Part 2 of 2

OREGON
ENVIRONMENTAL QUALITY
COMMISSION MEETING
MATERIALS 06/14/1991

DEQ

State of Oregon
Department of Environmental Quality

L

STATE OF OREGON

DEPARTMENT OF ENVIRONMENTAL QUALITY INTEROFFICE MEMORANDUM

DATE: June 7, 1991

TO: Environmental Quality Commission

FROM: Fred Hansen, Director

SUBJECT: Petition for Rule Amendment: Water Quality Standard 2,3,7,8 - TCDD

The Department would recommend to the Commission that the petition for rule making regarding the water quality standard for 2,3,7,8 - TCDD be denied. The denial at this time is based on several factors including:

1. The Department is in the process of completing the triennial review of the state's water quality standards. The standard for 2,3,7,8-TCDD was evaluated during this process. The Department, after careful review of the criteria, recommends to retain the standard as adopted in 1987.

   The Department reviewed all of the factors used to derive the criteria with special attention to three of the factors. These three factors were cancer potency, bioconcentration, and fish consumption. Various numbers have been forwarded for revision of all three of the factors. Review of the published literature indicated that the 0.013 pg/l water quality standard was an appropriate standard. When considering the possible changes to the cancer potency factor, the bioconcentration factor, and the fish consumption rate the 0.013 pg/l standard is an appropriate standard.

2. Since the Department's review of the water quality standard during the fall of 1990 the USEPA has announced that they will be conducting a review of the criteria. The USEPA expects to complete the review in one to two years. The agency expects to address wildlife, aquatic life, and human health issues related to the criteria. The agency is expected to review carcinogenic and reproductive effects to humans, wildlife and aquatic life; the rate of bioaccumulation; and, fish consumption rates.

3. Any review of the 2,3,7,8-TCDD standard which addresses wildlife and aquatic life risks could well result in a criteria value lower than the present Oregon standard. It should be noted that piscivorous wildlife have an increased risk of cancer mortality and reproductive

Based on the above information it would not be the best use of limited state resources to duplicate the present USEPA effort. State resources should be spent in other areas of toxin control such as the development of a comprehensive standard for all biologically and toxicologically active dioxins, furans and PCBs, technology based standards for the control of dioxins and furans in the pulp and paper industry and wood treating industry.

When the USEPA has completed their review of the 2,3,7,8-TCDD criteria, the Department would propose to immediately undertake a review of the standard if it is warranted.

If the Commission does not accept the Department's recommendation, we recommend, in accepting the petition for rule making, that a very specific statement be made regarding current regulatory actions, the items to be considered during the review and the time frame for the review. This would include:

1. The Department would continue all current regulatory activities using the current standards until such time as a new standard was adopted.

2. The re-evaluation of the state standard would be opened at this time, but the review would not be closed until the USEPA had completed its review.

3. The re-evaluation of the 2,3,7,8-TCDD water quality standard would include the review of criteria derivation for the other biologically available dioxins, furans, and co-planar PCBs to address as one standard the pollutants with similar biological/toxicological properties.

4. The Department would move forward to establish technology based standards for the control of dioxins and furans in the pulp and paper industry and wood treating industry.

Oregon

DEPARTMENT OF ENVIRONMENTAL QUALITY

STATE OF OREGON

DEPARTMENT OF ENVIRONMENTAL QUALITY **INTEROFFICE MEMORANDUM**

DATE: June 7, 1991

TO: Environmental Quality Commission

FROM: Fred Hansen

SUBJECT: Agenda Item L

Attached to this memoranda is written material pertaining to the Petition of James River II, Inc., and Boise Cascade Corporation. The materials were received in the Director's Office on June 7, 1991 by 4:30 p.m. Please review.

811 SW Sixth Avenue
Portland, OR 97204-1390
(503) 229-5696

Before the Environmental Quality Commission
of the State of Oregon

In the Matter of the Petition of James River II, Inc., and Boise Cascade Corporation to Amend Subparagraph (2)(p)(B) of Oregon Administrative Rules Chapter 340, Division 41, Sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965.	))))))))	NOTICE OF CONSIDERATION OF PETITION FOR RULE AMENDMENT

1. James River II, Inc., and Boise Cascade Corporation have filed a petition as noted above to amend Oregon's ambient water quality standard for 2,3,7,8-tetrachloro-dibenzo-p-dioxin (TCDD). Specifically, the petition proposes a standard of 2.3 parts per quadrillion (ppq) in place of the current standard of 0.013 ppq. The petitioners state that supporters include the Associated Oregon Industries, the Northwest Pulp & Paper Association, the Association of Western Pulp and Paper Workers, Local 1, and the United Paper Workers International, Local 1097. Petitioners requested opportunity to make an oral presentation to the Commission regarding the petition.

2. Petitioners have identified persons (and their attorneys) believed to be interested in the proposed rule change as follows: City of St. Helens, Northwest Coalition for Alternatives to Pesticides, Columbia River United, Pope and Talbot, Inc., UA Local 290, Plumbers and Steamfitters, and Mike Jerkiewicz. Petitioners have provided a copy of their petition and supporting documentation to the attorneys for those believed to be interested in the proposed rule change.

3. The Environmental Quality Commission (EQC) will consider, and may act upon, this petition at its regularly scheduled meeting on June 14, 1991. The item will be listed on the regular agenda as an action item. This meeting will be held in Room 3A of the DEQ offices at 811 S. W. 6th Avenue, Portland, Oregon, beginning at 8:30 a.m. Persons interested in this item should be present when the meeting begins.

4. Interested persons may submit written memoranda on the petition provided either that six (6) copies of all written materials are received by the Director's Office, Department of Environmental Quality, 811 S. W. 6th Avenue, Portland, Oregon 97204 of DEQ by no later than 4:00 p.m. on June 7, 1991, or in the alternative, that individual copies are served upon each Commission member and the Director by no later than 4:00 p.m. on June 10, 1991.

313 S.W. 2nd Street, Suite D
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

June 6, 1991

Office of the Director
Department of Environmental Quality
811 SW 6th Ave.
Portland, OR 97204

RE: Petition for reduction of Oregon's ambient water quality standard

Dear Mr. Fred Hansen:

At a very late date I was advised that this petition is once again before your department. I understand the EQC will consider and possibly act upon the petition submitted to you by James River Corporation and Boise Cascade at its June 14th meeting. For some reason this Commission has been excluded from any official notification by your department or by the petitioners. Instead I have been advised by a local citizen that this action has been about to take place.

This Commission remains opposed to lowering of our ambient water quality standards until and unless it can be shown that there will be zero negative effect upon the health of salmon runs in the affected waters. The basis of our concern is primarily for effects on the juvenile salmon who must use the fresh water habitat enroute to the ocean. We remain especially concerned in view of the recent petitions for endangered species status on several northwest salmon runs.

I include copies of testimony and correspondence already submitted to your department which I would like to have attached to the record for this particular petition.

In short, the Commission remains extremely concerned that even current loading of dioxins into the fresh water habitat may have deliterious effects on juvenile salmon survivability. Until it can be shown that those effects do not exist and until it can be shown that a reduction of our water quality standards will not further the problem, we remain opposed to any lessening of the standards.

Thank you for your considerations. I hope the oversight which led to the lack of communication with this Commission about these petitions will be corrected.

Sincerely yours,

Tom Robinson, Manager
Oregon Salmon Commission

TR/nf

313 S.W. 2nd Street, Suite D
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

May 10, 1990

Llewellyn Matthews
Northwest Pulp & Paper Association
1300 114th Ave. SE, Suite 110
Bellevue, WA 98004

Dear Mr. Matthews:

Thank you for your letter and overview statement pertaining to the dioxin issue. Although I was not personally in attendance, this Commission was represented at your Astoria briefing by Commissioner Robert Finzer. Mr. Finzer is a North Coast commercial fisherman and wholesaler. He gave a brief report on the situation at our last Commission meeting.

We are sensitive to your problems and we support your stated commitment to a solution which can allow a healthy pulp industry within a healthy environment. To us that continues to mean operations which do not pose risk to salmon food products nor to salmon survival, health or reproduction. It also means maintaining standards of water quality which are equal to those of our competitors in other nations which provide salmon to the world market.

So far, we are fairly comfortable with the food safety issue. Our public salmon are pure, clean food with all agencies finding salmon as the least likely of all fishes to be contaminated with toxins.

However, we remain steadfast in our position that standards equivalent to those in Europe and Canada be maintained here. Also, we continue to insist that our standards be met in fact. These are critical market demands.

We continue to be extremely concerned about salmon reproduction, smolt mortality, and immune systems, when exposed to effluent materials throughout the inland waterways they use. Even small percentages of mortality or fecundity loss represent large numbers of salmon losses at the harvest end. For example a 1% loss of down stream coho smolts represents a number of salmon roughly equal to the entire Oregon commercial troll harvest. We must learn the true impact on smolts and learn how to control it. I have not read the reports you cite as showing "no adverse affects on fish reproduction or fish tissue." Perhaps your staff can supply us with a copy.

Your offer to meet with us may be something we can explore later this fall, after our harvest season. We, like you, are an industry which supplies a valuable commodity to the market, relying on a healthy natural resource for the raw material. In the past, salmon resources industries have not viewed the wood products industry as a friend. I think you will agree that there is basis in fact for that view. Too much of our salmon resource has been lost to forest industries already. If that stops, perhaps we can ally as fellow industries, in common cause. If it does not, then our position is clear, and probably adversarial.

Sincerely yours,

Tom Robinson, Manager
Oregon Salmon Commission

cc: Dalton Hobbs, Department of Agriculture
Jill Zarnowitz, OR Dept. of Fish & Wildlife
Bob Eaton, Salmon for All
Oregon Salmon Commissioners

313 S.W. 2nd Street, Suite D
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON
TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

Date: May 1, 1990

To: DEQ
Water Quality Division
811 SW 6th Ave.
Portland, OR 97204

From: Tom Robinson, Manager
Oregon Salmon Commission

RE: Proposed Rule Changes Affecting Pulp Mill/Dioxin Effluents Standards.

Please be advised that the Oregon Salmon Commission on behalf of Oregon's commercial salmon trollers and on behalf of the consuming public which we serve under OAR 576.305 does not support any of the options for rule changes affecting standards applied to pulp mill effluents/dioxin contamination. The Oregon Salmon Commission has provided formal oral and written testimony to DEQ and to the Environment Quality Commission on this subject. Our position remains unchanged. We adamantly support stringent standards which will fully protect both food quality and the smolt survivability of salmon which use the Columbia River corridor. While we are satisfied that no danger to consumers of salmon food fish is imminent, we see this as no reason to relax any of the standards. We continue to be greatly concerned about mortality of juvenile salmon and about biological effects on adult salmon's immune systems and reproductive capacities when exposed to these effluents. Those biological and mortality concerns have not yet been addressed nor answered satisfactorily.

Attached are copies of written testimony already supplied to you by this Commission. Please apply them to this record.

On behalf of the Commission I also express a great dissatisfaction with the notification processes being used as this issue continues to run a gauntlet of meetings and reviews. I have not been formally contacted on a regular basis by your department about the schedule of hearings and comment deadlines. I remind you that we are a state agency which is very much affected by the decisions you will make. I find it extremely remarkable that my best source of up-to-date information continues to be the "grapevine" rather than official communications from your department. Furthermore, I know that the Pacific Fisheries Management Council and the states of Oregon and Washington fisheries divisions are greatly concerned about this issue. Are they not being directly contacted? Please take prompt action to correct this oversight in notification.

cc: William P. Hutchinson EQC
Randy Fisher ODFW
Joe Blum WDF
Richard Schwarz PFMC
Frank Warrens PFMC
Bob Eaton Salmon for All

313 S.W. 2nd Street, Suite C
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

Date: December 15, 1989

To: Fred Hansen, Director
Department of Environmental Quality
811 SW Sixth
Portland, OR 97204

From: Tom Robinson, Manager
Oregon Salmon Commission

Re: Proposed Rule Changes

We understand that Oregon's EQC is reviewing proposed rule changes on pulp mill pollution effluents January 1990. As you know we continue to provide comment on this matter as we find it to have significant impact on our industry through degradation of the environment. The details of our concern are outlined in previous communications and testimony submitted to you.

We also have some specific concerns and comments regarding proposed rule changes.

1. We ask for a return to full, open disclosure of all proceedings between the state and pulp mill industry representatives as this matter is resolved.
2. We support the status-quo of rules which require formal findings on pollution before EQC makes approvals. We recommend that food fish studies should be independently performed by other than industry contractors, to assure the objectivity of required findings.
3. We call your attention to the following items from the proposed rule changes:
   a) Proposed changes in paragraph 3, section (a) are alarming in that they appear to weaken existing permit processes, allowing too much subjective opinion, changing the phrase "would not", to read, "is not expected to", is clearly a move away from the level of control and protection which we must have through your commission, to assure safe, quality habitat for food fish in Oregon.
   b) Likewise, we support the status-quo for procedures which determine WQL status. There must not be a relaxing of processes which would remove the burden of positive proof of compliance with effluent standards, prior to removing a waterway, or a facility, from corrective activity. Speculative statements that compliance is expected may be encouraging news, but should not be substituted for actual achievement.

Thank you for your attention to our requests. We continue to rely on EQC, and DEQ to protect the habitat of Oregon's salmon resource as you execute your difficult tasks.

cc See attached sheet

June 2, 1991

Environmental Quality Commission
Directors Office
811 S. W. 6th Ave.
Portland, Oregon 97204

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 0 1991
OFFICE OF THE DIRECTOR

Dear Commission Member,

In reference to the giant pulp and paper manufacturers, notably James River Corporation and Boise Cascade, who brashly now request the Oregon E.Q.C. to set lower ambient water quality standards.

Needless to say, the Oregon standard is absolutely necessary to the maintenance of our waterways now and for the future. Certainly industrial needs must be given some consideration. However all members of the state's citizenry should also be granted the highest water quality standards in our great Northwest. Oregon as a leader in all environmental concerns is a model for the nation.

As owners of property on the Columbia River in Columbia County, we implore the E.Q.C. to reject the proposed change in water quality standards. Industry cannot provide any real evidence that would support any modification of the D.E.Q. standard.

Thank you for your vote against such a negative approach to our water quality.

Sincerely,

Roger and Mary Thompson

Roger and Mary Thompson
4144 S. E. Boardman Ave.
Milwaukie, Oregon 97267

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 07 1991

OFFICE OF THE DIRECTOR

NORTHWEST
PULP&PAPER

June 6, 1991

Fred Hansen, Director
Department of Environmental Quality
811 SW Sixth Avenue
Portland, OR 97204

Dear Mr. Hansen:

The Northwest Pulp and Paper Association is writing to support the James River Corp. and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Oregon's current water quality standard of 0.013 parts per quadrillion (ppq) is a human-health-based standard. However, the science upon which this standard was developed has been challenged — and its conclusions radically altered — by the very scientist who conducted the original research. Therefore, the premise for the current standard is now highly questionable.

In addition, the Environmental Protection Agency has recently approved water quality standards 100-times less stringent than its guideline criterion (which Oregon adopted, along with a variety of other EPA recommendations for toxic discharges). Thus, EPA has indirectly conceded that, when taking new science and regional factors into consideration, its criterion of 0.013 ppq may be more restrictive than necessary to protect human health.

In recognizing this apparent conflict, EPA has announced a review of the science on dioxin. I have enclosed a May 17 report from *Science* that notes the one-year time frame EPA Administrator William Reilly has established for this review. However, should Oregon decide to wait on the EPA review before commencing a review of its standard — and not suspend its imposition of dioxin discharge restrictions — the two mills in question are bound by state law to invest millions of dollars in what may prove to be unnecessary environmental controls.

Oregon needs a scientifically-based water quality standard for dioxin that is fully protective of human health. The Clean Water Act delegates this responsibility to the states, in part so that states may incorporate regional data, such as fish consumption information, into their decision. It is time for Oregon to develop such a state-specific water quality standard for dioxin. We hope that the Environmental Quality Commission will accept the James River and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Sincerely,

Kathy E. Gill

Kathy E. Gill, CAE
Public Affairs Director

enclosure
c: EQC members

EPA Moves to Reassess the Risk of Dioxin

Urged on by the scientific community, EPA is developing a new model for estimating dioxin's risk

GALVANIZED BY THE RESULTS OF A RECENT scientific meeting on dioxin's molecular actions, Environmental Protection Agency (EPA) administrator William K. Reilly has launched a major new effort to reassess the toxicity of this ubiquitous—and infamous—chemical.

Responding to criticism that the model EPA now uses to assess dioxin's risk is obsolete, Reilly has asked agency scientists to come up with a new "biologically based" model that will draw on an emerging understanding of the first steps that take place as dioxin enters a cell (for example, see pages 924 and 954). Reilly and others call the new effort "precedent-setting" not only for how the agency regulates carcinogens but also for EPA's quick response to new scientific developments—not its strong suit in the past.

Until now, EPA has gauged the risk of dioxin exposure by using the same model it applies to most carcinogens: the linear multistage model, which assumes that risk rises in proportion to dose. Agency officials have long viewed the model as a "default"—one adopted for lack of a real understanding of how carcinogens work—and their intent was always to replace it with something more realistic once mechanisms were understood. But so far, they say, such evidence has been lacking. Now it may at last be in hand, at least for dioxin and perhaps a handful of other chemicals that behave similarly.

The turning point came in an 8 March briefing for Reilly and his top deputies given by three agency scientists: William Farland and Peter Preuss, both at EPA headquarters in Washington, D.C., and Linda Birnbaum of EPA's Health Effects Research Laboratory in North Carolina. Part of the briefing was devoted to recent epidemiologic studies, including the new one by Marilyn Fingerhut of the National Institute for Occupational Safety and Health (NIOSH), which found perhaps the strongest link yet between high doses of dioxin and human cancer (see *Science*, 8 February, page 625). The EPA scientists also discussed a reanalysis of data from a 1976 study of cancer in dioxin-exposed rats that figured heavily in EPA's original risk assessment. After reexamining the original slides of liver tissue, investigators have concluded that the animals developed fewer tumors than was originally believed.

But it was Birnbaum and Farland's description of a meeting last November at the Banbury Center at Cold Spring Harbor Laboratory that Reilly says made the most compelling case for change. At that meeting a group of dioxin experts agreed that before dioxin can cause any of the ill effects it has been linked to—cancer, immune system suppression, chloracne, and birth defects—one "necessary but not sufficient" event must occur: the compound must bind to and activate a receptor, known as the aryl hydrocarbon or AH receptor (see *Science*, 8 February, p. 625). After that, the dioxin-receptor complex is transported to the nucleus, where it binds to specific sequences of DNA and turns genes on and off, thereby causing its myriad effects. It had long been known that dioxin binds to a receptor, but before the Banbury meeting it had been unclear whether all of dioxin's effects or just some were mediated this way.

Key mover. *Linda Birnbaum had been urging EPA to change how it does dioxin risk assessment.*

The Banbury group also agreed that dioxin has to occupy a certain number of AH receptors on a cell before any biological response can ensue. The result is a practical "threshold" for dioxin exposure, below which no toxic effects occur. That conclusion flies in the face of the linear model's underlying assumption: that the risk of harmful effects begins with exposure to a single molecule and increases from there. Faced with this new picture of dioxin's action, the Banbury participants urged EPA to develop a new, receptor-based model for dioxin risk assessment.

Reilly bit. He has now asked scientists in EPA's Office of Research and Development, in collaboration with academic researchers around the country, to come up with just such a model. The goal, explains Michael Gallo of the Robert Wood Johnson Medical School, one of the organizers of the Banbury meeting who is now working with EPA, is to pinpoint the threshold or "safe" dose below which none of dioxin's ill effects should occur.

In building the model, Gallo and his EPA colleagues hope to draw on work on the dioxin receptor now under way in a number of labs around the country. In this issue of *Science*, for example, a group headed by Oliver Hankinson of the University of California at Los Angeles reports on the cloning of a protein that is necessary for the receptor to function. Various roles have been proposed for the new protein; one intriguing possibility is that it is part of the receptor itself. The dioxin receptor thus might contain at least two proteins, one that binds to dioxin (and presumably whatever natural molecule dioxin mimics) and another that binds to DNA. "Boy, is that exciting," says Gallo, who adds that the new findings will feed directly into the model.

Until the model is complete, no one can say for sure whether it will show dioxin to be more or less risky than EPA now calculates, though Gallo and others speculate that it will turn out to be less risky. One of the major questions is how close the presumed "safe" dose is to the background levels of dioxin to which the general population is exposed. If background exposure is already near the "safe" dose, then there may not be much room for additional exposure.

Those background levels are largely unknown, so Reilly has added that question to the EPA scientists' assignment. Over the next year Birnbaum and other EPA scientists, in collaboration with researchers from NIOSH, the Centers for Disease Control, and the Air Force, hope to get a fix on blood levels of dioxin and the handful of polychlorinated biphenyls that behave similarly and thus could increase its risk. Meanwhile, other researchers will be studying the sources and routes of dioxin exposure—most of which are dietary—and how it is passed up the food chain.

Reilly wants the new model and related work complete within a year, at which time the results will go on to EPA's Scientific Advisory Board (SAB) for peer review. Three years ago, the SAB sent EPA scientists back to the drawing board when they tried to revise the dioxin standard, saying the science wasn't sound enough. Birnbaum and other EPA researchers predict a different outcome this time. ■ LESLIE ROBERTS

Environmental Quality Commission
Directors Office
811 SW 6th Avenue
Portland, OR 97204

June 4, 1991

Dear Commission Member,

I urge you to please reject the latest proposal by the pulp industry to reduce the water quality standards in Oregon.

In a time of increased environmental awareness, it seems indefensible that certain companies would propose to lessen the standards for economic reasons, while neglecting and potentially harming a very large and complex ecological system.

My interest as a partner in land in Clatskanie prompts me to write this letter not only for myself, but for everyone who lives on or near the rivers in Oregon. You have the opportunity to effect a positive result for the people of Oregon. Please do so.

Respectfully,

Robert J. Thompson

Robert J. Thompson

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 07 1991

OFFICE OF THE DIRECTOR

MILES

SAND AND GRAVEL COMPANY

P.O. BOX 130, AUBURN, WASHINGTON 98071

AUBURN
JUN 5 '91
WASH.

U.S. POSTAGE
0 5 2
METER
8219290

Environmental Quality Commission
Directors Office
811 S.W. 6th Ave.
Portland, OR 97204

SAT., JUNE 8, 1991

The Register-Guard

ALTON F. BAKER, Publisher, 1927-1961
ALTON F. BAKER Jr., Editor and Publisher, 1961-1982
EDWIN M. BAKER, Publisher, 1982-1987

ALTON F. BAKER III, Editor and Publisher
FLETCHER LITTLE, General Manager
ALLAN A. GEMMELL, Finance Director

PATRICK A. YACK, Managing Editor
DON ROBINSON, Editorial Page Editor
HENNY WILLIS, Associate Editor
JACKMAN WILSON, Associate Editor

An Independent Newspaper

The Register-Guard's policy is the impartial publication in its news pages of all news and statements on news. On this page, the editors offer their opinions on events of the day and matters of importance, endeavoring to be candid but fair and helpful in the development of constructive community policy. A newspaper is a CITIZEN OF ITS COMMUNITY.

No retreat on dioxin

Meeting state standards limiting dioxin pollution will be difficult and expensive for the pulp and paper industry. But it's hard to muster much sympathy for two mills in Oregon that are complaining about the standards when a third, Pope & Talbot's mill near Halsey, already has a plan to comply with the dioxin rules. If one can do it, the others can.

Dioxins are chemicals created as byproducts of certain chemical and industrial processes, including paper bleaching. Some dioxins are highly toxic; one is the most powerful known carcinogen. The federal Environmental Protection Agency studied fish living downstream from pulp and paper mills nationwide and found that dioxin had accumulated in their tissues.

The EPA told the states to regulate mills' dioxin emissions. Oregon's Department of Environmental Quality obliged by requiring that water downstream from pulp and paper mills contain no more than 0.013 parts per quadrillion of dioxin. That small a portion of the United States' total land area is one-tenth of a square inch — a fact that illustrates both the strictness of the DEQ standard and the potency of the deadliest dioxin.

Last year, Pope & Talbot reached an agreement with the DEQ that will allow it to meet the state's standard. Improving current industrial processes will reduce dioxin emissions by about 60 percent. By 1993 the mill expects to meet the 0.013 parts per quadrillion standard. And in concert with an expansion project, Pope & Talbot intends to change its paper-bleaching process so that by 1997 it will be able to triple its production and still meet the state standard.

The two companies that operate Oregon's other two bleached-pulp mills, James River II Inc. and Boise Cascade Corp., haven't kept up with Pope & Talbot. Instead, they're urging the DEQ to loosen its regulations and allow them to put 177 times as much dioxin in the Columbia River as is permitted under the 0.013 parts per quadrillion standard.

\#1

The two companies argue that dioxins are not as carcinogenic as was once believed. One of the scientists who did the original evaluations has now concluded that dioxins pose only a small threat to human and animal health, they say. The companies accuse the DEQ of forcing them to spend tens of millions of dollars to meet a standard that is based on an exaggerated assessment of the dioxin threat.

The DEQ, however, is not directly responsible for determining whether dioxin is dangerous. That determination has been made by the federal EPA, which told the states to limit dioxin discharges to levels that would cause fewer than one cancer case among a million people. Oregon's standard is in response to that order, and complaints about its scientific basis should be directed to the EPA, not the DEQ.

\#2

Even if there are doubts about the magnitude of the health risk posed by dioxins, it's plain that some hazard exists. Barring a conclusive finding that would allow the EPA to downgrade its assessment of the danger from dioxin, a cautious approach offers the best protection for human health and river-dwelling fish and wildlife. At least one pulp and paper mill intends to grow and prosper while meeting the standard that recognizes the wisdom of caution. The other two should be expected to do the same.

While one Oregon mill is moving toward papermaking methods that produce less dioxin and two others are dragging their heels, the pulp and paper industry in other parts of the world is moving away from dioxin-producing processes altogether. The elimination of dioxin should be the industry's goal. Pope & Talbot's reductions are welcome but incomplete, and a lack of progress by the other two companies should be unacceptable.

3

JAMES RIVER CORPORATION
P.O. Box 2218, Richmond, VA 23217 (804) 644-5411

RONALD B. ESTRIDGE
Senior Vice President, Group Executive
Technology
(804) 649-4209

May 17, 1991

The Honorable William K. Reilly
Administrator
United States Environmental Protection Agency
Washington, DC 20460

Re: Industrial Toxics Project

Dear Mr. Reilly:

James River Corporation is pleased to participate in EPA's proposed voluntary Industrial Toxics Project.

Our 1995 goals are:

- The 17 high priority chemicals - 50% reduction in annual releases
- Dioxin - 90% reduction in annual releases

In addition to our U.S. operations, these goals include reductions of chloroform and dioxin at our pulp mill in Marathon, Ontario, which is located on Lake Superior. Where possible, pollution prevention methods will be used to reach these goals.

Although we fully intend to meet these goals, we understand that this project is completely voluntary and that the goals are not firm, enforceable requirements under any laws or regulations. Also, there are several concerns about the program which have been communicated by the American Paper Institute in its May 8 letter to you; EPA's prompt attention to these issues will be appreciated.

The Industrial Toxics Project represents a real step forward from the current "command-and-control" approach favored to date by Congress and the Agency. We look forward to a success that will set a new tone for industry/agency cooperation in environmental protection.

Very truly yours,

Ronald B Estridge

Ronald B. Estridge

RBE/kr

cc: The Honorable Linda J. Fisher
Assistant Administrator
Office of Pesticides and Toxic Substances

signed mixing zone, as measured relative to a control point immediately upstream from a discharge when stream temperatures are 58° F. or greater; or more than 0.5° F. increase due to a single-source discharge when receiving water temperatures are 57.5° F. or less; or more than 2° F. increase due to all sources combined when stream temperatures are 56° F. or less, except for specifically limited duration activities which may be authorized by DEQ under such conditions as DEQ and the Department of Fish and Wildlife may prescribe and which are necessary to accommodate legitimate uses or activities where temperatures in excess of this standard are unavoidable and all practical preventive techniques have been applied to minimize temperature rises. The Director shall hold a public hearing when a request for an exception to the temperature standard for a planned activity or discharge will in all probability adversely affect the beneficial uses.

(C) Marine and estuarine waters: No significant increase above natural background temperatures shall be allowed, and water temperatures shall not be altered to a degree which creates or can reasonably be expected to create an adverse effect on fish or other aquatic life.

(c) Turbidity (Jackson Turbidity Units, JTU): No more than a 10 percent cumulative increase in natural stream turbidities shall be allowed, as measured relative to a control point immediately upstream of the turbidity causing activity. However, limited duration activities necessary to address an emergency or to accommodate essential dredging, construction or other legitimate activities and which cause the standard to be exceeded may be authorized provided all practicable turbidity control techniques have been applied and one of the following has been granted:

(A) Emergency activities: Approval coordinated by DEQ with the Department of Fish and Wildlife under conditions they may prescribe to accommodate response to emergencies or to protect public health and welfare.

(B) Dredging, Construction or other Legitimate Activities: Permit or certification authorized under terms of Section 401 or 404 (Permits and Licenses, Federal Water Pollution Control Act) or OAR 141-85-100 et seq. (Removal and Fill Permits, Division of State Lands), with limitations and conditions governing the activity set forth in the permit or certificate.

(d) pH (hydrogen ion concentration): pH values shall not fall outside the following ranges:

(A) Marine waters: 7.0 – 8.5.

(B) Estuarine and fresh waters: 6.5 – 8.5.

(e) Organisms of the coliform group where associated with fecal sources (MPN or equivalent MF using a representative number of samples):

(A) Columbia River from the Highway 5 bridge between Vancouver and Portland to the mouth: A log mean of 200 fecal coliform per 100 milliliters based on a minimum of 5 samples in a 30-day period with no more than 10 percent of the samples in the 30-day period exceeding 400 per 100 ml.

(B) Marine waters and estuarine shellfish growing waters: A fecal coliform median concentration of 14 organisms per 100 milliliters, with not more than 10 percent of the samples exceeding 43 organisms per 100 ml.

(C) Estuarine waters other than shellfish growing waters: A log mean of 200 fecal coliform per 100 milliliters based on minimum of 5 samples in a 30-day period with no more than 10 percent of the samples in the 30-day period exceeding 400 per 100 ml.

(f) Bacterial pollution or other conditions deleterious to waters used for domestic purposes, livestock watering, irrigation, bathing, or shellfish propagation, or otherwise injurious to public health shall not be allowed.

(g) The liberation of dissolved gases, such as carbon-dioxide, hydrogen sulfide, or other gases, in sufficient quantities to cause objectionable odors or to be deleterious to fish or other aquatic life, navigation, recreation, or other reasonable uses made of such waters shall not be allowed.

(h) The development of fungi or other growths having a deleterious effect on stream bottoms, fish or other aquatic life, or which are injurious to health, recreation, or industry shall not be allowed.

(i) The creation of tastes or odors or toxic or other conditions that are deleterious to fish or other aquatic life or affect the potability of drinking water or the palatability of fish or shellfish shall not be allowed.

(j) The formation of appreciable bottom or sludge deposits or the formation of any organic or inorganic deposits deleterious to fish or other aquatic life or injurious to public health, recreation, or industry shall not be allowed.

(k) Objectionable discoloration, scum, oily sleek, or floating solids, or coating of aquatic life with oil film shall not be allowed.

(l) Aesthetic conditions offensive to the human senses of sight, taste, smell, or touch shall not be allowed.

(m) Radioisotope concentrations shall not exceed maximum permissible concentrations (MCP's) in drinking water, edible fishes or shellfishes, wildlife, irrigated crops, livestock and dairy products, or pose an external radiation hazard.

(n) The concentration of total dissolved gas relative to atmospheric pressure at the point of sample collection shall not exceed one hundred and ten percent (110%) of saturation, except when stream flow exceeds the 10-year, 7-day average flood. However, for Hatchery receiving waters and waters of less than 2 feet in depth, the concentration of total dissolved gas relative to atmospheric pressure at the point of sample collection shall not exceed one hundred and five percent (105%) of saturation.

(o) Total Dissolved Solids: Guide concentrations listed below shall not be exceeded unless otherwise specifically authorized by DEQ upon such conditions as it may deem necessary to carry out the general intent of this plan and to protect the beneficial uses set forth in rule 340-41-202:

(A) Columbia River – 500.0 mg/l:

(B) All other Fresh Water Streams and Tributaries – 100.0 mg/l;

340-41-205(2)(p)

(p) Toxic Substances:

(A) Toxic substances shall not be introduced above natural background levels in the waters of the state in amounts, concentrations, or combinations which may be harmful, may chemically change to harmful forms in the environment, or may bioaccumulate to levels that adversely affect public health, safety, or welfare; adquatic life; or other designated beneficial uses.

(B) Levels of toxic substances shall not exceed the most recent criteria values for organic and inorganic pollutants established by EPA and published in Quality Criteria for Water (1986). A list of the criteria is presented in Table 20.

(C) The criteria in paragraph (B) of this subsection shall apply unless data from scientifically valid studies demonstate that the most sensitive designated beneficial uses will not be adversely affected by exceeding a criterion or that a more

June 2, 1991

Environmental Quality Commission
Directors Office
811 S. W. 6th Ave.
Portland, Oregon 97204

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 04 1991
OFFICE OF THE DIRECTOR

Dear Commission Member,

In reference to the giant pulp and paper manufacturers, notably James River Corporation and Boise Cascade, who brashly now request the Oregon E.Q.C. to set lower ambient water quality standards.

Needless to say, the Oregon standard is absolutely necessary to the maintenance of our waterways now and for the future. Certainly industrial needs must be given some consideration. However all members of the state's citizenry should also be granted the highest water quality standards in our great Northwest. Oregon as a leader in all environmental concerns is a model for the nation.

As owners of property on the Columbia River in Columbia County, we implore the E.Q.C. to reject the proposed change in water quality standards. Industry cannot provide any real evidence that would support any modification of the D.E.Q. standard.

Thank you for your vote against such a negative approach to our water quality.

Sincerely,

Roger and Mary Thompson

Roger and Mary Thompson
4144 S. E. Boardman Ave.
Milwaukie, Oregon 97267

Environmental Quality Commission
Directors Office
811 SW 6th Avenue
Portland, OR 97204

June 4, 1991

Dear Commission Member,

I urge you to please reject the latest proposal by the pulp industry to reduce the water quality standards in Oregon.

In a time of increased environmental awareness, it seems indefensible that certain companies would propose to lessen the standards for economic reasons, while neglecting and potentially harming a very large and complex ecological system.

My interest as a partner in land in Clatskanie prompts me to write this letter not only for myself, but for everyone who lives on or near the rivers in Oregon. You have the opportunity to effect a positive result for the people of Oregon. Please do so.

Respectfully,

Robert J. Thompson

Robert J. Thompson

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED

MILES
SAND AND GRAVEL COMPANY
P.O. BOX 130, AUBURN, WASHINGTON 98071

AUBURN
JUN 5 '91
WASH.

U.S. POSTAGE
0 5
METER
821S

Environmental Quality Commission
Directors Office
811 S.W. 6th Ave.
Portland, OR 97204

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 07 1991

OFFICE OF THE DIRECTOR

304(l)

64,000
159,000

NORTHWEST PULP&PAPER

June 6, 1991

$2000.00

Fred Hansen, Director
Department of Environmental Quality
811 SW Sixth Avenue
Portland, OR 97204

Dear Mr. Hansen:

The Northwest Pulp and Paper Association is writing to support the James River Corp. and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Oregon's current water quality standard of 0.013 parts per quadrillion (ppq) is a human-health-based standard. However, the science upon which this standard was developed has been challenged — and its conclusions radically altered — by the very scientist who conducted the original research. Therefore, the premise for the current standard is now highly questionable.

In addition, the Environmental Protection Agency has recently approved water quality standards 100-times less stringent than its guideline criterion (which Oregon adopted, along with a variety of other EPA recommendations for toxic discharges). Thus, EPA has indirectly conceded that, when taking new science and regional factors into consideration, its criterion of 0.013 ppq may be more restrictive than necessary to protect human health.

In recognizing this apparent conflict, EPA has announced a review of the science on dioxin. I have enclosed a May 17 report from *Science* that notes the one-year time frame EPA Administrator William Reilly has established for this review. However, should Oregon decide to wait on the EPA review before commencing a review of its standard — and not suspend its imposition of dioxin discharge restrictions — the two mills in question are bound by state law to invest millions of dollars in what may prove to be unnecessary environmental controls.

Oregon needs a scientifically-based water quality standard for dioxin that is fully protective of human health. The Clean Water Act delegates this responsibility to the states, in part so that states may incorporate regional data, such as fish consumption information, into their decision. It is time for Oregon to develop such a state-specific water quality standard for dioxin. We hope that the Environmental Quality Commission will accept the James River and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Sincerely,

Kathy E. Gill

Kathy E. Gill, CAE
Public Affairs Director

enclosure
c: EQC members

EPA Moves to Reassess the Risk of Dioxin

Urged on by the scientific community, EPA is developing a new model for estimating dioxin's risk

GALVANIZED BY THE RESULTS OF A RECENT scientific meeting on dioxin's molecular actions, Environmental Protection Agency (EPA) administrator William K. Reilly has launched a major new effort to reassess the toxicity of this ubiquitous—and infamous—chemical.

Responding to criticism that the model EPA now uses to assess dioxin's risk is obsolete, Reilly has asked agency scientists to come up with a new "biologically based" model that will draw on an emerging understanding of the first steps that take place as dioxin enters a cell (for example, see pages 924 and 954). Reilly and others call the new effort "precedent-setting" not only for how the agency regulates carcinogens but also for EPA's quick response to new scientific developments—not its strong suit in the past.

Until now, EPA has gauged the risk of dioxin exposure by using the same model it applies to most carcinogens: the linear multistage model, which assumes that risk rises in proportion to dose. Agency officials have long viewed the model as a "default"—one adopted for lack of a real understanding of how carcinogens work—and their intent was always to replace it with something more realistic once mechanisms were understood. But so far, they say, such evidence has been lacking. Now it may at last be in hand, at least for dioxin and perhaps a handful of other chemicals that behave similarly.

The turning point came in an 8 March briefing for Reilly and his top deputies given by three agency scientists: William Farland and Peter Preuss, both at EPA headquarters in Washington, D.C., and Linda Birnbaum of EPA's Health Effects Research Laboratory in North Carolina. Part of the briefing was devoted to recent epidemiologic studies, including the new one by Marilyn Fingerhut of the National Institute for Occupational Safety and Health (NIOSH), which found perhaps the strongest link yet between high doses of dioxin and human cancer (see *Science*, 8 February, page 625). The EPA scientists also discussed a reanalysis of data from a 1976 study of cancer in dioxin-exposed rats that figured heavily in EPA's original risk assessment. After reexamining the original slides of liver tissue, investigators have concluded that the animals developed fewer tumors than was originally believed.

But it was Birnbaum and Farland's description of a meeting last November at the Banbury Center at Cold Spring Harbor Laboratory that Reilly says made the most compelling case for change. At that meeting a group of dioxin experts agreed that before dioxin can cause any of the ill effects it has been linked to—cancer, immune system suppression, chloracne, and birth defects—one "necessary but not sufficient" event must occur: the compound must bind to and activate a receptor, known as the aryl hydrocarbon or AH receptor (see *Science*, 8 February, p. 625). After that, the dioxin-receptor complex is transported to the nucleus, where it binds to specific sequences of DNA and turns genes on and off, thereby causing its myriad effects. It had long been known that dioxin binds to a receptor, but before the Banbury meeting it had been unclear whether all of dioxin's effects or just some were mediated this way.

Key mover. *Linda Birnbaum had been urging EPA to change how it does dioxin risk assessment.*

The Banbury group also agreed that dioxin has to occupy a certain number of AH receptors on a cell before any biological response can ensue. The result is a practical "threshold" for dioxin exposure, below which no toxic effects occur. That conclusion flies in the face of the linear model's underlying assumption: that the risk of harmful effects begins with exposure to a single molecule and increases from there. Faced with this new picture of dioxin's action, the Banbury participants urged EPA to develop a new, receptor-based model for dioxin risk assessment.

Reilly bit. He has now asked scientists in EPA's Office of Research and Development, in collaboration with academic researchers around the country, to come up with just such a model. The goal, explains Michael Gallo of the Robert Wood Johnson Medical School, one of the organizers of the Banbury meeting who is now working with EPA, is to pinpoint the threshold or "safe" dose below which none of dioxin's ill effects should occur.

In building the model, Gallo and his EPA colleagues hope to draw on work on the dioxin receptor now under way in a number of labs around the country. In this issue of *Science*, for example, a group headed by Oliver Hankinson of the University of California at Los Angeles reports on the cloning of a protein that is necessary for the receptor to function. Various roles have been proposed for the new protein; one intriguing possibility is that it is part of the receptor itself. The dioxin receptor thus might contain at least two proteins, one that binds to dioxin (and presumably whatever natural molecule dioxin mimics) and another that binds to DNA. "Boy, is that exciting," says Gallo, who adds that the new findings will feed directly into the model.

Until the model is complete, no one can say for sure whether it will show dioxin to be more or less risky than EPA now calculates, though Gallo and others speculate that it will turn out to be less risky. One of the major questions is how close the presumed "safe" dose is to the background levels of dioxin to which the general population is exposed. If background exposure is already near the "safe" dose, then there may not be much room for additional exposure.

Those background levels are largely unknown, so Reilly has added that question to the EPA scientists' assignment. Over the next year Birnbaum and other EPA scientists, in collaboration with researchers from NIOSH, the Centers for Disease Control, and the Air Force, hope to get a fix on blood levels of dioxin and the handful of polychlorinated biphenyls that behave similarly and thus could increase its risk. Meanwhile, other researchers will be studying the sources and routes of dioxin exposure—most of which are dietary—and how it is passed up the food chain.

Reilly wants the new model and related work complete within a year, at which time the results will go on to EPA's Scientific Advisory Board (SAB) for peer review. Three years ago, the SAB sent EPA scientists back to the drawing board when they tried to revise the dioxin standard, saying the science wasn't sound enough. Birnbaum and other EPA researchers predict a different outcome this time. ■ LESLIE ROBERTS

(4) Residential generators of yard debris participating in a regularly scheduled yard debris collection service, where yard debris is a principal recyclable material, may be charged a fee for yard debris recycling. <u>No fee may be charged for the first setout per month of up to a unit of yard debris.</u> [This fee may be charged in addition to the base fee for garbage collection only if the volume of yard debris material collected exceeds one unit of yard debris for the collection period.] The first unit of yard debris collection [shall not be less than] <u>is defined as</u> the equivalent of a thirty-two gallon can<u>, or the standard unit of yard debris service provided, whichever is greater</u>.

(503) 229-5502
FAX (503) 226-1355
TDD-Nonvoice (503) 229-5497

Oregon

DEPARTMENT OF HUMAN RESOURCES

Health Division

June 11, 1991

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 12 1991
OFFICE OF THE DIRECTOR

Environmental Quality Commission
Director's Office
Dept. of Environmental Quality
811 SW 6th Avenue
Portland, Oregon 97204

Dear Commissioners:

I am writing as the spokesperson for the Oregon Health Division to recommend that the Environmental Quality Commission deny James River II, Inc. and Boise Cascade's petition to amend Oregon's ambient water quality standard for TCDD. Increasing the ambient water quality criteria for TCDD could potentially undermine the future protection of public health in the State of Oregon.

As the Public Health Toxicologist for the Oregon Health Division (OHD), I am very familiar with scientific information regarding the health effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). A substantial amount of scientific data exists to support a receptor-based mechanism of toxicity for this chemical. Empirical as well as epidemiologic information provide support that animal to man inferences, and high to low dose theoretical extrapolation models have not accurately estimated TCDD's true human toxicity.

The OHD is currently monitoring the scientific debates and developments regarding the assessment of human health effects of TCDD. We are also in the process of developing a public health policy regarding dioxin and furan contaminated media of public health concern in the State of Oregon. This policy is not expected to be finalized before the end of the year.

The OHD policy will provide information about whether or not human health effects would be expected from a certain type of dioxin or furan exposure. The policy will address pre-existing environmental contamination, and provide the mechanism to initiate appropriate public health protection activities.

The OHD approach will not be unlike other agency's "acceptable daily intake" estimates which identify a dose that is not expected to result in adverse health effects. However, such estimates are not useful for developing pollution prevention or antidegradation environmental protection policies. To be protective of public health,

BARBARA ROBERTS
Governor

1400 SW 5th Avenue
Portland, OR 97201
(503) 229-5599 Emergency
(503) 252-7978 TDD
Emergency

concentrations of contaminants in the environment of highly persistent chemicals such as dioxins and furans for which substantial evidence exists for the potential for adverse health effects should not be allowed to increase, and should not be as high as an "acceptable daily intake".

Even if pollution prevention or antidegradation is not an issue in this particular case, it still remains that many assumptions and extrapolations that are not scientifically based, and can not be validated must be made in order to utilize an "acceptable daily intake" in the calculation of an ambient water quality criteria.

In conclusion, the OHD believes that revision of Oregon's ambient water quality criteria should be scientifically based on information that can be substantiated with actual data. Such information is not presently available; therefore, increasing the water quality criteria has the potential for undermining the future protection of public health in the State of Oregon.

Sincerely,

Roseanne M. Lorenzana

Roseanne M. Lorenzana, DVM, PhD
Public Health Toxicologist
Environmental Toxicology Section
Office of Environment and Health Systems

RML:ab

CC: Gene Foster, DEQ
Larry Foster, Acting State Health Officer
Kathleen A. Gaffney, MD, MPH, State Health Officer Elect

June 2, 1991

Environmental Quality Commission
Directors Office
811 S. W. 6th Ave.
Portland, Oregon 97204

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 04 1991
OFFICE OF THE DIRECTOR

Dear Commission Member,

In reference to the giant pulp and paper manufacturers, notably James River Corporation and Boise Cascade, who brashly now request the Oregon E.Q.C. to set lower ambient water quality standards.

Needless to say, the Oregon standard is absolutely necessary to the maintenance of our waterways now and for the future. Certainly industrial needs must be given some consideration. However all members of the state's citizenry should also be granted the highest water quality standards in our great Northwest. Oregon as a leader in all environmental concerns is a model for the nation.

As owners of property on the Columbia River in Columbia County, we implore the E.Q.C. to reject the proposed change in water quality standards. Industry cannot provide any real evidence that would support any modification of the D.E.Q. standard.

Thank you for your vote against such a negative approach to our water quality.

Sincerely,

Roger and Mary Thompson

Roger and Mary Thompson
4144 S. E. Boardman Ave.
Milwaukie, Oregon 97267

Environmental Quality Commission
Directors Office
811 SW 6th Avenue
Portland, OR 97204

June 4, 1991

Dear Commission Member,

I urge you to please reject the latest proposal by the pulp industry to reduce the water quality standards in Oregon.

In a time of increased environmental awareness, it seems indefensible that certain companies would propose to lessen the standards for economic reasons, while neglecting and potentially harming a very large and complex ecological system.

My interest as a partner in land in Clatskanie prompts me to write this letter not only for myself, but for everyone who lives on or near the rivers in Oregon. You have the opportunity to effect a positive result for the people of Oregon. Please do so.

Respectfully,

Robert J. Thompson

Robert J. Thompson

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED

MILES
SAND AND GRAVEL COMPANY
P.O. BOX 130, AUBURN, WASHINGTON 98071

AUBURN
JUN 5 '91
WASH.

U.S. POST
05
MET
8219

Environmental Quality Commission
Directors Office
811 S.W. 6th Ave.
Portland, OR 97204

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 07 1991

OFFICE OF THE DIRECTOR

NORTHWEST PULP&PAPER

June 6, 1991

Fred Hansen, Director
Department of Environmental Quality
811 SW Sixth Avenue
Portland, OR 97204

Dear Mr. Hansen:

The Northwest Pulp and Paper Association is writing to support the James River Corp. and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Oregon's current water quality standard of 0.013 parts per quadrillion (ppq) is a human-health-based standard. However, the science upon which this standard was developed has been challenged — and its conclusions radically altered — by the very scientist who conducted the original research. Therefore, the premise for the current standard is now highly questionable.

In addition, the Environmental Protection Agency has recently approved water quality standards 100-times less stringent than its guideline criterion (which Oregon adopted, along with a variety of other EPA recommendations for toxic discharges). Thus, EPA has indirectly conceded that, when taking new science and regional factors into consideration, its criterion of 0.013 ppq may be more restrictive than necessary to protect human health.

In recognizing this apparent conflict, EPA has announced a review of the science on dioxin. I have enclosed a May 17 report from *Science* that notes the one-year time frame EPA Administrator William Reilly has established for this review. However, should Oregon decide to wait on the EPA review before commencing a review of its standard — and not suspend its imposition of dioxin discharge restrictions — the two mills in question are bound by state law to invest millions of dollars in what may prove to be unnecessary environmental controls.

Oregon needs a scientifically-based water quality standard for dioxin that is fully protective of human health. The Clean Water Act delegates this responsibility to the states, in part so that states may incorporate regional data, such as fish consumption information, into their decision. It is time for Oregon to develop such a state-specific water quality standard for dioxin. We hope that the Environmental Quality Commission will accept the James River and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Sincerely,

Kathy E. Gill

Kathy E. Gill, CAE
Public Affairs Director

enclosure
c: EQC members

EPA Moves to Reassess the Risk of Dioxin

Urged on by the scientific community, EPA is developing a new model for estimating dioxin's risk

GALVANIZED BY THE RESULTS OF A RECENT scientific meeting on dioxin's molecular actions, Environmental Protection Agency (EPA) administrator William K. Reilly has launched a major new effort to reassess the toxicity of this ubiquitous—and infamous—chemical.

Responding to criticism that the model EPA now uses to assess dioxin's risk is obsolete, Reilly has asked agency scientists to come up with a new "biologically based" model that will draw on an emerging understanding of the first steps that take place as dioxin enters a cell (for example, see pages 924 and 954). Reilly and others call the new effort "precedent-setting" not only for how the agency regulates carcinogens but also for EPA's quick response to new scientific developments—not its strong suit in the past.

Until now, EPA has gauged the risk of dioxin exposure by using the same model it applies to most carcinogens: the linear multistage model, which assumes that risk rises in proportion to dose. Agency officials have long viewed the model as a "default"—one adopted for lack of a real understanding of how carcinogens work—and their intent was always to replace it with something more realistic once mechanisms were understood. But so far, they say, such evidence has been lacking. Now it may at last be in hand, at least for dioxin and perhaps a handful of other chemicals that behave similarly.

The turning point came in an 8 March briefing for Reilly and his top deputies given by three agency scientists: William Farland and Peter Preuss, both at EPA headquarters in Washington, D.C., and Linda Birnbaum of EPA's Health Effects Research Laboratory in North Carolina. Part of the briefing was devoted to recent epidemiologic studies, including the new one by Marilyn Fingerhut of the National Institute for Occupational Safety and Health (NIOSH), which found perhaps the strongest link yet between high doses of dioxin and human cancer (see *Science*, 8 February, page 625). The EPA scientists also discussed a reanalysis of data from a 1976 study of cancer in dioxin-exposed rats that figured heavily in EPA's original risk assessment. After reexamining the original slides of liver tissue, investigators have concluded that the animals developed fewer tumors than was originally believed.

But it was Birnbaum and Farland's description of a meeting last November at the Banbury Center at Cold Spring Harbor Laboratory that Reilly says made the most compelling case for change. At that meeting a group of dioxin experts agreed that before dioxin can cause any of the ill effects it has been linked to—cancer, immune system suppression, chloracne, and birth defects—one "necessary but not sufficient" event must occur: the compound must bind to and activate a receptor, known as the aryl hydrocarbon or AH receptor (see *Science*, 8 February, p. 625). After that, the dioxin-receptor complex is transported to the nucleus, where it binds to specific sequences of DNA and turns genes on and off, thereby causing its myriad effects. It had long been known that dioxin binds to a receptor, but before the Banbury meeting it had been unclear whether all of dioxin's effects or just some were mediated this way.

Key mover. *Linda Birnbaum had been urging EPA to change how it does dioxin risk assessment.*

The Banbury group also agreed that dioxin has to occupy a certain number of AH receptors on a cell before any biological response can ensue. The result is a practical "threshold" for dioxin exposure, below which no toxic effects occur. That conclusion flies in the face of the linear model's underlying assumption: that the risk of harmful effects begins with exposure to a single molecule and increases from there. Faced with this new picture of dioxin's action, the Banbury participants urged EPA to develop a new, receptor-based model for dioxin risk assessment.

Reilly bit. He has now asked scientists in EPA's Office of Research and Development, in collaboration with academic researchers around the country, to come up with just such a model. The goal, explains Michael Gallo of the Robert Wood Johnson Medical School, one of the organizers of the Banbury meeting who is now working with EPA, is to pinpoint the threshold or "safe" dose below which none of dioxin's ill effects should occur.

In building the model, Gallo and his EPA colleagues hope to draw on work on the dioxin receptor now under way in a number of labs around the country. In this issue of *Science*, for example, a group headed by Oliver Hankinson of the University of California at Los Angeles reports on the cloning of a protein that is necessary for the receptor to function. Various roles have been proposed for the new protein; one intriguing possibility is that it is part of the receptor itself. The dioxin receptor thus might contain at least two proteins, one that binds to dioxin (and presumably whatever natural molecule dioxin mimics) and another that binds to DNA. "Boy, is that exciting," says Gallo, who adds that the new findings will feed directly into the model.

Until the model is complete, no one can say for sure whether it will show dioxin to be more or less risky than EPA now calculates, though Gallo and others speculate that it will turn out to be less risky. One of the major questions is how close the presumed "safe" dose is to the background levels of dioxin to which the general population is exposed. If background exposure is already near the "safe" dose, then there may not be much room for additional exposure.

Those background levels are largely unknown, so Reilly has added that question to the EPA scientists' assignment. Over the next year Birnbaum and other EPA scientists, in collaboration with researchers from NIOSH, the Centers for Disease Control, and the Air Force, hope to get a fix on blood levels of dioxin and the handful of polychlorinated biphenyls that behave similarly and thus could increase its risk. Meanwhile, other researchers will be studying the sources and routes of dioxin exposure—most of which are dietary—and how it is passed up the food chain.

Reilly wants the new model and related work complete within a year, at which time the results will go on to EPA's Scientific Advisory Board (SAB) for peer review. Three years ago, the SAB sent EPA scientists back to the drawing board when they tried to revise the dioxin standard, saying the science wasn't sound enough. Birnbaum and other EPA researchers predict a different outcome this time. ■ LESLIE ROBERTS

313 S.W. 2nd Street, Suite D
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON
TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 07 1991
OFFICE OF THE DIRECTOR

June 6, 1991

Office of the Director
Department of Environmental Quality
811 SW 6th Ave.
Portland, OR 97204

RE: Petition for reduction of Oregon's ambient water quality standard

Dear Mr. Fred Hansen:

At a very late date I was advised that this petition is once again before your department. I understand the EQC will consider and possibly act upon the petition submitted to you by James River Corporation and Boise Cascade at its June 14th meeting. For some reason this Commission has been excluded from any official notification by your department or by the petitioners. Instead I have been advised by a local citizen that this action has been about to take place.

This Commission remains opposed to lowering of our ambient water quality standards until and unless it can be shown that there will be zero negative effect upon the health of salmon runs in the affected waters. The basis of our concern is primarily for effects on the juvenile salmon who must use the fresh water habitat enroute to the ocean. We remain especially concerned in view of the recent petitions for endangered species status on several northwest salmon runs.

I include copies of testimony and correspondence already submitted to your department which I would like to have attached to the record for this particular petition.

In short, the Commission remains extremely concerned that even current loading of dioxins into the fresh water habitat may have deliterious effects on juvenile salmon survivability. Until it can be shown that those effects do not exist and until it can be shown that a reduction of our water quality standards will not further the problem, we remain opposed to any lessening of the standards.

Thank you for your considerations. I hope the oversight which led to the lack of communication with this Commission about these petitions will be corrected.

Sincerely yours,

Tom Robinson, Manager
Oregon Salmon Commission

TR/nf

313 S.W. 2nd Street, Suite D
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

May 10, 1990

Llewellyn Matthews
Northwest Pulp & Paper Association
1300 114th Ave. SE, Suite 110
Bellevue, WA 98004

Dear Mr. Matthews:

Thank you for your letter and overview statement pertaining to the dioxin issue. Although I was not personally in attendance, this Commission was represented at your Astoria briefing by Commissioner Robert Finzer. Mr. Finzer is a North Coast commercial fisherman and wholesaler. He gave a brief report on the situation at our last Commission meeting.

We are sensitive to your problems and we support your stated commitment to a solution which can allow a healthy pulp industry within a healthy environment. To us that continues to mean operations which do not pose risk to salmon food products nor to salmon survival, health or reproduction. It also means maintaining standards of water quality which are equal to those of our competitors in other nations which provide salmon to the world market.

So far, we are fairly comfortable with the food safety issue. Our public salmon are pure, clean food with all agencies finding salmon as the least likely of all fishes to be contaminated with toxins.

However, we remain steadfast in our position that standards equivalent to those in Europe and Canada be maintained here. Also, we continue to insist that our standards be met in fact. These are critical market demands.

We continue to be extremely concerned about salmon reproduction, smolt mortality, and immune systems, when exposed to effluent materials throughout the inland waterways they use. Even small percentages of mortality or fecundity loss represent large numbers of salmon losses at the harvest end. For example a 1% loss of down stream coho smolts represents a number of salmon roughly equal to the entire Oregon commercial troll harvest. We must learn the true impact on smolts and learn how to control it. I have not read the reports you cite as showing "no adverse affects on fish reproduction or fish tissue." Perhaps your staff can supply us with a copy.

Your offer to meet with us may be something we can explore later this fall, after our harvest season. We, like you, are an industry which supplies a valuable commodity to the market, relying on a healthy natural resource for the raw material. In the past, salmon resources industries have not viewed the wood products industry as a friend. I think you will agree that there is basis in fact for that view. Too much of our salmon resource has been lost to forest industries already. If that stops, perhaps we can ally as fellow industries, in common cause. If it does not, then our position is clear, and probably adversarial.

Sincerely yours,

Tom Robinson, Manager
Oregon Salmon Commission

cc: Dalton Hobbs, Department of Agriculture
Jill Zarnowitz, OR Dept. of Fish & Wildlife
Bob Eaton, Salmon for All
Oregon Salmon Commissioners

313 S.W. 2nd Street, Suite D
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON
TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

Date: May 1, 1990

To: DEQ
Water Quality Division
811 SW 6th Ave.
Portland, OR 97204

From: Tom Robinson, Manager
Oregon Salmon Commission

RE: Proposed Rule Changes Affecting Pulp Mill/Dioxin Effluents Standards.

Please be advised that the Oregon Salmon Commission on behalf of Oregon's commercial salmon trollers and on behalf of the consuming public which we serve under OAR 576.305 does not support any of the options for rule changes affecting standards applied to pulp mill effluents/dioxin contamination. The Oregon Salmon Commission has provided formal oral and written testimony to DEQ and to the Environment Quality Commission on this subject. Our position remains unchanged. We adamantly support stringent standards which will fully protect both food quality and the smolt survivability of salmon which use the Columbia River corridor. While we are satisfied that no danger to consumers of salmon food fish is imminent, we see this as no reason to relax any of the standards. We continue to be greatly concerned about mortality of juvenile salmon and about biological effects on adult salmon's immune systems and reproductive capacities when exposed to these effluents. Those biological and mortality concerns have not yet been addressed nor answered satisfactorily.

Attached are copies of written testimony already supplied to you by this Commission. Please apply them to this record.

On behalf of the Commission I also express a great dissatisfaction with the notification processes being used as this issue continues to run a gauntlet of meetings and reviews. I have not been formally contacted on a regular basis by your department about the schedule of hearings and comment deadlines. I remind you that we are a state agency which is very much affected by the decisions you will make. I find it extremely remarkable that my best source of up-to-date information continues to be the "grapevine" rather than official communications from your department. Furthermore, I know that the Pacific Fisheries Management Council and the states of Oregon and Washington fisheries divisions are greatly concerned about this issue. Are they not being directly contacted? Please take prompt action to correct this oversight in notification.

cc: William P. Hutchinson EQC
Randy Fisher ODFW
Joe Blum WDF
Richard Schwarz PFMC
Frank Warrens PFMC
Bob Eaton Salmon for All

313 S.W. 2nd Street, Suite C
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON
TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

Date: December 15, 1989

To: Fred Hansen, Director
Department of Environmental Quality
811 SW Sixth
Portland, OR 97204

From: Tom Robinson, Manager
Oregon Salmon Commission

Re: Proposed Rule Changes

We understand that Oregon's EQC is reviewing proposed rule changes on pulp mill pollution effluents January 1990. As you know we continue to provide comment on this matter as we find it to have significant impact on our industry through degradation of the environment. The details of our concern are outlined in previous communications and testimony submitted to you.

We also have some specific concerns and comments regarding proposed rule changes.

1. We ask for a return to full, open disclosure of all proceedings between the state and pulp mill industry representatives as this matter is resolved.
2. We support the status-quo of rules which require formal findings on pollution before EQC makes approvals. We recommend that food fish studies should be independently performed by other than industry contractors, to assure the objectivity of required findings.
3. We call your attention to the following items from the proposed rule changes:
    a) Proposed changes in paragraph 3, section (a) are alarming in that they appear to weaken existing permit processes, allowing too much subjective opinion, changing the phrase "would not", to read, "is not expected to", is clearly a move away from the level of control and protection which we must have through your commission, to assure safe, quality habitat for food fish in Oregon.
    b) Likewise, we support the status-quo for procedures which determine WQL status. There must not be a relaxing of processes which would remove the burden of positive proof of compliance with effluent standards, prior to removing a waterway, or a facility, from corrective activity. Speculative statements that compliance is expected may be encouraging news, but should not be substituted for actual achievement.

Thank you for your attention to our requests. We continue to rely on EQC, and DEQ to protect the habitat of Oregon's salmon resource as you execute your difficult tasks.

cc See attached sheet

NORTHWEST ENVIRONMENTAL ADVOCATES

June 10, 1991

Fred Hansen, Director
Oregon Department
of Environmental Quality
811 S.W. Sixth
Portland, OR 97204

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 10 1991
OFFICE OF THE DIRECTOR

Bill Hutchinson, Chair
Oregon Environmental Quality
Commission
Tooze, Shenker Holloway, & Duden
333 SW Taylor St.
Portland, OR 97204

Re: Notice of Consideration of Petition for Rule Amendment
(Water Quality Standard for 2,3,7,8-TCDD)

Dear Fred and Bill:

I am writing to urge the Commission to deny the pulp and paper industry's petition to change the criterion in the water quality standard for dioxin. There are numerous reasons for the Commission not to take up this issue, not the least of which is the fact that the Department recently reevaluated this standard in its most recent "triennial review." In addition, as I am sure you are aware, U.S. EPA is reexamining the criterion.

It would be redundant for the State of Oregon to reevaluate the very same issue that EPA is currently reviewing, and Oregon is certainly less well equipped to do so. It is also premature to second guess the outcome of that evaluation. In fact, EPA Administrator Reilly has urged that regulatory actions based on the existing dioxin criterion proceed as scheduled.

For as many reasons as the pulp and paper industry can come up with to argue for an increase in the allowable limits for dioxin, there are at least an equal number of arguments that the existing standard is not conservative enough. For example, the current criterion is based on a bioconcentration factor of 5,000. Yet studies show that the bioconcentration factor in fish can range up to 156,000. The existing dioxin standard does not take into account the other media by which dioxin contaminates human beings, i.e. inhalation, eating food other than fish. General human background exposure to dioxin compounds (1 to 10 parts per kilogram (equivalent to part per quadrillion) in toxicity equivalent units for all dioxins) is known to already exceed the acceptable daily intake set by EPA for protection against reproductive effects (1 part per quadrillion). In addition there are the synergistic and

408 Southwest Second Avenue, Governor Bldg. Suite 406, Portland, Oregon 97204 Telephone (503) 295-0490

additive effects caused by exposure to dioxin in tandem with other toxic pollutants.

Industry is fond of pointing out that the risk to humans from dioxin is far less than to lab rats, for which dioxin is clearly a hazard. Presumably industry would include other 'lower life forms' in its assessment of the hazards of dioxin. This is relevant to the Commission's decision because, whether or not the existing criterion for dioxin adequately protects human beings, it certainly does not take into account the increased effects dioxin has on wildlife. These effects are increased due to the lower body weight and greater consumption of contaminated aquatic life (e.g. fish) by eagles, mink, otter, and other pisciverous wildlife. States' water quality standards are supposed to protect the most sensitive beneficial uses. The Commission should not even consider this or any other petition to change the dioxin standard unless petitioners can demonstrate that a higher level of dioxin contamination will not result in a lower level of protection for the most sensitive uses.

It is an old ploy of industry's to seek to have the rules changed when it doesn't want to meet them. It is inexcusable when government accedes to this. The Commission should enforce the standards it has adopted, not bend them when the going gets tough for a segment of industry which has had the benefit of over-polluting public waters for many years.

Sincerely,

Eugene Rosolie for

Nina Bell
Executive Director

cc: Emery N. Castle
Henry Lorenzen
Carol Whipple
William W. Wessinger

VICTOR M. SHER (WSB# 16853)
TODD D. TRUE (WSB# 12864)
REBECCA E. TODD (WSB# pending)
Sierra Club Legal Defense Fund
216 First Avenue S., Suite 330
Seattle, Washington 98104
(206) 343-7340

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 10 1991
OFFICE OF THE DIRECTOR

BEFORE THE ENVIRONMENTAL QUALITY COMMISSION
OF THE STATE OF OREGON

In the Matter of the Petition of James River II, Inc. and Boise Cascade Corporation to Amend Subparagraph (2)(p)(B) of Oregon Administrative Rules Chapter 340, Division 41, Sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965.)	MEMORANDUM IN OPPOSITION TO THE PETITION FOR RULE AMENDMENT

I. Introduction

This Memorandum in Opposition to the Petition for Rule Amendment is submitted by the Sierra Club Legal Defense Fund, Inc. on behalf of the American Oceans Campaign, the Campaign for Puget Sound, the Dioxin/Organochlorine Center, Friends of the Earth, National Audubon Society, Puget Sound Alliance, the Washington Environmental Council, and the Washington Toxics Coalition.[1] These organizations are non-profit environmental groups dedicated to and actively working toward the preservation and protection of water resources and all life dependent on them.

[1] American Oceans Campaign, 4007 Latona Avenue NE Seattle, WA 98105; Campaign for Puget Sound, P.O. Box 2807 Seattle, WA 98111-2807; Dioxin/Organochlorine Center, 1247 Willamette Street Eugene OR 97401; Friends of the Earth, 4512 University Way NE Seattle WA 98105; National Audubon Society, P.O. Box 462 Olympia, WA 98502; Puget Sound Alliance, 4516 University Way NE Seattle WA 98105; Washington Environmental Council, 5200 University Way NE Seattle WA 98105; and the Washington Toxics Coalition, 4516 University Way NE Seattle WA 98105.

In specific, the organizations seek to reduce and eliminate entirely the discharge of toxic organochlorines to the waters of the Pacific Northwest, including 2,3,7,8 tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD), commonly known as dioxin.[2]

We strongly oppose the Petition for Rule Amendment and urge the Environmental Quality Commission to deny the Petition. We are a group of national, regional, and Washington State environmental groups concerned about the water quality of the Pacific Northwest, Oregon, and the water resources shared by Oregon, Washington, and Idaho. The Columbia River receives much of the region's pulp and paper mill organochlorine discharge and for many hundreds of miles is a shared resource and border for Oregon and Washington.[3] The ambient water quality standard for 2,3,7,8-TCDD in Oregon necessarily affects these shared ecosystems and the livelihood and recreation of those living in both states. We are also concerned with the precedential implications that the Petition for Rule Amendment may have nationwide and for the Pacific Northwest.

---

[2] "Dioxin" as it refers to 2,3,7,8-TCDD is actually a misnomer. Dioxins are a family of approximately 75 separate chlorinated organic compounds, each of which is characterized by the existence of two oxygen atoms connecting two chlorinated benzene rings.

[3] The interdependence of the Pacific Northwest states with regard to the Columbia River has been recognized by the formation by Oregon and Washington of the Bistate Commission for the Columbia River, and the basin-wide protection strategies for the River established by the Environmental Protection Agency [EPA], including the establishment of Total Maximum Daily Loadings and Individual Control Strategies pursuant to the Federal Water Pollution Control Act, 33 U.S.C. §§ 1313(d) and 1314(l), respectively.

2,3,7,8-TCDD is a known human carcinogen, teratogen, and immunosuppressant.[4] Other types of damage caused by 2,3,7,8-TCDD include skin disorders, reproductive disorders, hormonal and metabolic effects, developmental defects, damage to the liver, kidney and thymus, wasting syndrome, neurobehavioural effects, and learning disabilities.[5] Furthermore, 2,3,7,8-TCDD is

---

[4] Some pertinent papers regarding this include:

Fingerhut, Marilyn A., William E. Halperin, David A. Marlow, Laurie A. Piacitelli, Patricia A. Honchar, Marie H. Sweeney, Alice L. Greife, Patricia A. Dill, Kyle Steenland, and Anthony J. Suruda, Cancer Mortality in Workers Exposed to 2,3,7,8 Tetrachlorodibenzo-p-dioxin, The New England Journal of Medicine 324: 212-218 (1991).

Schwartz, E., A Proportionate Mortality Ratio Analysis of Pulp and Paper Mill Workers in New Hampshire, British Journal of Industrial Medicine 45:234-238 (1988).

Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 (1989).

Skene, S.A., I.C. Dewhurst, and M. Greenberg, Polychlorinated Dibenzo-p-dioxins and Polychlorinated Dibenzofurans: The Risks to Human Health: A Review, Human Toxicology 8:173-203 (1989).

[5] Some pertinent papers regarding this include:

Bowman, R.E., S.L. Schantz, M.L. Gross, and S.A. Ferguson, Behavioral Effects in Monkeys Exposed to 2,3,7,8-TCDD Transmitted Maternally During Gestation and for Four Months of Nursing, Chemosphere 18:235-242 (1989).

Fish and Wildlife Service, Dioxin Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review, Biological Report 85, May 1986.

Jacobson, Joseph L., Sandra W. Jacobson, and Harold E.B. Humphrey, Effects of In Utero Exposure to Polychlorinated Biphenyls and Related Contaminants on Cognitive Functioning in Young Children, Journal of Pediatrics 116:38-45 (1990).

Larsson, Ake, T. Andersson, L. Forlin, and J. Hardig, Physiological Disturbances in Fish Exposed to Bleached Kraft Mill Effluents, Wat. Sci. Tech. 20:67-76, 1988.

McCormack, Craig and David Cleverly, United States Environmental Protection Agency, Analysis of the Potential Populations at Risk From the Consumption of Freshwater Fish Caught Near Paper Mills, Draft Report, April 23, 1990.

Schantz, Susan L., and Robert E. Bowman, Learning in Monkeys Exposed Perinatally to 2,3,7,8 Tetrachlorodibenzo-p-dioxin (TCDD), Neurotoxicology and Teratology 11:13-19, 1989.

bioaccumulative, bioconcentrative, and persistent.[6]

Moreover, while 2,3,7,8-TCDD is the most toxic substance ever identified, and hence the most toxic of the organochlorines, chlorine bleaching pulp and paper production generates tons of chlorinated organics which are toxicologically equivalent to 2,3,7,8-TCDD. In other words, these other organochlorines act within the body and the environment in virtually the same toxicological manner as 2,3,7,8-TCDD. For example, in issuing a recent Fish Consumption Advisory for Lake Roosevelt, the Washington State Department of Health recognized that 90% of the dioxin toxicity is due to 2,3,7,8 tetrachlorodibenzofuran.[7] As one of the leading scientific experts has written,

---

Svensson, Bengt-Goran, Anita Nilsson, Marianne Hansson, Christopher Rappe, Bjorn Akesson, and Staffan Skerving, Exposure to Dioxins and Dibenzofurans Through the Consumption of Fish, The New England Journal of Medicine 116:8-12 (1991).

Swain, Wayland R., Human Health Consequences of Consumption of Fish Contaminated with Organochlorine Compounds, Aquatic Toxicology 11:357-377 (1988).

Tanabe, S., N. Kannan, An. Subramanian, S. Watanabe, and R. Tatsukawa, Highly Toxic Coplanar PCBs: Occurrence, Source, Persistency and Toxic Implications to Wildlife and Humans, Environmental Pollution 47:147-163 (1987).

[6] The toxicokinetic half-life of 2,3,7,8-TCDD in human tissue has been predicted to be approximately 5 to 8 years and the half-life in sediments is even longer. See, Bowman, R.E., S.L. Schantz, N.C.A. Weerasinghe, M.L. Gross, and D.A. Barsotti, Chronic Dietary Intake of 2,3,7,8 Tetrachlorodibenzo-p-dioxin (TCDD) at 5 or 25 Parts Per Trillion in the Monkey: TCDD Kinetics and Dose-Effect Estimate of Reproductive Toxicity, Chemosphere 18:243-252 at 250 (1989), and Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 at 458 (1989).

[7] Washington Department of Ecology, First Progress Report on Ecology's Dioxin/Furan Survey in Lake Roosevelt, Memorandum from Art Johnson, Dave Serdar, and Stuart Magoon to Carl Nuechterlein, August 8, 1990.

> it is misleading to consider dioxin as a single entity, and the potential health risks are properly evaluated by taking into account exposures to mixtures of the hundreds of isomers and related compounds in this group.[8]

An approach, therefore, which focuses on the cancer risks from 2,3,7,8-TCDD necessarily underestimates cancer risks from pulp and paper mill effluent[9] and also ignores other arguably more important organismic and ecosystem level impacts from 2,3,7,8-TCDD such as adverse reproductive, developmental, and wildlife effects.

//

//

//

//

//

---

[8] Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 at 456 (1989).

[9] EPA itself recognizes that its cancer risk and attendant water quality standard of .013 ppq vastly underestimate the actual cancer risk suffered by certain sensitive populations. EPA estimates that a Native American adult consuming Columbia River Basin fish in an amount average for Native Americans per day contaminated with 6.5 parts per trillion (ppt) 2,3,7,8-TCDD equivalents exceeds the EPA threshold of concern for reproductive effects by over nine times. See, McCormack, Craig and David Cleverly, United States Environmental Protection Agency, Analysis of the Potential Populations at Risk From the Consumption of Freshwater Fish Caught Near Paper Mills, Draft Report, April 23, 1990.

Furthermore, in calculating the cancer risk and water quality standard for 2,3,7,8-TCDD, EPA assumed a fish consumption rate of only 6.5 grams per day, while actual fish consumption rates are approximately five times higher than this, and Native American fish consumption rates are approximately fifteen times higher. More realistic fish consumption rates, therefore, would make the cancer risk standards five to fifteen times higher, respectively. Id.

II. The Environmental Quality Commission Should Deny the Petition for Rule Amendment.

We strongly urge the Commission to deny the Petition for Rule Amendment filed by James River II and the Boise Cascade Corporation on May 23, 1991. A new rulemaking effort makes little sense in light of the limited resources of the State of Oregon. Indeed, Oregon initially adopted the .013 ppq standard established by EPA's Quality Criteria for Water 1986 with the express realization that the State had insufficient resources to undertake adequately a separate analysis of the health risks of 2,3,7,8-TCDD. As the State continues to suffer from limited resources, it continues to be ill-advisable for the State to undertake the complex analysis of human and environmental health risks from 2,3,7,8-TCDD necessary in deciding the water quality standard.

The adoption of a water quality criterion or standard is a significant task. EPA regulations mandate that every water quality criteria

> must be based on sound scientific rational and must contain sufficient parameters or constituents to protect the designated use. For waters with multiple use designations, the criteria shall support the most sensitive use.

40 C.F.R. § 131.11(b)(1)(1990). To adopt a new water quality standard requires that the rulemaking body employ "scientifically defensible methods" in assuring that the most sensitive uses are protected. 40 C.F.R. § 1313.11(b)(1)(1990) Establishing a new water quality standard for 2,3,7,8-TCDD would be extremely resource intensive, consuming the kind of time and energy that the State of Oregon has already recognized that it lacks.

Furthermore, the issue of the proper water quality standard for 2,3,7,8-TCDD will be debated shortly in another forum. EPA established the Total Maximum Daily Loadings [TMDL] for the Columbia River on February 25, 1991, regarding the total allowable discharge of 2,3,7,8-TCDD into the Basin. We anticipate legal challenges to the TMDL asserting that the .013 ppq standard is inadequate to protect human health and wildlife. In this connection, we believe that the appropriate water quality standard for 2,3,7,8-TCDD is zero, as detailed in Section III below.

Furthermore, from an ecosystem perspective it is nonsensical to allow mills in Oregon to discharge bioaccumulative and persistent organochlorines into the Columbia River Basin at 2.3 ppq, while Idaho and Washington mills comply with the applicable .013 ppq state standards, a difference of orders of magnitude. Fish, endangered Bald Eagles feeding on them, mink, otter, other wildlife, as well as sensitive human populations such as Native Americans, Asian Americans, and subsistence and sport fishers cannot differentiate among the 2,3,7,8-TCDD contamination from Oregon and that from other states. With regard to these especially sensitive groups, the State of Oregon has a duty to protect all of the people that compose the population of the State. While the .013 ppq standard is not adequately protective of either humans and wildlife, the suggested 2.3 ppq standard is even less so.

//

//

At this time and given the limited resources of the State, the most logical and protective course of action for the Commission is to deny the Petition for Rule Amendment.

III. Alternatively, If the Environmental Quality Commission Revisits the Rulemaking Procedure, the Proper Water Quality Standard for 2,3,7,8-TCDD is Zero.

The chlorine bleaching pulp and paper mills insist that new data indicate that the ambient water quality standard for 2,3,7,8-TCDD should be loosened. It is our position, and the position of the best scientific experts in the field, that available data militate for a <u>more stringent and protective</u> standard. These data include human reproductive and developmental effects, the effects on wildlife reliant on contaminated ecosystems, and the bioaccumulation, bioconcentration, and persistence of 2,3,7,8-TCDD in animal tissue and sediments. If the Petition for Rule Amendment is granted, we expect that the Commission will find itself in the midst of an extremely involved and complex dispute, with both sides presenting evidence and expert opinion regarding the proper water quality standard for 2,3,7,8-TCDD.

If the Commission does indeed elect to reopen rulemaking, we anticipate arguing that the standard for 2,3,7,8-TCDD is properly zero, that is, that the Commission should allow no discharges of 2,3,7,8-TCDD at all.

//

//

//

We are not the first to suggest to the State of Oregon that the water quality standard for 2,3,7,8-TCDD should be zero. Over the past several years, the United States Fish and Wildlife Service has consistently advised that because of the long-term health effects on wildlife that 2,3,7,8-TCDD discharges be reduced and eliminated:

> We recommend that the DEQ consider limiting the [pulp and paper mills' National Discharge Elimination System, or NPDES] permit[s] to a discharge of no dioxins...

Letter from the United States Fish and Wildlife Service to the Oregon Department of Environmental Quality dated July 10, 1989. Six months later the Fish and Wildlife reiterated that

> we believe it is appropriate for DEQ to develop a long-term goal that decreases and eventually eliminates the production of dioxin and other chlorinated byproducts.

Letter from the United States Fish and Wildlife Service to the Oregon Department of Environmental Quality dated January 19, 1990.

In recognition of the severity of the organochlorine contamination in the Columbia River Basin, the Fish and Wildlife Service most recently explained that

> considering the longevity of organochlorine compounds and the potential impact of small quantities of dioxins on fish, waterfowl, and endangered species, we recommend that the EPA strive towards limiting NPDES permits to zero discharge of dioxins to the Columbia River Basin.

Letter from the United States Fish and Wildlife Service to Region 10 EPA dated November 21, 1990. The zero discharge standard is the only standard for 2,3,7,8-TCDD that will adequately protect human, wildlife, and environmental health.

There are many technologies available and in use worldwide that reduce and eliminate the use of chlorine or chlorine compounds that are the necessary precursors for all chlorinated organic compounds. Without chlorine or chlorine compounds present in the production process, organochlorines cannot be formed and discharged to the environment. Many European mills and some North American mills currently employ chlorine-free technology in their pulp and paper production. Many if not all the mills in the United States are at the very least exploring ways in which they can reduce their use of chlorine and the subsequent discharge of toxic organochlorines.

Furthermore, the public is becoming increasingly aware of the human and environmental health risks associated with chlorine bleaching and is demanding chlorine-free pulp and paper products. The mill in Lyons Falls, New York is one example of a mill that has converted to a chlorine-free technology and has subsequently experienced an increase in its market share. As consumers increasingly demand chlorine-free paper products, those mills that can supply them are enjoying competitive success in the marketplace.

As has been long recognized elsewhere, there are no functional uses of pulp and paper products that demand the super bright whiteness normally achievable with chlorine bleaching processes. Non-chlorine bleaching renders pulp and paper products that are nearly as bright white as chlorine bleached products. These chlorine-free products are suitable for every use to which pulp and paper products are put today.

Because of the availability of chlorine-free technologies, the complete lack of need for chlorine bleached pulp and paper, and the serious and persistent risks to human and environmental health, if the Commission grants the Petition for Rule Amendment, we anticipate returning to urge the Commission to promulgate an ambient water quality standard of zero for 2,3,7,8-TCDD.

IV. Conclusion

On behalf of the organizations listed above, we offer this Memorandum in Opposition to the Petition for Rule Amendment. We will gladly provide the Commission with any of the data discussed above. As we have not had the opportunity to view all the information submitted by the mills, we are unable to respond directly to their particular scientific or other assertions. Should the Commission like us to provide a more detailed response to their specific claims, we will arrange to procure the mills' lengthy submission and provide a detailed scientific analysis for the Commission's review. That being said, however, we believe that the wisest, most protective, and most efficient course of

//

//

//

//

//

//

//

//

action for the Commission is to deny the Petition for Rule Amendment and we urge the Commission to do so.

Dated this 10th day of June, 1991.

Respectfully submitted,

Victor M. Sher /RET

VICTOR M. SHER

Todd D. True /RET

TODD D. TRUE

Rebecca E. Todd

REBECCA E. TODD

Sierra Club Legal Defense Fund, Inc.
216 First Avenue S. Suite 330
Seattle, WA 98014
(206) 343-7340

Attorneys for American Oceans Campaign, Campaign for Puget Sound, Dioxin/Organochlorine Center, Friends of the Earth, National Audubon Society, Puget Sound Alliance, Washington Environmental Council, and Washington Toxics Coalition.

Sent by telecopy to:

Chair William P. Hutchison, Jr.	(503) 223-5550
Vice Chair Emery N. Castle	(503) 737-1574
Commissioner Henry Lorenzen	(503) 276-3148
Commissioner Carol A. Whipple	(503) 584-2129
Commissioner William W. Wessinger	(503) 229-4689
Director Fred Hansen	(503) 229-6124

cc: Mr. Larry Edelman
Ms. Dana Rasmussen
Mr. Rick Albright
Ms. Adrianne Allen

CHARLES R. "CHUCK" NORRIS
UMATILLA COUNTY
DISTRICT 57

REPLY TO ADDRESS INDICATED:
House of Representatives
Salem, Oregon 97310-1347
P.O. 121, 725 E. Highland Ave.
Hermiston, Oregon 97838

378-8050

HOUSE OF REPRESENTATIVES
SALEM, OREGON
97310-1347

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 12 1991

OFFICE OF THE DIRECTOR

June 11, 1991

William P. Hutchison, Jr., Chair
Environmental Quality Commission
c/o Department of Environmental Quality
811 SW Sixth
Portland, OR 97204

Dear Mr. Hutchison:

I understand that the EQC is in receipt of petitions to reconsider the permissible ambient level of 2,3,7,8 TCDD (dioxin) in Oregon's water. You may recall that I had previously shared some concerns on this issue, basically questioning a criterion of .013 ppq. A copy of some relevant correspondence under date of March 19, 1990 is enclosed.

A lot has happened in this matter since my letter of March 19, most notably Dr. Robert A. Squire's letter of the same date refuting the research which led to the .013 ppq criterion. I'm sure you are aware of and have seen that letter, but I enclose a copy for your convenient reference.

While I am certainly committed to avoiding realistic biological risk, I remain concerned that we do not label certain bodies of water, especially the Columbia River John Day and McNary Pools, unsafe based on other than credible scientific evidence and principles.

As stated earlier, eventually the west end of Umatilla County must rely on the Columbia as a major source of water for a variety of uses, and it would be extremely unfortunate to have such use denied because of alleged contamination based on flawed criteria. No doubt you are aware that certain other states, in concert with the EPA, have adopted standards far less stringent then .013 ppq.

Your attention in this matter will be appreciated.

Sincerely,

CRN

C.R. "Chuck" Norris

2 enclosures: As stated above.

cc: Henry Lorenzen, Member, FQC
Fred Hansen, Director, DEQ

REPLY TO ADDRESS INDICATED:
[ ] House of Representatives
Salem, Oregon 97310-1347
[✓] P.O. 121, 725 E. Highland Ave.
Hermiston, Oregon 97838

567-8638, ofc

HOUSE OF REPRESENTATIVES
SALEM, OREGON
97310-1347

March 19, 1990

SUBJECT: Dioxin in the Columbia River

TO: Fred Hansen, Director, Department of Environmental Quality
811 SW Sixth, Portland, OR 97204

Dear Fred:

During my comments to the Environmental Quality Commission on March 1 in Pendleton I raised two basic issues regarding dioxin in the Columbia.

1. Is there a scientific basis for the limiting standard of .013 parts per quadrillion? My best recollection is that I was informed that the standard was set by the EPA.

2. I commented that the water future of parts of District 57 (primarily the west end of Umatilla County) will rest on tapping the Columbia River to replace our current dependence on deep wells. I expressed the hope that we wouldn't get there just in time to learn that dioxin contamination above McNary Dam precluded our use of that source. My best recollection is that there was no response suggesting that there is or is likely to be such a problem. My thoughts and comments at the time are reported with reasonable accuracy in the enclosed article from the Hermiston Herald. (See Enclosure 1.)

Several days after the EQC meeting I read with dismay the enclosed article from the East Oregonian of March 12. It jarred me on two counts. (See Enclosure 2.)

1. It reported that the McNary pool was already badly contaminated.

2. It reported that the Oregon (DEQ) standard is .013 parts per quadrillion but that the Federal (EPA) standard is "only" .07 parts per trillion and the Federal FDA acceptable level is more lenient yet at 25 parts per trillion--the Oregon standard being more stern by factors of 5,000 and 35,000, respectively. (I have made no effort to check the math on those factors.)

I am confused and concerned and request a clear statement on acceptable levels of dioxin in the Columbia River (or any other water source) and whether or not the interagency disparity suggested in Enclosure 2 does in fact exist. I repeat my question and concern of March 1 regarding acceptable levels--scientific or arbitrary?

Your attention in this matter will be appreciated.

2 encl: As ~~stated above~~. Not included

Sincerely,

Chuck

C.R. "Chuck" Norris

cc: Wm. P. Hutchison, JR, Chair, EQC
Henry Lorenzen, Member, EQC

ROBERT A. SQUIRE ASSOCIATES, INC.
1515 LABELLE AVENUE
RUXTON, MARYLAND 21204
301-821-0054

March 19, 1990

Robert A. Michaels, Ph.D., Chairperson
Maine Scientific Advisory Panel
RAM TRAC Corporation
931 Northumberland Drive
Schenectady, N.Y. 12309

Dear Dr. Michaels:

I enclose a copy of the independent Pathology Working Group (PWG) Report on 2,3,7,8-Tetrachlorodibenzo-P-Dioxin conducted by Pathco, Inc. This report constitutes an objective reevaluation of the female rat liver lesions, by recognized experts, based upon current pathological criteria. I am certain the other observers of the PWG, Dr. Moch from FDA and Dr.'s Singh and Chiu from EPA, would agree with me that the review was conducted in a balanced, unbiased manner by highly qualified pathologists.

The conclusions reached by the PWG are consistent with my recent findings, as reported to you in my letter of January 8, 1990. A recalculation of potential human risk, based upon these new data, is clearly necessary. One of the most important statements in the report is that the morphological findings indicate that TCDD had only a weak oncogenic effect in female rat livers. This is in contrast to the view often expressed that TCDD is a potent animal carcinogen.

The Maine Scientific Panel should be commended for raising this issue and seeking an objective review based upon current scientific evidence. Without your request, it would have been difficult to obtain the slides for reevaluation and, more importantly, there would have been little impetus to conduct the review.

Please contact me if I may be of further assistance.

Sincerely,

Robert A. Squire

Robert A. Squire, D.V.M., Ph.D.

RAS:fts

cc:Dr. Robert Frakes

MAY 04 1990

(503) 229-5502
FAX (503) 226-1355
TDD-Nonvoice (503) 229-5497

Oregon

DEPARTMENT OF HUMAN RESOURCES

Health Division

June 11, 1991

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 12 1991
OFFICE OF THE DIRECTOR

Environmental Quality Commission
Director's Office
Dept. of Environmental Quality
811 SW 6th Avenue
Portland, Oregon 97204

Dear Commissioners:

I am writing as the spokesperson for the Oregon Health Division to recommend that the Environmental Quality Commission deny James River II, Inc. and Boise Cascade's petition to amend Oregon's ambient water quality standard for TCDD. Increasing the ambient water quality criteria for TCDD could potentially undermine the future protection of public health in the State of Oregon.

As the Public Health Toxicologist for the Oregon Health Division (OHD), I am very familiar with scientific information regarding the health effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). A substantial amount of scientific data exists to support a receptor-based mechanism of toxicity for this chemical. Empirical as well as epidemiologic information provide support that animal to man inferences, and high to low dose theoretical extrapolation models have not accurately estimated TCDD's true human toxicity.

The OHD is currently monitoring the scientific debates and developments regarding the assessment of human health effects of TCDD. We are also in the process of developing a public health policy regarding dioxin and furan contaminated media of public health concern in the State of Oregon. This policy is not expected to be finalized before the end of the year.

The OHD policy will provide information about whether or not human health effects would be expected from a certain type of dioxin or furan exposure. The policy will address pre-existing environmental contamination, and provide the mechanism to initiate appropriate public health protection activities.

The OHD approach will not be unlike other agency's "acceptable daily intake" estimates which identify a dose that is not expected to result in adverse health effects. However, such estimates are not useful for developing pollution prevention or antidegradation environmental protection policies. To be protective of public health,

BARBARA ROBERTS
Governor

1400 SW 5th Avenue
Portland, OR 97201
(503) 229-5599 Emergency
(503) 252-7978 TDD
Emergency

concentrations of contaminants in the environment of highly persistent chemicals such as dioxins and furans for which substantial evidence exists for the potential for adverse health effects should not be allowed to increase, and should not be as high as an "acceptable daily intake".

Even if pollution prevention or antidegradation is not an issue in this particular case, it still remains that many assumptions and extrapolations that are not scientifically based, and can not be validated must be made in order to utilize an "acceptable daily intake" in the calculation of an ambient water quality criteria.

In conclusion, the OHD believes that revision of Oregon's ambient water quality criteria should be scientifically based on information that can be substantiated with actual data. Such information is not presently available; therefore, increasing the water quality criteria has the potential for undermining the future protection of public health in the State of Oregon.

Sincerely,

Roseanne M. Lorenzana, DVM, PhD
Public Health Toxicologist
Environmental Toxicology Section
Office of Environment and Health Systems

RML:ab

CC: Gene Foster, DEQ
Larry Foster, Acting State Health Officer
Kathleen A. Gaffney, MD, MPH, State Health Officer Elect

LIZ VanLEEUWEN
LINN COUNTY
DISTRICT 37

REPLY TO ADDRESS INDICATED:
☑ House of Representatives
Salem, OR 97310-1347
Capitol Message 378-8772

☐ 27070 Irish Bend Loop
Halsey, Oregon 97348
Home Phone 369-2544

HOUSE OF REPRESENTATIVES
SALEM, OREGON
97310-1347

COMMITTEES
Chairman:
Intergovernmental Affairs
Vice-Chairman:
Agriculture, Forestry, and
Natural Resources
Member:
Enviroment and Energy

June 11, 1991

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 13 1991
OFFICE OF THE DIRECTOR

Mr. William P. Hutchison
Chairman, Environmental Quality Commission
811 S.W. Sixth Avenue
Portland, OR 97204

Dear Mr. Hutchison:

I am writing to support the James River Corporation and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Oregon's current water quality standard of .0013 parts per quadrillion (ppq) may be more restrictive than necessary to protect human health. Recently, the EPA approved water quality standards in other states that are 100 times less stringent than the original EPA guideline criterion which Oregon adopted. Now EPA has called for a review of the science on dioxin. However, if Oregon awaits the outcome of the EPA study before reviewing its own dioxin standard, the two pulp and paper companies listed above will be bound by state law to invest millions of dollars in what may prove to be unnecessary environmental controls. That is why we need rule-making now.

James River will spend close to $20 million in the next three years to further reduce the discharge of dioxin from its Wauna pulp and paper mill on the Columbia River. If the Wauna mill were located in Maryland, Virginia or elsewhere in the Southeast, the mill already would be in compliance with EPA-approved standards, and the expenditures would not be necessary.

<u>We must establish a scientifically-based water quality standard for dioxin that protects Oregonians, but at the same time does not overwhelmingly disadvantage Oregon industry.</u> I urge you and other commission members to accept the petition to review Oregon'' water quality standard for dioxin when you meet June 14.

Sincerely,

Liz VanLeeuwen

Liz VanLeeuwen
State Representative
District 37

GREENPEACE

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 10 1991
OFFICE OF THE DIRECTOR

7 June, 1991

Oregon Environmental Quality Commission
c/o Oregon DEQ Director's Office
811 S.W. 6th Avenue
Portland, OR 97204

Director
Oregon Department of Environmental Quality
811 S.W. 6th Avenue
Portland, OR 97204

Dear Commissioners and Director:

We understand that James River, Inc. and Boise Cascade Corp., along with several co-petitioners have asked the Commission and the DEQ to amend the state's ambient water quality standard for 2,3,7,8-TCDD from a current level 0.013 ppq to 2.3ppq.

We wish to offer comments regarding the wisdom of honoring such a petition that we hope you will make part of the public record in this decision.

INADEQUATE PUBLIC NOTICE

First we must question the lack of public notification involved in this pending decision. We have, on more than one occasion, asked to be placed on the DEQ notification list for any water quality actions the Department has pending, particularly with respect to pulp mills.

Our requests have to date been ignored, and we find that the only way to obtain a copy of a notice or a draft permit is to hear of its existence from a third party and then to call the DEQ to request a copy be sent us. Nor have we received word of final decisions regarding permits or any response to permit comments we have offered. To say that this archaic and haphazard method of public notice is deficient is an understatement. It is certainly not consistent with the mandate for public participation inherent in EPA's having delegated the water quality program to the state of Oregon.

That the petitioners themselves have the temerity to suggest they have identified all interested parties as the few listed in item 2 of the Commission Chair's notice, is absurd. A gutting of the state's water quality standard for the most potent chemical known to mankind is not something to be decided privately after consultation with just a few individuals.

Even the more narrow decision the Commission intends to make about whether or not to initiate a rulemaking that could potentially weaken the standard should have received broader notice, e.g. tribal governments, fishing interests, the state health department and those state and federal agencies charged with protecting wildlife (e.g. the U.S. Fish and Wildlife Service).

THRESHOLD MODEL CITED BY PETITIONERS AS FAVORING THE WEAKENING OF A STANDARD HAS NOT BEEN PEER REVIEWED

We remind the Commission that the much touted theory regarding a supposed threshold mechanism for 2,3,7,8-TCDD has not yet been peer reviewed. The forum in which it was first advanced, at a Banbury conference last fall, has itself become known for the controversy it created among attendees (see attachment 1). No version of the theory has yet been published in the scientific literature, and the theory has been challenged by other dioxin scientists (see attachments 2, 3).

EPA's own review of it's dioxin standard is still underway and far from finalization, and any attempt by the state of Oregon to presuppose EPA's conclusions would be ill-advised. EPA Administer William Reilly himself warned against second guessing the Agency's dioxin review, advising that in the interim state governments should go on with business as usual.

There is also new evidence coming from other quarters that tends to refute the threshold theory cited so enthusiastically by the petitioners. Abstracts for two papers to be presented at this fall's dioxin symposium are attached which argue against reliance on such a theory (see attachment 4).

Moreover, a paper by Sargent, et al published in a recent issue of <u>Carcinogenesis</u> (see attachment 5) suggests alarmingly that even non-planar PCB's can act by a mechanism identical to that of coplanar compounds such as 2,3,7,8-TCDD, and that exposure to mixtures resulted in superadditive effects. The authors further state that humans already are exposed to levels at which adverse effects would certainly be occurring. This in turn suggests why the epidemiology concerning exposure to 2,3,7,8-TCDD is at best equivocal, except in very exaggerated doses, as was indeed the case for a recently published NIOSH study (see attachment 6).

EVIDENCE CITED BY PETITIONERS REGARDING BIOCONCENTRATION IN FISH AND FISH CONSUMPTION RATES DIFFERS DRAMATICALLY FROM THAT OFFERED BY MORE CREDIBLE SOURCES

Petitioners suggest that the prevailing way of estimating bioconcentration (BCF) factors in fish used to calculate the current standard should be scrapped, and that a different (less conservative) method for estimating BCF's should be substituted. The method they suggest yields a number in the same ballpark as

the existing one. Yet there is much evidence from EPA's lab in Duluth to suggest that fish are far better at taking up and storing dioxin than the 5000 factor now in use supposes (see attachments 7, 8), and the Agency has requested funds in its 1992 budget to re-evaluate its BCF assumptions.

In fact it has been shown that even Columbia River salmon, species thought to be more protected from uptake because of their mobility and feeding patterns, are harboring levels of dioxin in their edible tissues (see attachment 9).

Patterns of human fish consumption in the Pacific Northwest also argue for a much stronger standard. EPA has long acknowledged that the average fish consumption rate of 6.5 grams per day per person assumed in the setting of its current standard seriously underestimates actual eating patterns, and this has been confirmed by surveys in several states. Moreover, work by EPA's Cleverly and McCormack indicates that Columbia River sports and subsistence fishers, Native Americans, and Asian Americans eat far more fish than the levels suggested by petitioners (see attachment 10). One wonders how petitioners could have arrived at the impossibly low figures they suggest.

Petitioners also make the illogical claim that only fish consumption from the Columbia River need be considered, irrespective of the rest of one's fish diet, as if to suppose that all other sources of fish (or food) are free from contamination.

THE STATE HAS A DUTY TO PROTECT US FROM OTHER HARM THAN JUST CANCER, AND FROM OTHER POLLUTANTS THAN JUST 2,3,7,8-TCDD

Petitioners make mention of Keenan, et al's re-evaluation of the Kociba rat study from which EPA's current acceptable daily intake is derived. They suggest that we should take heart from the fact that slightly more than half a team of 9 scientists funded by the industry should find that many of the liver lesions identified by Kociba as cancerous might only be pre-cancerous after all. A critique of this study is enclosed.

In any case, it is hardly reassuring to expect that one's liver be riddled with dioxin-induced lumps and bumps of any kind. We similarly find no comfort in the fact that women thoughout the industrialized world are passing dioxins and other organo-chlorines on to future generations through the placenta and via breast-feeding.

Studies on primates have shown that dioxins can cause profound behavioral and reproductive effects at very low doses. The petitioners ignore all non-cancerous effects in arguing for a weaker standard.

It must also be noted that 2,3,7,8-TCDD never occurs in

isolation. Discharges from the pulp and paper industry include other dioxins and furans and numerous other compounds which exhibit similar mechanisms of toxicity. The Sargent study mentioned above gives added weight to the likelihood that these compounds can act synergistically.

THE STATE HAS A DUTY TO PROTECT THE ENVIRONMENT AS WELL AS HUMAN HEALTH

Petitioners have offered no evidence to suggest that a weakened ambient water quality standard will be sufficiently protective of aquatic life or fish-eating birds and mammals.

Nor have petitioners demonstrated that a weakening of the current dioxin standard will not adversely effect bald eagle populations on the lower Columbia River, as required under the Endangered Species Act. Much evidence already exists to suggest that dioxins and other organochlorines are negatively impacting these birds. The pending listing of various wild salmon species will further increase the burden of proof necessary to justify any continued discharge of dioxin and other organochlorines.

A RELAXING OF THE DIOXIN STANDARD AS PROPOSED BY INDUSTRY WILL NOT RELIEVE THE INDUSTRY OF ANY FINANCIAL BURDEN FOR POLLUTION CONTROL

The same technologies that must be implemented by petitioners to meet the state's current dioxin standard will in any case be required in order to meet the technology-based standards already in their NPDES permits. Indeed, the longer the industry waits to install new bleaching technology, the greater will be their ultimate financial burden.

Capital costs for equipment will only be more expensive, and the money invested in stopgap measures such as chlorine-dioxide generators will only be money wasted. The U.S. industry can also be expected to lose market share in Europe as a result of its recalcitrance, as is already proving the case in Canada. Fletcher Challenge's failure to produce chlorine-free pulp for its foreign market has already cost them an estimated $ 5 million dollars in loss of sales.

THE ONLY ACCEPTABLE STANDARD FOR DIOXIN IS ZERO, AND THE STATE OF OREGON SHOULD TAKE IMMEDIATE STEPS TO ELIMINATE ALL KNOWN SOURCES

Dioxin is the most intensively studied compound in history, and will doubtless remain the darling of the scientific community for years to come. Even so we still do not know its precise toxicity to humans, and given the degree to which we are all already contaminated with dioxin and dioxin-like compounds, we probably never will. There is simply no such thing as a control group to serve as a baseline.

But what we do know is serious enough to make moot any further quibbling about precisely how much is too much dioxin. What we know is more than enough to justify elimination of all known sources.

We urge the Department and the Commission to deny the petition to set a weaker dioxin standard, and instead use your limited resources to moving the pulp and paper industry into chlorine-free technology. The technologies exist, and only await implementation.

Sincerely,

Shelley Stewart

Shelley Stewart
U.S. Pulp/Paper Project

***

Please note that these comments are printed on chlorine-free paper imported from Europe. No North American manufacturer has yet been willing to produce chlorine-free bleached office or printing paper.

Attachment 1

UNIVERSITY OF MARYLAND AT BALTIMORE

The University Program In Toxicology
660 West Redwood Street
Howard Hall, Room 544
Baltimore, Maryland 21201-1596
(301) 328-8196

January 29, 1991

Dr. Jan Witkowski
Director
Banbury Center
Cold Spring Harbor Laboratory
P O Box 534
Cold Spring Harbor, NY 11724

Dear Dr. Witkowski:

I was a participant in the recent Banbury Conference on "Biological Basis for Risk Assessment of Dioxins and Related Compounds" held at the Banbury Center in October 1990. I am writing you becuase I have just been informed of a very disturbing result of that conference, a press release sent out by a public relations firm along with statements by Drs Scheuplein, van der Heiden, and Gallo purporting to represent the "consensus" views of the participants at that conference with espect to regulatory conclusions related to risk assessment of dioxins. I only learned of this press release from a reporter who called me last week (Marguerite Holloway of Scientific American).

This press release, copy enclosed, was never shown to me or to most of the participants in the conference, as far as I know. Thus, in terms of process alone, it should not be represented as a "consensus" document. Morover, its contents do not accurately reflect the views of all participants, or even a consensus of those views, as best I can determine. I resent the circulation of this press release as reflecting the views of a meeting in which I was a participant, and I feel that my name attached to it somehow implies my agreement with it.

I am in fact rather astounded by such a product from a Banbury Conference. While it was rather obvious to some of us that the organizers, and some of the sponsors, of this confernece had some trans-scientific objectives in mind related to regulations concerning dioxin, I had expected that the Banbury Center would be able to keep these motives under control. The press releases and statements imply that a major focus of the conference was a discussion of the regulatory risk assessments that have been applied to the dioxins; this was not the focus of this meeting. I agreed to participate based upon my previously held high regard for Banbury and Cold Spring Harbor. I did not expect to be manipulated by industry and government spokespeople

(who are not dioxin researchers, incidentally) to be made into a supporter of their political views on dioxins and risk assessment. This is particularly annoying to me because I was invited to present the main conference paper on the topic of the scientific basis for dioxin risk assessment. In this paper, I have attempted to present the complexity of integrating the basic molecular biology of dioxins into a receptor-based model. I do not feel that the state of knowledge on this complex topic can be reduced to a simplistic press release.

The preparation and release of these documents by Drs Scheuplein, van der Heijden, Carlo, and Gallo, with the assistance of a public relations firm, discredits all of us. It challenges the precious institution of free scientific discussion, epitomized by such places as Banbury, Dahlem, and the Gordon conferences. I hope you believe that I would be just as angry if this action had been taken by an environmental group. I trust you will take aciton to dissociate Banbury from this attempt to manipulate science and scientists. Because these people have acted without consulting the rest of us, and because I have heard about this only through the press, I am with great regret also sending this letter to the persons shown under my signature, as well as to my colleagues at the conference, an action not taken by these people.

Yours sincerely,

Ellen K Silbergeld

Ellen Silbergeld, PhD
Visiting Professor of Toxicology and
Adjunct Professor of Pharmacology
and Experimental Therapeutics

cc: Leslie Roberts, Science
Marguerite Holloway, Scientific American
Cristine Russell, Washington Post
Chris Joyce, New Scientist
Judy Randall, The Economist
Betty Mushak, NIEHS
William Farland, EPA

attendees, Banbury Conference on Dioxins

History Lessons

Warfare analysts offer some disturbing—and hopeful—news

Political leaders always claim to be steering us by the lights of history toward a peaceful future. But what does a comprehensive analysis of our past actually reveal about our present course? A pessimist could conclude that our leaders are completely misreading—or misrepresenting—history. An optimist could find hope that warfare might become obsolete anyway—if the tentative spread of democracy worldwide continues.

These conclusions are both supported by the Correlates of War project, a computerized storehouse of information on 118 wars (defined as conflicts leading to at least 1,000 deaths) and more than 1,000 lesser disputes from the early 1800s to the present. Researchers at the University of Michigan created the data base in the 1970s to find statistical associations between warfare and various economic, political and social factors.

The data offer no support for the bromide "peace through strength," according to J. David Singer, a political scientist at Ann Arbor who oversees the Correlates project. A buildup of military armaments, far from deterring war, is one of the most frequent precursors of it. At the very least, Singer says, such a finding suggests that the U.S. policy of supplying arms to nations in an unstable region—such as the Middle East—is seriously flawed.

There is also no evidence that alliances help to keep the peace. In fact, a nation's participation in one or more alliances increases its risk of warfare, Singer says, particularly against its allies. History even casts doubt on the argument—used by the U.S. to justify both its current war against Iraq and its past one against Vietnam—that allowing aggression to proceed unchecked always leads to more aggression. Although Hitler's Europe certainly provides an important counterexample, Correlates of War data yielded little statistical correlation between warfare in a given region and prior unchecked aggression, Singer says.

A somewhat more hopeful finding

A Press Release on Dioxin Sets the Record Wrong

When the Chlorine Institute shopped around for a place to hold a scientific conference, they did not want just any host. "We were looking for an organization that was squeaky clean, that would not in any way, shape or form be questioned about the conference," says Robert G. Smerko, president of the Washington, D.C.-based institute, which is supported by some 170 chemical, paper and other manufacturers.

Smerko seemed to have met his requirements when he finally landed Cold Spring Harbor Laboratory. Last October the laboratory's respected Banbury Center held a conference—jointly sponsored by the Chlorine Institute and the Environmental Protection Agency—on the toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, or TCDD. That chlorinated compound achieved notoriety during the Vietnam War, when it was identified as a contaminant of the defoliant Agent Orange. It remains controversial because it is found in some commercial herbicides and is produced in other chemical processes, such as paper bleaching.

Cold Spring Harbor Laboratory may have been squeaky clean, but the conference apparently was not. And the outcome of that meeting—attended by 38 of the world's dioxin experts, few of whom say they knew it was industry sponsored—is every bit as controversial as the substance that was the topic of discussion.

The issue is a press release sent out at the conclusion of the meeting by the Chlorine Institute's public relations firm, Daniel J. Edelman, Inc. It announced that the experts had agreed on a model for the toxicity of dioxin that "allows for the presence of a substance in the environment, with no risk experienced below a certain level of exposure." The release said that the scientists had rejected a linear exposure model, in which any level of exposure would have a biological effect, in favor of a receptor-based model that implies a threshold level. (This part of the release was approved by Cold Spring Harbor Laboratory, says the Banbury Center's director, Jan A. Witkowski—although he now says Edelman made several changes after he saw it.)

Such a consensus, of course, would have implications for setting permissible levels of the substance in the environment. But those at the conference insist that no such agreement was reached. "There was no consensus in terms of risk assessment," says George W. Lucier of the National Institute of Environmental Health Sciences. In addition, none of the scientists saw the press release, although their names accompanied it. "We were being used, clearly, and that's unfortunate," declares Arnold J. Schecter, professor of preventive medicine at the State University of New York at Binghamton. "Political layering is not particularly good, especially when it is unbeknownst," Lucier adds.

Few of the participants seem to dispute that the receptor-based mechanism of dioxin is relevant to human exposure. Nor did they before the conference, observes Alan P. Poland of the University of Wisconsin at Madison, who discovered the receptor in 1976. "The basic tenets were all known since 1981 or 1982," Poland says. But Lucier notes that now "we are at the point where we can reevaluate the linear model."

Indeed, the EPA intends to explore the question of whether there is a threshold response. The agency will investigate the receptor-based model with Michael A. Gallo, one of the conference organizers and a professor of toxicology at the University of Medicine and Dentistry of New Jersey–Robert Wood Johnson Medical School. But Gallo and others agree that discussion of thresholds in a regulatory context may be premature. At the conference, "some regulators got real excited by back-of-the-envelope calculations" and thought dioxin standards could be eased, says Linda S. Birnbaum, director of the EPA's environmental toxicology division. "Clearly, we don't know that."

Although many of the Banbury attendees were the last to know about the consensus they reportedly reached, news about the conference traveled quickly in political circles. At a recent hearing on dioxin standards in Alabama, expert witness for the pulp and paper industry Russell E. Keenan invoked the Banbury results in his testimony. "There was general agreement among the attending scientists that dioxin is much less toxic to humans than originally believed," Keenan claimed. Obviously, "it is not useless to tout Banbury results if you have a political ax to grind," comments Cate Jenkins, a chemist in the EPA's hazardous waste division. —*Marguerite Holloway*

Attachment 2

To: Dioxin Nerds, et al.
From: Tom Webster, CBNS Queens College, Flushing NY 11367
Date: 3/14/91
RE: Banbury Dioxin Model, Part 1 A Critique

A recent two article series in Science(1) covered the infamous Banbury conference on dioxin toxicity. The second article addresses the scandal aspect of the story, particularly the involvement of the Chlorine Institute. The first article (attached) addresses some of the scientific aspects, but does so in what I consider a rather opaque fashion.

In particular, the article shows an S-shaped graph which appears to show why dioxin has a threshold. Science indicates, using the graph, that "responses to dioxin increase slowly at first but then shoot up after passing a critical concentration."

However, all is not as simple as it seems at first. Since there has been some confusion regarding this business, I will address the graph in this memo.

(1) Background: The Ah receptor

First, a bit of background. 2,3,7,8-TCDD and other dioxin-like compounds (PCDFs, co-planar PCBs, chlorinated naphthalenes, etc.) are generally thought to cause toxicity through a receptor mediated mechanism. This receptor also binds aromatic hydrocarbons such as 3-methylcholanthrene and other non-halogenated aromatic hydrocarbons; hence it is termed the Ah receptor.

The Ah receptor is a protein which is normally found in the fluid (cytosol) of the cell (There is some controversy here; some people think it is found solely in the nucleus). Only certain molecules ("ligands") with certain properties (size ,shape, etc.) fit it, like a key into a lock. 2,3,7,8-TCDD has the best fit of any known compound. When this occurs, the receptor-ligand complex changes shape and moves into the nucleus. The change in shape helps it to recognize and bind to certain sequences in the DNA. This in turn causes the transcription and translation of adjacent DNA into protein. (This is quite similar to the mechanism of steroid hormones.)

The most well understood effect is the production an enzyme called P450IA1 which makes aromatic hydrocarbons more water soluble--and therefore easier to excrete--by adding hydoxyl (-OH) groups. One measure of this enzyme activity is called aryl hydrocarbon hydroxylase (AHH).

Many of the types of toxicity associated with dioxin-like compounds correlate with binding to the Ah receptor or AHH activity (also with EROD, a related enzyme activity). This provides good evidence that dioxin toxicity is mediated by the Ah receptor, i.e., binding to Ah is the first (but not only) step. It also provides both a theoretical justification and a measurement technique for 2,3,7,8-TCDD equivalents. If all dioxin-like compounds act through the receptor, then the potency of a given compound can be rated against 2,3,7,8-TCDD by their relative ability to bind Ah and induce AHH or EROD activity.

Nevertheless, other experiments show that many toxic effects are probably not directly caused by enzyme induction. Hence, other genes are probably being turned on by the Ah receptor as

well. The nature of these other genes and the biochemical mechanism of many toxic responses is not so well understood. I'll discuss some of this in a future memo.

(2) Receptor Kinetics

If the toxicity of dioxin-like compounds is mediated by the Ah receptor, clearly we need to understand this first step. Receptor-ligand relationships are mathematically described by the Michaelis-Menten equation, a standard tool for describing enzymes. This is schematically described as:

$$L + R \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} LR \qquad (1)$$

where "R" is the unbound receptor, "L" is the ligand (molecule binding to the receptor) and "LR" is the receptor-ligand complex. k_1 and k_{-1} are, respectively, the association and dissociation rate constants. At equilibrium, we find

$$K_D = [L][R]/[LR] \qquad (2)$$

$$K_D = k_{-1}/k_1$$

where the items in the brackets "[ ]" are concentrations and K_D is the dissociation equilibrium constant. The constant K_D tells us, in an inverse way, about the strength of the binding between the ligand and the receptor. A small K_D means the binding is strong, and thus the receptor-ligand complex is less likely to dissociate. Conversely, a large K_D means that the receptor-ligand binding is weak.

Equation (2) can be solved in terms of the amount of occupied (bound) receptor:

$$[LR] = [L]*R0/(K_D + [L]) \qquad (3)$$

where R0 is the total amount of receptor, bound and unbound.

Equation (3) gives the relationship between the amount of 2,3,7,8-TCDD (or other ligand) and the amount of bound receptor (LR). Remember that the toxic activity of 2,3,7,8-TCDD (and other dioxin-like compounds) is thought to be associated with the concentration of dioxin-receptor complexes. We could infer a dose-response curve with two additional pieces of information: 1) the relationship between external dose (e.g., amount of exposure per day) and [L] and ii) the relationship between [LR] and toxicity.

Note that when the concentration of 2,3,7,8-TCDD is significantly less than K_D, the relationship is linear:

$$[LR] = [L]*R0/K_D \qquad \text{for } [L] \ll K_D \qquad (4)$$

Indeed, this equation indicates that even one molecule of 2,3,7,8-TCDD could bind to the receptor, indicating that there may be no theoretical threshold for activity. The slope of the curve is governed by the number of Ah receptors (R0) and the dissociation constant (K_D). Since 2,3,7,8-TCDD has a very small K_D compared to

other dioxin-like compounds, it binds tightly, and has a large slope.

For a high concentration of 2,3,7,8-TCDD, the curve saturates. One can't produce more receptor-dioxin complexes than there are receptors:

$$[LR] = R0 \qquad \text{for } [L] >> K_D \qquad (5)$$

(We'll ignore for now so-called "supermaximal" induction as well as circumstances which alter the number of receptors).

Finally, note that when the concentration of a compound equals its K_D, the number of bound receptors is equal to one-half the total number of receptors.

$$[LR] = R0/2 \qquad \text{for } [L] = K_D \qquad (6)$$

(3) Analysis of the Science graph

When equation (3) is plotted on normal graph paper it looks like my Figure 1, linear at low levels of 2,3,7,8-TCDD--the concentration of receptor-ligand complexes directly proportional to the concentration of ligand--and plateauing--at 100% bound receptor--at high levels of 2,3,7,8-TCDD.

When the same equation is replotted using the logarithm of the concentration of 2,3,7,8-TCDD, the graph looks like Figure 2, the same S-shaped curve seen in Science. Note that the horizontal axis in the Science graph gives concentration of 2,3,7,8-TCDD increasing by a factor of ten at each step; this is equivalent to using logarithms.

Finally, 50% of the receptors are shown as occupied in the Science graph when the concentration of 2,3,7,8-TCDD equals about 10^{-9} (Although not given, the units are undoubtably the standard moles per liter). This is the old K_D value for 2,3,7,8-TCDD. Actually, recent experiments indicate that the K_D is probably even smaller, on the order of 10^{-12} to 10^{-11} moles per liter. This means that 2,3,7,8-TCDD binds Ah more tightly than previously thought.

(4) Discussion

As a result, it should be clear that the graph in Science does not by itself indicate a threshold. The S-shape of the curve is an artifact of the graphing technique. Plotted on linear axes, the equation for ligand-receptor interaction indicates that the number of occupied receptors rises linearly from zero. In other words, this response should theoretically be linear at low doses with no threshold.

What then is really going on? Clearly, there must be more to the story. I'll be writing another memo on this, but let me give a few hints.

i) There may be other compounds inside the cell which bind to Ah, albeit with less affinity, complicating the picture.

ii) Binding to the receptor is just the first step. The other steps, binding to DNA, generation of protein, action of protein, etc., might not be linear. Hence, even though the first step might be linear, the final toxic response might not be.

ii) Binding to the receptor is reversible. However, the long half-life of dioxin-like compounds and the background exposure to them diminishes the strength of this argument.

iv) The Birnbaum[2] memo makes the following assumptions: 1) all toxicity is mediated by the Ah receptor binding; 2) induction of P450IA1 (AHH activity) is the most sensitive response of this system; 3) no effect occurs until one can measure an increase in enzyme activity. This defines a "practical" threshold that one can use to determine no-effect levels, etc.

In response to this last argument (briefly), enzyme induction may be the most sensitive response, but we don't really know. Also, lack of measurable activity doesn't necessarily mean no activity. Ability to measure a response is determined by many things including the sensitivity of the assay, the statistical power of the experiment, etc. In addition, 2,3,7,8-TCDD has a very long lifetime in the human body. Finally, the already existing body-burden of dioxin-like compounds in humans and other animals needs to be taken into consideration when examining such threshold models.

References

(1) Roberts, L. (1991a). Dioxin Risks Revisited. Science 251: 624-626. February 8.

Roberts, L. (1991b). Flap Erupts Over Dioxin Meeting. Science 251: 866-867. February 22.

(2) Birnbaum, L. (1990). Memo to E. Bretthauer (EPA-ORD) regarding Consensus at Banbury Dioxin Conference. October 31.

Figure 1 : Linear Plot

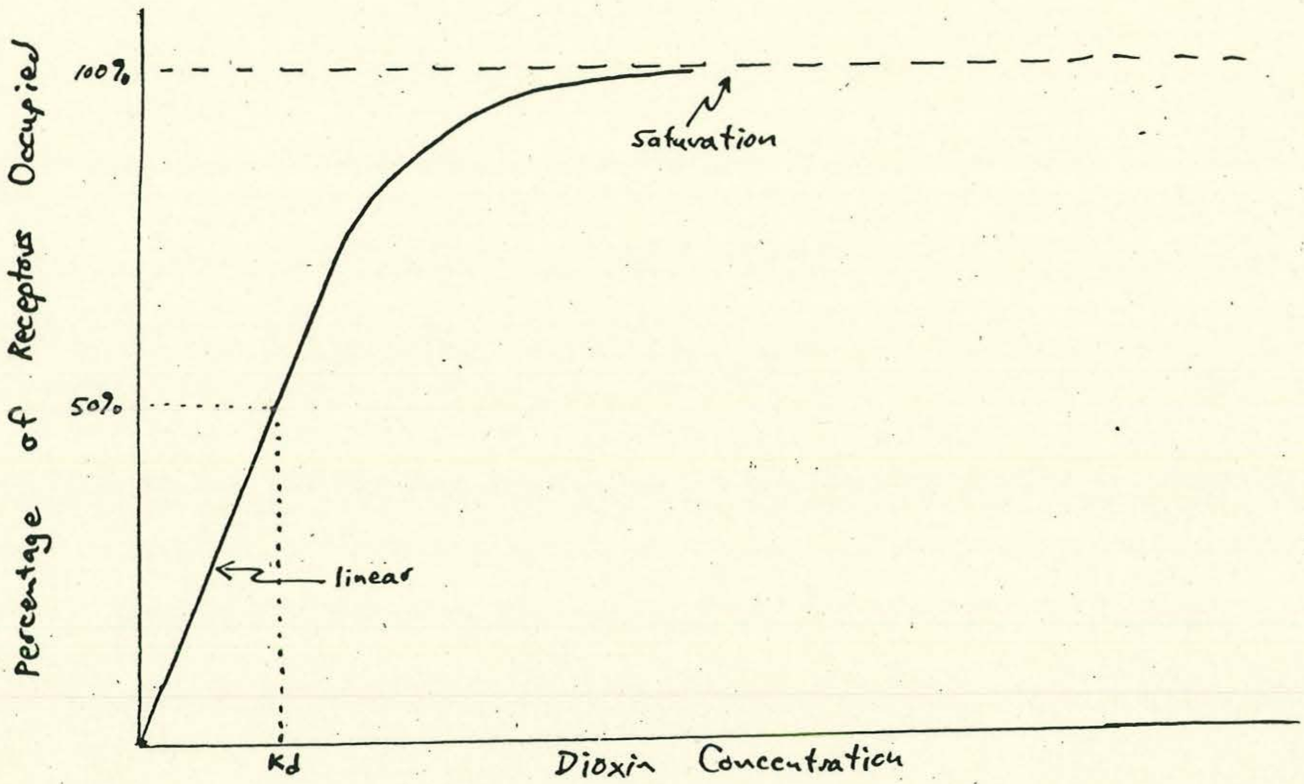
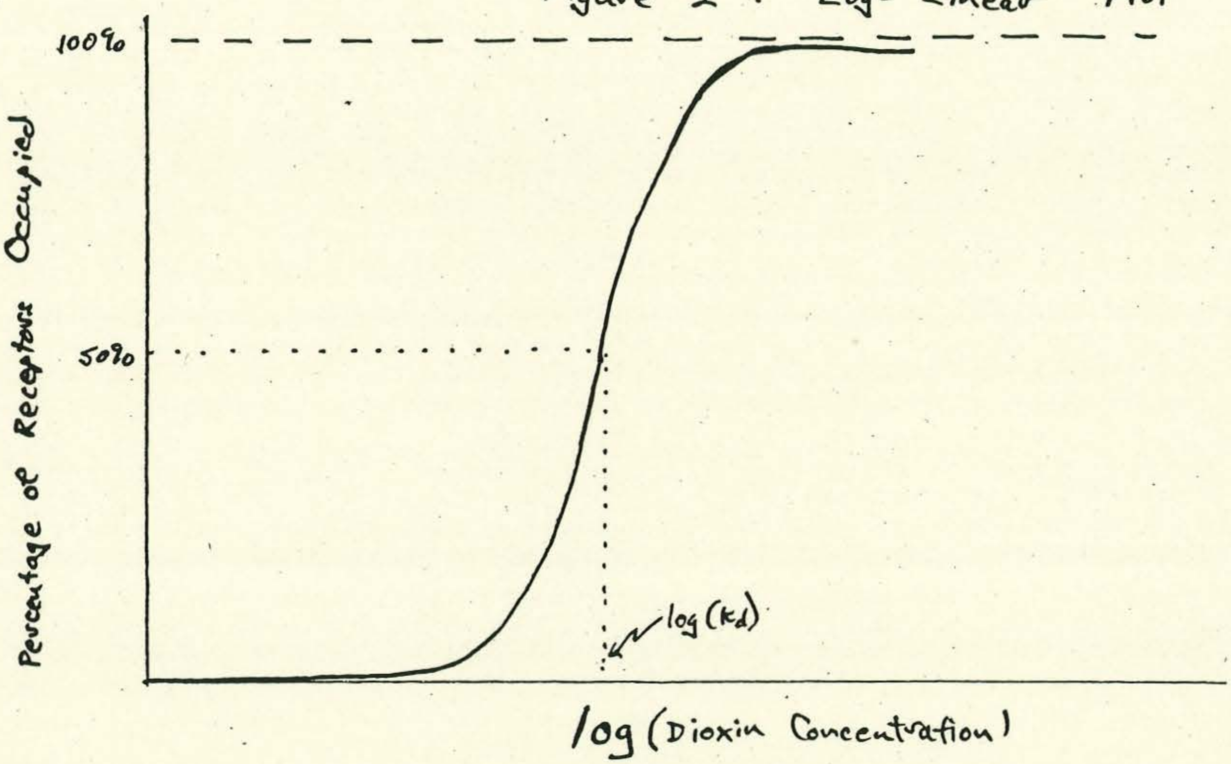


Figure 2 : Log-Linear Plot



Attachment 3

Downgrading Dioxin's Cancer Risk: Where's the Science?

By Tom Webster

Some of the concerns about the toxicity of the wood preservative pentachlorophenol have resulted because of its contamination with dioxins and furans. During manufacturing, pentachlorophenol is contaminated with several members of this family of compounds, with hexadioxins being most abundant.[1] 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD, commonly called dioxin), the most toxic dioxin, has been found in commercial pentachlorophenol formulations[1] and is often found in the soil and waste products from wood treatment plants.[2,3] This article discusses recent attempts to weaken regulatory standards for 2,3,7,8-TCDD.

-Ed.

The pulp and paper industry and certain consultants are once again attempting to relax the regulatory standards for dioxin. The consulting company ChemRisk has proposed an increase in the so-called "acceptable" dose of 2,3,7,8-TCDD by a factor as large as one thousand.[4,5] Many states are currently setting water quality standards for dioxin,[6] a regulation that depends on the "acceptable" dose.[7]

Despite assertions that the proposed change is based on new scientific evidence showing that dioxin "may be far less dangerous than previously imagined,"[8] the new information is actually a reinterpretation of the 1978 rat experiment that forms the basis for the U.S. Environmental Protection Agency's (EPA's) current estimate of dioxin's ability to cause cancer. In this reanalysis, a group of pathologists voted, according to a new set of guidelines, on the classification of tumors found in the test animals.[9]

However, if all other assumptions are left unchanged, recounting the tumors according to the revised rules [10] would result in an "acceptable" daily dioxin dose that is only two to three times larger than the current estimate. This is an insignificant change given the uncertainty in risk assessment. 2,3,7,8-TCDD is currently rated as millions of times more carcinogenic than many other compounds.

> *"Indeed, new scientific evidence on the amount of fish people consume, the degree to which dioxin is concentrated in fish, and the toxic equivalencies of other dioxins and furans supports stronger, not weaker, dioxin standards."*

The much larger change proposed by ChemRisk was derived by altering a number of other assumptions without proper justification. Indeed, new scientific evidence on the amount of fish people consume, the degree to which dioxin is concentrated in fish, and the toxic equivalencies of other dioxins and furans (JPR 10(2):23-27) supports stronger, not weaker, dioxin standards.[7]

Human Health Effects Controversy

This episode is neither the first nor last attempt to downgrade or dismiss the toxicity of dioxin. Perhaps the best known and continuing controversy surrounds Agent Orange. 2,3,7,8-TCDD was a contaminant in the herbicide 2,4,5-T, a component of Agent Orange, which was sprayed in parts of the United States as well as in Vietnam.

Despite the claim by some that the only long-term effect of dioxin on humans is chloracne, a serious skin disorder, the compound has been hypothesized to cause a number of other health effects in humans. Several recent epidemiological studies support this position. The Agent Orange Scientific Task Force[11] linked phenoxyacetic acid herbicides (such as Agent Orange) and their dioxin contaminants to a number of diseases including certain cancers. Dioxin's close chemical relatives PCBs and dibenzofurans may cause birth defects and learning/behavioral changes in the children of exposed women.[12,13] Certain key earlier studies that found no increase in cancer in chemical workers exposed to dioxin are faulty or possibly even fraudulent,[14,15] a charge now under investigation by EPA. Recent studies of German and American chemical workers exposed to dioxin found statistically significant increases in cancer rates.[16,17]

EPA rates cancer-causing compounds qualitatively (how good is the evidence for cancer causation in humans?) and quantitatively (how much cancer is caused by a given dose?). As a result of the recent epidemiology, it is likely that EPA will upgrade the qualitative standing of 2,3,7,8-TCDD to a Class B1 probable human carcinogen (limited human data and sufficient animal data),[18] an action with important regulatory ramifications.[19]

Constructing an "Acceptable" Daily Intake of Dioxin

EPA typically assumes that cancer-causing agents have no threshold, meaning that any amount of exposure can cause damage. Some people argue that there is no acceptable exposure for dioxin, an unintentional chemical by-product with no use or benefit, and that the goal should be zero exposure to this compound. EPA, however, has stated that some level of risk is "acceptable," a decision that is a matter of policy, not science. In setting ambi-

---

Tom Webster is a researcher with the Center for the Biology of Natural Systems (CBNS) of Queens College. He is currently working on a project for Greenpeace concerning chlorinated compounds.

CBNS; Queens College; City University of New York; Flushing, NY 11367; (718) 670-4180.

ent water quality standards, EPA often uses an acceptable lifetime risk of cancer of one case in a million (10^{-6}).

Based on this policy, the acceptable daily dose of a chemical is established by dividing the acceptable risk level by the "potency" of the compound. EPA calls such values risk specific doses (RsD). The potency is the quantitative estimate of the strength of the carcinogen. The more potent a chemical is, the smaller the dose that is required to pose a certain level of risk.

For dioxin, as with the overwhelming majority of toxic chemicals, there are insufficient human data to establish a potency. (The new study cancer among chemical workers[17] may, however, prove sufficient.) Consequently, dioxin's potency is based on laboratory experiments with animals. The current estimate for 2,3,7,8-TCDD[1] was based on a 1978 experiment on female rats, the most sensitive sex and species tested.[20]

EPA projected from the number of tumors found in animals at experimental doses to effects at the lower doses that people might encounter using a standard mathematical technique, the linear multistage model. This model assumes that the carcinogen has no threshold and that effects at low doses are linear, i.e., directly proportional to dose.

Finally, the potency in humans is estimated by multiplying the animal value by a "scaling factor." This adjusts for differences between the experimental animal and humans. For dioxin, EPA employed the default "surface area" scaling factor, since many differences between animals and humans (e.g., metabolism) depend on relative surface area.[1,21]

The 1988 Attempt to Downgrade Dioxin

In 1988, a proposal was made by EPA's Dioxin Workgroup to decrease the carcinogenic potency of 2,3,7,8-TCDD by a factor of sixteen. The Workgroup argued that dioxin might cause cancer through several mechanisms rather than being simply a complete carcinogen (the basis of the 1985 estimate). It might, therefore, be a less potent cancer-causing agent than previously thought. The Workgroup concluded that there was "no definitive scientific basis" for determining how much less potent dioxin might be.[22]

They noted that other agencies (the Center for Disease Control, the Food and Drug Administration) as well as other countries have less stringent "acceptable" levels of dioxin. They argued that "for strictly policy purposes, there is great benefit in federal agencies adopting consistent positions in the absence of compelling scientific information" and that an order of magnitude (factor of ten) estimate conveys the uncertainty involved. Based on this somewhat arbitrary logic, the Working Group recommended increasing the "acceptable" level (RsD) from 0.006 picograms (one picogram is one trillionth of a gram) per kilogram per day (pg/kg/day) to 0.1 pg/kg/day.

In their review of this proposal, EPA's Science Advisory Panel acknowledged some criticisms of the application of the linear multistage model to dioxin. However, they rejected the Workgroup's proposal, stating that "there is no reason to necessarily believe that a new mechanism model would lead to a relaxation of the risk specific dose for 2,3,7,8-TCDD induced cancer...The Panel therefore finds no scientific basis at this time for the proposed change."[23]

Acceptable Doses of Dioxin: ChemRisk versus EPA

At about the same time that the Science Advisory Panel was rejecting the 1988 case for increasing the "acceptable" risk of dioxin by a factor of sixteen, ChemRisk's new proposal supported an increase by as much as a factor of one thousand.[4,5] Three main factors are used by ChemRisk and EPA in their respective dioxin computations (see Table 1):

"ChemRisk selects an "acceptable" risk of 10^{-5}. Since the level of acceptable risk is a question of policy, not science, ChemRisk's choice of this factor is arbitrary."

• **"Acceptable" Lifetime Cancer Risk:** For water quality standards, EPA recommends an "acceptable" lifetime cancer risk ranging from one in ten million (10^{-7}) to one in one hundred thousand (10^{-5}). However, one in one million (10^{-6}) is both the default and most commonly used value.[6,24] ChemRisk selects an "acceptable" risk of 10^{-5}. Since the level of acceptable risk is a question of policy, not science, ChemRisk's choice of this factor is arbitrary.

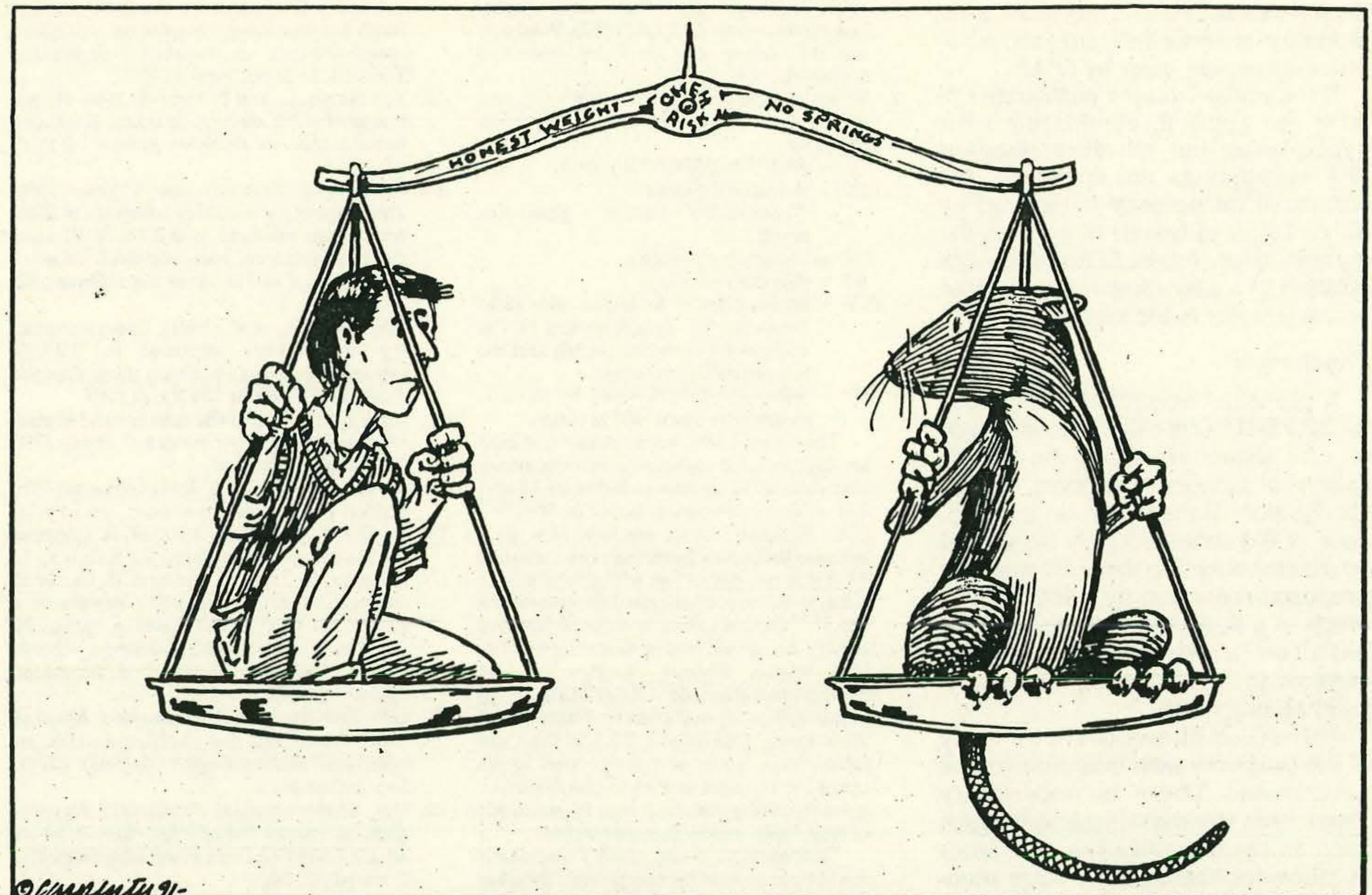
• **Interspecies Scaling Factor:** ChemRisk uses a body weight scaling factor to extrapolate from rats to humans. Since dose is commonly expressed as an amount per kilogram of body weight, ChemRisk's approach assumes that humans and rats are equally sensitive. EPA's surface area scaling factor assumes that humans will be more sensitive than rats per unit body weight by a

Table 1
Constructing an "Acceptable" Dose of Dioxin

	USEPA[1]	ChemRisk[4,5]	Factor[a]
1. Cancer potency in rats $(mg/kg/day)^{-1}$ (95% upper-bound estimate with linear multi-stage model)	29000	1500	19.3[b]
2. Scaling factor, rat to human (surface area)	5.38 (body weight)	1	5.38
3. "Acceptable" Lifetime Cancer Risk	10^{-6}[c]	10^{-5}	10
4. Risk-Specific Dose of 2,3,7,8-TCDD (pg/kg/day)	0.006[d]	6.74	1040

a. Factor by which ChemRisk is less stringent.
b. This factor would be 2-3 if the only change was the reclassification of tumors.
c. One in a million is a default and common value for water quality standards.[6,25]
d. An earlier draft by ChemRisk proposed an acceptable dose of 2.5 pg/kg/day.[4]

Note: RsD = (acceptable risk)/(rat potency * scaling factor)



Jim Carpenter

factor of about five.

ChemRisk argues that the use of the dose per body weight scaling factor is "more biologically relevant" because 2,3,7,8-TCDD is itself the active compound rather than any metabolite as is common with many carcinogens. EPA has disagreed with this line of reasoning in general,[25] but the case against body weight scaling is even stronger for 2,3,7,8-TCDD.

Since EPA's 1985 dioxin potency estimate, 2,3,7,8-TCDD half-life in humans has been determined to be 5-10 years, much longer than previously thought. In rats, the half-life of 2,3,7,8-TCDD is only about one month. Taking into account differences in tissue distribution, a scientist with EPA's Carcinogen Assessment Group estimated a scaling factor for the liver of as high as 37, much higher than ChemRisk's body weight scaling factor of one as well as EPA's surface area scaling factor of 5.38.[25] ChemRisk's reliance on the body weight scaling factor is not supportable.

• **Cancer Potency In Rats:** EPA's 1985 computation of dioxin potency was based on the occurrence in the 1978 rat study of carcinomas (cancerous tumors) and neoplastic nodules (lesions which may develop into cancerous tumors) in the liver, as well as tumors in other organs where the increase over control animals was statistically significant. In 1986, researchers proposed dividing neoplastic nodules into two groups: hepatocellular hyperplasia (a noncancerous proliferation of liver cells caused by toxicity) and hepatocellular adenomas (benign liver tumors).[10] This change has been questioned by some toxicologists.[26]

ChemRisk used the new classification system to argue in 1989 that the EPA's 1985 analysis was incorrect.[4]

At about the same time, Dr. Squire, a consulting pathologist involved in the original analysis of the female rat cancer data, was asked to re-examine the in conjunction with the setting of a water quality standard for Maine.[27] (Squire was involved earlier in a controversy over dioxin contaminants of pentachlorophenol: see article beginning on p. 4). After an initial review of the rat data, Dr. Squire helped convene a group of pathologists to re-examine the liver tissue slides from the experiment using the new classification system.

During this re-evaluation, in which "consensus" was defined as agreement by four out of seven pathologists (not all votes were unanimous), the group identified fewer carcinomas as well as fewer total tumors (carcinomas plus adenomas) than EPA's earlier analyses. The group concluded that because "the tumors were predominantly benign and usually associated with lesions of hepatic [liver] toxicity" the rat study demonstrated "a weak oncogenic [cancer-causing] effect of TCDD."[9] The implication of this controversial conclusion is that liver toxicity somehow caused or magnified the carcinogenic response.

ChemRisk used these results to calculate a new potency factor for 2,3,7,8-TCDD in rats, but counted only carcinomas in the liver (the primary target organ in this animal). They ignored carcinomas in other tissues as well as all adenomas, benign tumors that may progress into carcinomas. Both omissions are contrary to EPA guidelines for carcinogen risk assessment.[21]

ChemRisk also failed to adjust for early mortality of some test animals, another correction used by EPA.[1]

If the revised tumor pathology criteria are applied, eliminating liver hyperplasias, but all other standard EPA assumptions are employed, the calculated rat potency is reduced by only a factor of two to three from the current value. Again, ChemRisk's calculation of a new dioxin carcinogenic potency factor is indefensible.

Conclusion

A proposed acceptable daily dose for 2,3,7,8-TCDD is claimed to be based on new science regarding the classification of tumors. However, if this change alone is made, the "acceptable" dose of dioxin would only be altered by a factor of two to three. ChemRisk's proposed reduction by a factor of as much as a thousand is fundamentally based on scientifically indefensible changes in a number of other unrelated assumptions.

This series of events shows many of the problems with quantitative risk assessment. There is uncertainty about even the most basic questions such as the classification of tumors in laboratory animals. A large number of assumptions are required, each of which must be independently justified. Because of the uncertainty and the number of assumptions, it may be possible, in the absence of checks and balances, to construct nearly any result. ■

References and Notes

1. U.S. Environmental Protection Agency. 1985. *Health assessment document for polychlorinated dibenzo-p-dioxins.* EPA/600/8-84/014F. Washington, D.C.: Office of Health and Environmental Assessment.
2. U.S. Environmental Protection Agency. 1987. National dioxin study. EPA/530-SW-87-025. Washington, D.C.: Office of Solid Waste and Emergency Response.
3. State Water Resources Control Board. 1988. Chlorinated dibenzo-p-dioxin and dibenzofuran contamination in California from chlorophenol wood preservative use. Report 88-5WQ. Sacramento, CA: Division of Water Quality.
4. Keenan, R., R. Wenning, A. Parsons. 1989. Sensitivity analysis for dioxin risk assessment and implications for determining acceptable daily exposure: Executive summary. Portland, ME.: ChemRisk, October 20.
5. Keenan, R. Letter to Dr. R. Loehr, Chair, Executive Committee, Science Advisory Board, U.S. Environmental Protection Agency. March 20, 1990.
6. U.S. Environmental Protection Agency. 1990. *Tracking report: State water quality criteria for dioxin (2,3,7,8-TCDD).* Washington, D.C.: Office of Water Regulations and Standards. May.
7. Where people can consume both fish and water, the water quality standard is computed as:

   C = (RsD*BW)/((FC*BCF)+WC)

   RsD = risk specific dose ("acceptable" dose at a given risk level)

   BW = human body weight

   FC = fish consumption

   BCF = bioconcentration factor, the ratio between the concentration of the compound found in the fish and the concentration in water.

   WC = water consumption rate by humans (negligible when BCF is large).

   The current EPA water quality standard for 2,3,7,8-TCDD assumes a fish consumption rate of 6.5 grams per day (0.23 oz.) and a bioconcentration factor of 5000.[6,24] Both of these factors are low. New data indicate that sport fishermen can consume 30 grams per day of fish while subsistence fishermen may consume 140 grams per day.[24,28] These values are about five and twenty two times higher than the current EPA value. Recent studies of the bioconcentration of 2,3,7,8-TCDD have found values from 39,000 to 140,000.[29,30] Thus, even if the RsD for 2,3,7,8-TCDD was raised by a factor of two to three to account for changes in tumor classification, a water quality standard tens to hundreds of time lower could be constructed.

   Furthermore, water quality standards are set compound by compound, ignoring the fact that compounds closely related to 2,3,7,8-TCDD—such as 2,3,7,8-tetrachlorodibenzofuran, also emitted by pulp and paper mills that bleach with chlorine—are added together in other regulatory contexts, after adjusting for relative potency using the 2,3,7,8-TCDD equivalence methodology.
8. Gladwell, M. 1990. Scientists temper views on cancer-causing potential of dioxin. *Washington Post*, May 31, p. A3.
9. Sauer, R. and PATHCO, Inc. 1990. Pathology Working Group 2,3,7,8-tetrachlorodibenzo-p-dioxin in Sprague-Dawley Rats. 10075 Tyler Place #16, Ijamsville, MD 21754. March 13.
10. Maronpot, R., C. Montgomery, G. Boorman, and E. McConnell 1986. National Toxicology Program nomenclature for hepatoproliferative lesions of rats. *Toxicologic Pathology* 14(2): 263-273.
11. Agent Orange Scientific Task Force. 1990. *Human health effects associated with exposure to herbicides and/or their associated contaminants - chlorinated dioxins.* Washington, D.C.: National Veterans Legal Services Project.
12. Rogan, W., B. Gladen, C. Hsu, Y. Chen, and H. Ko. 1990. Yucheng: Studies in children. Presented at Dioxin '90, The Tenth International Meeting. Bayreuth, Germany.
13. Jacobson, J., S. Jacobson, and H. Humphrey. 1990. Effects of in utero exposure to polychlorinated biphenyls and related contaminants on cognitive functioning in young children. *J. Pediatrics* 116: 38-45.
14. Rohleder, F. 1989. Dioxins and cancer mortality: Reanalysis of the BASF cohort. Ninth International Symposium on Chlorinated Dioxins and Related Compounds, Toronto, Ontario, Sept. 17-22.
15. Van Strum, C. and P. Merrell. 1990. Dioxin human health damage studies: Damaged data? *Journal of Pesticide Reform* 10(1): 8-12.
16. Zober, A., P. Messerer, and P. Huber. 1990. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. *International Archives of Occupational and Environmental Health.* 62: 139-157.
17. Fingerhut, M., et al. (1991). Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324(4): 212-218.
18. "EPA likely to upgrade dioxin cancer classification to reflect new data." *Inside EPA.* February 1, 1991. p.4.
19. Jenkins, C. 1991. U.S. Environmental Protection Agency Memorandum. January 24.
20. Kociba, R., D. Keyes, J. Beyer, R. Carreon, C. Wade, D. Dittenber, R. Kalnins, L. Frauson, C. Park, S. Barnard, R. Hummel, and and C. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicology and Applied Pharmacology* 46: 279-303.
21. U.S. Environmental Protection Agency. 1986. Guidelines for carcinogen risk assessment. *Federal Register* 51(185): 33991. September 24.
22. U.S. Environmental Protection Agency. 1988. *A cancer risk-specific dose estimate for 2,3,7,8-TCDD: Draft.* EPA/600/6-88/007Aa. June. pp. 49-50.
23. Goldstein, B., N. Kim. 1989. Letter from the Chair and Co-Chair of the Ad Hoc Dioxin Panel to Dr. R. Loehr, Chair, Science Advisory Board Executive Committee, U.S. Environmental Protection Agency. November 28.
24. U.S. Environmental Protection Agency. 1990. EPA's position on Georgia's adoption of a dioxin water quality standard. Region IV. March.
25. Bayard, S. 1988. Quantitative implications of the use of different extrapolation procedures for low-dose cancer risk estimates from exposure to 2,3,7,8-TCDD. Appendix A of reference 22.
26. Alsen-Hinrichs, C, Department of Toxicology, University of Kiel School of Medicine, Kiel, Germany. Letter to the *Washington Post* (unpublished). June 21, 1990.
27. Squire, R. 1990. Letter to Dr. Robert Michaels acknowledging the request of November 28, 1989. January 8.
28. U.S. Environmental Protection Agency (1989). *Exposure factors handbook.* Versar, Inc. EPA 600/8-89-043. Washington, D.C.: EPA.
29. Mehrle, P., et al. 1988. Toxicity and bioconcentration of 2,3,7,8-tetrachlorodibenzo-p-dioxin and 2,3,7,8-tetrachlorodibenzofuran in rainbow trout. *Environ. Toxicol. Chem.* 7: 47-62.
30. Cook, P., A. Batterman, and B. Butterworth. 1990. *Laboratory study of TCDD bioaccumulation by lake trout from Lake Ontario sediments, food chain and water.* Duluth, MN: U.S. Environmental Protection Agency Environmental Research Laboratory.

Attachment 4

MAR 20 1991

Eleventh International Symposium on Chlorinated Dioxins and Related Compounds

cc Steve
CR
[illegible]
Jim K

DIOXIN '91

September 23-27, 1991

Conference Information

School of Public Health
Office of Continuing Education
The University of North Carolina
at Chapel Hill
CB# 8165, Miller Hall
Chapel Hill, NC 27599-8165
Phone: 919/966-1104
Fax: 919/966-7141

Organizing Committee

Memo

To: Conference Participants Who Plan to Submit Papers

From: Sharon Johnson Wills
Program Assistant

Date: February 10, 1991

Re: Abstract Format Instructions

The Organizing Committee of Dioxin '91 invites you to submit your abstract for the 11th International Symposium on Chlorinated Dioxins and Related Compounds. The conference will be held in Research Triangle Park, North Carolina, Sept. 23-27, 1991. Enclosed please find one instruction sheet and two forms for submitting your abstract. Also enclosed is an acknowledgment card that you should send back with your completed package. Fill in the lines marked "title" and "author" and return it with your abstract package to the Office of Continuing Education. I will return the card to you to acknowledge receipt of your abstract.

Please read the instructions carefully and take note of all mailing advisories so that we may include your abstract in this year's program. Remember that all abstracts must be received no later than April 1, 1991. Abstracts received after this date will not be considered for acceptance, published or printed.

If you have any questions or concerns, please call or write.

P.S. A complete brochure describing this program will be mailed to you in April. To register for Dioxin '91 before that time, please call me at 919/966-1104.

DOSE RESPONSE RELATIONSHIPS FOR CHRONIC EXPOSURE TO 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD) IN A RAT TUMOR PROMOTION MODEL: 2. QUANTIFICATION AND IMMUNOLOCALIZATION OF CYTOCHROMES P450c(1A1) AND P450d(1A2) IN THE LIVER. A Tritscher, G Clark, Z McCoy, C Portier, W Greenlee, J Goldstein, and G Lucier. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

TCDD and its structural analogs produce a broad spectrum of biochemical and toxic effects in animals and humans. The mechanisms responsible for these effects involve interactions with the Ah receptor but many of the steps necessary for biological response remain unknown. One of the troublesome knowledge gaps that causes uncertainty in risk assessments for TCDD is the lack of adequate dose-response relationships following chronic exposure to TCDD. One of the most sensitive responses to TCDD and its structural analogs is the induction of specific isozymes of cytochrome P450 (CYP1A1 and CYP1A2). CYP1A1 is induced in many tissues whereas CYP1A2 is induced only in liver. We have employed a two-stage model for hepatocarcinogenesis in female Sprague-Dawley rats to evaluate dose-response relationships for CYP1A1 and CYP1A2. A single dose of diethylnitrosamine was used as the initiating agent followed by biweekly gavage of TCDD at doses equivalent to 3.5, 10, 35 and 125 ng/kg/day for 30 weeks. CYP1A1 and CYP1A2 were quantified in liver microsomes from control and treated rats by immunoassay. Data revealed a maximum induction of CYP1A2 of 10-fold and induction was nearly 3-fold at the 3.5 ng/kg/day dose. The no detectable effect for 1A2 induction was estimated to be 0.1 to 0.3 TCDD ng/kg/day. A chronic dosing experiment is in progress to determine if this is an accurate estimate of the no detectable effect. Interestingly, TCDD-mediated induction of 1A2 appeared to occur at lower doses in DEN-initiated rats compared to non-initiated rats. Also, CYP1A2 induction appeared to be a slightly more sensitive marker of TCDD exposure than CYP1A1 in our rat liver tumor promotion model. We also analyzed liver TCDD concentrations by GC-MS. These data revealed a linear relationship between administered dose and TCDD liver concentrations throughout the entire dose range of our study. Therefore, induction of 1A2 does not enhance TCDD retention in liver, a hypothesis that had been proposed because 1A2 is a binding protein for TCDD. We also used immunocytochemical techniques to analyze the pattern of CYP1A1 and CYP1A2 distribution in livers of control and TCDD-treated rats. 1A2 was localized primarily in the centrolobular region with small amounts in the midzonal and periportal regions. Induction by TCDD increases the number of cells containing detectable amounts of 1A2 but not the intensity of staining of cells constitutively expressing this cytochrome. Localization patterns, in induced rats, were similar for 1A1 and 1A2. Taken together, these studies are characterizing dose response relationships for CYP1A1 and CYP1A2 that represent characteristic Ah receptor dependent responses to TCDD exposure. (Funding for TCDD analyses provided by the American Paper Institute.

DOSE RESPONSE RELATIONSHIPS FOR CHRONIC EXPOSURE TO 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD) IN A RAT LIVER TUMOR PROMOTION MODEL: 1. RELATIONSHIPS OF TCDD TISSUE CONCENTRATIONS TO SERUM CLINICAL CHEMISTRY, CELL PROLIFERATION, AND PRENEOPLASTIC FOCI. G Clark, A Tritscher, Z McCoy, C Portier, M Thompson, R Wilson, J Foley, R Maronpot, [1]T Goldsworthy, W Greenlee, and G Lucier. National Institute of Environmental Health Sciences, Research Triangle Park, NC and [1]Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

One of the important issues in a risk assessment for exposure to dioxins is the pharmacokinetic distribution of TCDD in a long term chronic exposure regimen and the biological responses associated with a potential carcinogenic outcome. A specific cytoplasmic binding protein, the Ah receptor, is generally thought to mediate most of the biological responses to TCDD including its action as a tumor promoter. We have used a rat liver tumor promotion model to investigate biochemical responses that may be associated with promotion of carcinogenesis. In previous studies we have found that alterations of hepatic cell proliferation and the appearance of enzyme altered foci (γ-glutamyl transpeptidase and glutathione S-transferase-positive foci) correlate with liver tumor formation but that the ovaries are necessary for the expression of these effects. In the current study we are investigating dose response relationships in female Sprague-Dawley rats with an initiating dose of 175 mg/kg DEN and biweekly exposure to TCDD for 30 weeks to give doses equivalent to 3.5, 10.7, 35.7, and 125 ng/kg/day TCDD. A linear distribution of TCDD in livers of exposed animals was found. The mean liver concentration of TCDD was 19.9 ppb at 125 ng/kg/day and the mean liver concentration was 0.5 ppb at 3.5 ng/kg/day. In serum samples from the rats exposed to 125 ng/kg/day the TCDD concentration was 23.9 ppt while the concentration at the lowest dose was 8 ppt. Several serum clinical chemistry parameters were measured including alkaline phosphatase, glucose, alanine transaminase, total cholesterol, triglycerides, sorbitol dehydrogenase, 5' nucleotidase, and total bile acids. A significant dose effect for TCDD exposure was determined for serum alkaline phosphatase, 5' nucleotidase activities and on the levels of serum cholesterol. We are in the process of analyzing cell proliferation in livers from these animals by incorporation of bromodeoxyuridine into newly-formed cells and immunohistochemical analysis. We are also quantifying γ-glutamyl transpeptidase and placental glutathione S-transferase-positive foci as indicators of preneoplastic lesions. These parameters will be correlated with the applied dose, the tissue specific dose, and the levels of occupied Ah receptors. We hope to determine a) what is the most sensitive biochemical response to TCDD exposure and b) which parameter correlates with carcinogenicity. These data will be useful in the development of mechanistic models for dioxin risk assessment. (Funding for TCDD analyses provided by the American Paper Institute).

Carcinogenesis vol.12 no.5 pp.793–800, 1991 Attachment 5

Study of the separate and combined effects of the non-planar 2,5,2′,5′- and the planar 3,4,3′,4′-tetrachlorobiphenyl in liver and lymphocytes *in vivo*

Linda Sargent[1], Yvonne P.Dragan, Chris Erickson, Chris J.Laufer and Henry C.Pitot[2]

McArdle Laboratory for Cancer Research, Department of Oncology and the Center for Environmental Toxicology, The Medical School, University of Wisconsin, Madison, WI 53706, USA

[1]Present address: Chemical Industry Institute of Toxicology, 6 Davis Drive, Research Triangle Park, NC 27709, USA
[2]To whom reprint requests should be sent

Polychlorinated biphenyls (PCBs) are a group of industrial chemicals that are widely distributed in the environment. Because these compounds occur as mixtures, studies of their possible interactive effects are essential for an understanding of the mechanism of the toxicity of these mixtures. For the determination of a possible interaction of the effects *in vivo* of 2,5,2′,5′-tetrachlorobiphenyl (TCB) and 3,4,3′,4′-TCB, rats were exposed to a single dose of diethylnitrosamine (DEN) and subsequently to 0.1 p.p.m. 3,4,3′,4′-TCB and/or 10 p.p.m. 2,5,2′,5′-TCB in the feed for 1 year. The two major targets of PCB toxicity, the liver and the peripheral blood, were examined after these treatments. TCB treatment after DEN exposure caused a predominance of increased placental glutathione S-transferase (PGST) and deficiencies of ATPase as preneoplastic markers in focal hepatic lesions. When 0.05% phenobarbital (PB) was administered after DEN exposure, the distribution of markers in altered hepatic foci (AHF) was essentially equal for increased PGST and γ-glutamyltranspeptidase (GGT) and for ATPase deficiency. Many of these AHF also exhibited increased P450 b/e expression. Our results demonstrated that the two PCB congeners interacted *in vivo* to produce an increase in AHF that were PGST positive and ATPase negative. PGST-positive and ATPase-negative AHF correlated best with focal areas of P450 b/e expression. The combination of the two PCBs caused a greater than additive decrease in the total number of lymphocytes and antibody-producing B-cells. Also the thymocyte-dependent T-helper cells isolated from the animals receiving the combination of TCBs demonstrated a morphologically abnormal subpopulation. The results indicate that the interaction of 2,5,2′,5′-TCB and 3,4,3′,4′-TCB *in vivo* induced much greater toxicity and mutagenicity in peripheral lympyhocytes and hepatocytes than treatment with either congener alone.

Introduction

Polychlorinated biphenyls (PCBs*) are a group of industrial chemicals that, in the past, had diverse uses owing to their chemical stability and their miscibility in organic solvents. These properties resulted in the use of PCBs as hydraulic fluids, plasticizers, adhesives, heat transfer fluids, wax extenders, dedusting agents, organic diluents, lubricants, flame retardants and as dielectric fluids in capacitors and transformers (1). The advantages that made PCBs such a versatile industrial chemical proved to be the source of their problem in the environment. Traces of PCBs have been found in environmental samples world-wide (2,3). Analyses of human breast milk, blood and adipose tissue have demonstrated that most individuals have been exposed to PCBs (2,3). The primary route of human exposure is through oral ingestion of contaminated products.

Technical mixtures of PCBs contain a combination of planar and non-planar congeners. The planar congeners bind to the Ah receptor, induce cytochrome P450 c and P450 d (4–7), and cause a cascade of events primarily in the liver and immune cells, including weight loss, thymic atrophy, decreased spleen weights (8), reduction of circulating lymphocytes of both the bursae and thymic cell populations (9–11), hepatomegaly, and subcapsular and midzonal hepatic necrosis. They are also potent promoters of the growth of preneoplastic hepatic foci (12). The non-planar congeners are less toxic, have a low affinity for the Ah receptor, and induce P450 b/e. The non-planar congeners cause hepatic enlargement and are relatively weak promoting agents in hepatocarcinogenesis (12,13). They do not cause thymic atrophy or reduction in immune function (5,6,14).

Planar and non-planar congeners occur as mixtures, yet there are few studies which have examined the potency of specific combinations of PCB congeners. The planar 3,4,3′,4′-tetrachlorobiphenyl (TCB) and the non-planar 2,5,2′,5′-TCB are found in the Aroclor mixtures 1254, 1248 and 1242. The ratio of the concentration of these two congeners in the major Aroclors was used to determine the concentration ratio for this study. In addition, we chose to use low-level, environmentally relevant doses of these TCBs in order to assess the potency of the combination for the determination of doses in this experiment. The sample of Aroclor that was used as a standard contained 0.002 μg of 3,4,3′,4′-TCB/ml and 0.2 μg of 2,5,2′,5′-TCB/ml. Hepatocytes and lymphocytes were chosen as target cells to study a possible superadditive toxicity and promotion potency of the combination of the planar and the non-planar TCBs, since these two target cell types are among the most sensitive to PCB toxicity.

Materials and methods

Chemicals

The Pariza purified diet was purchased from Teklad (Madison, WI). Diethylnitrosamine (DEN) was obtained from the Eastman Kodak Co. (Rochester, NY). 3,4,3′,4′-TCB was purchased from Ultra Scientific (Hope, RI) and 2,5,2′,5′-TCB was a gift from Dr James Miller (McArdle Laboratory, Madison, WI). All of the antibodies used for immunohistochemistry were obtained from Bioproducts for Science Inc. (Indianapolis, IN).

Animals and treatment protocol

Female Sprague–Dawley rats (Harlan Sprague Dawley, Madison, WI) weighing an average of 90 g were housed in wire mesh cages and fed the Pariza diet (30% casein, 5% corn oil, 10% partially hydrogenated corn oil, 40% sucrose, 15% cornstarch) and water *ad libitum*. A 70% partial hepatectomy was performed under ether anesthesia and 24 h later 50% of the animals were intubated with

*Abbreviations: PCBs, polychlorinated biphenyls; TCB, tetrachlorobiphenyl; DEN, diethylnitrosamine; PB, phenobarbital; AHF, altered hepatic foci; GGT, γ-glutamyl transpeptidase; PGST, placental form of glutathione S-transferase; ATP, canalicular ATPase; G6P, glucose-6-phosphatase; HCC, hepatocellular carcinoma; TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin; HCB, hexachlorobiphenyl.

10 mg DEN in trioctanoin/kg. After 1 week, the animals were randomly assigned to the treatment groups outlined in Figure 1. TCBs were dissolved in methylene chloride, added to the powdered chow, and mixed thoroughly in plastic bags. The solvent was evaporated in the hood for 24 h. Randomly selected rats were then placed on a control diet or control diet with one of the following additions: 0.1 p.p.m. 3,4,3′,4′-TCB only, 10 p.p.m. 2,5,2′,5′-TCB only, 0.1 p.p.m. 3,4,3′,4′-TCB and 10 p.p.m. 2,5,2′,5′-TCB, or 100 p.p.m. 2,5,2′,5′-TCB. Another group was fed phenobarbital (PB) at a level of 0.05% in the diet as a positive control (15,16).

Analysis of lymphocytes

Rats were treated with 100 mg cyclophosphamide/kg and anesthetized with ether; blood was drawn by cardiac puncture 48 h later. The red blood cells were lysed with 2 ml hypotonic buffer (1000 ml of deionized water, 8.29 g NH_4Cl, 1.0 g KH_2CO_3, 0.372 g disodium EDTA, pH 7.4) and washed with phosphate-buffered saline. Washed lymphocytes were then mixed with fluorescein-conjugated antibodies generated against the CD-4 protein, the CD-8 protein, the 1.1 Thy protein and a general B-cell protein (17). The stained cells were then analyzed on the flow cytometer by standard methods (18). Lymphocytes of abnormal morphology were examined by scanning electron microscopy according to standard methods. Sections of the spleen were frozen on solid CO_2 and fixed in 10% buffered formalin.

Analysis of preneoplastic foci (altered hepatic foci, AHF)

The liver was removed, weighed, and sections from each liver lobe were immediately frozen on solid CO_2. Five 10-μ-thick serial sections were stained for γ-glutamyl transpeptidase (GGT), the placental form of glutathione S-transferase (PGST), canalicular ATPase (ATP), cytochrome P450 b/e, P450 c/d and glucose-6-phosphatase (G6P), according to the methods for staining outlined by Xu *et al.* (19). AHF were then quantitated by the procedure of Campbell *et al.* (20). Additional slices of tissue were stored in 10% formalin for histopathological analysis.

Statistics

Non-parametric Wilcoxon statistics were used to compare groups. For the determination of additivity, Steel and Torrie's χ-square test for additivity (21) was used.

Results

Lymphocyte analysis

The total number of circulating antibody-producing cells (B-cells) was reduced in the peripheral blood prepared from animals treated with 3,4,3′,4′-TCB, but not from those treated with 2,5,2′,5′-TCB (groups 3 and 5, Figure 2) when compared with untreated controls. The number of circulating B-cells isolated from animals treated with both TCBs was reduced by a greater than additive level ($P < 0.001$, group 7) when analyzed by flow cytometry. When DEN was included in the treatment protocol (Figure 3), the level of circulating B-cells was reduced in the 2,5,2′,5′-TCB group as well as the 3,4,3′,4′-TCB group ($P < 0.05$, groups 4 and 6). The level of B-cells in the group with DEN plus both TCBs (group 8) was reduced to 1%. A reduction to this level was greater than would be expected by an additive model when analyzed by the χ-square test for additivity.

There was no statistical reduction in the number of CD-4, CD-8 or Thy 1.1 cells. Although the total number of cells was the same, a population of light-staining CD-4 cells was observed by flow cytometry (Figure 4). Of the CD-4 cells, 50 ± 8% from group 7 (both TCBs) and 95 ± 5% of the samples from group 8 (DEN + both TCBs) had an abnormal population of light-staining CD-4 cells. The forward scatter of these cells was the same as that of the normal CD-4 cells, but the side scatter was different (Figure 4). A difference in the side scatter would indicate a difference in size or morphology. When these light-staining CD-4 cells were separated and examined by scanning electron microscopy, the surface morphology of all of the cells examined was distinctly different from the normal population (Figure 5). By standard methods (17), these abnormal cells were further examined for esterase activity and were determined to be negative and therefore not monocytes.

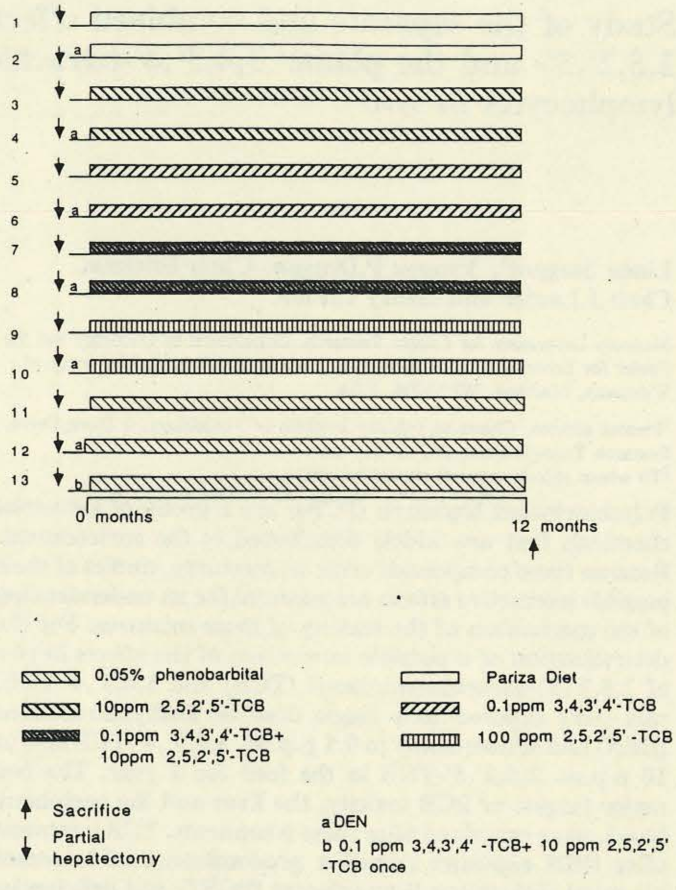


Fig. 1. Format of the protocol used for the initiation and promotion of AHF in female Sprague–Dawley rats.

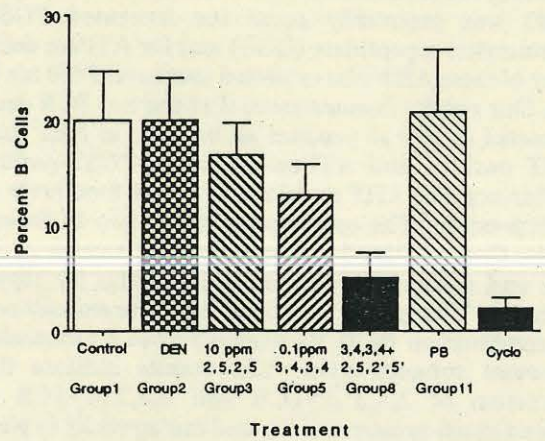


Fig. 2. Percentage of B-cells in the peripheral blood after chronic exposure to DEN alone or followed by 0.05% PB, 3,4,3′,4′-TCB, 2,5,2′,5′-TCB, or a combination of 3,4,3′,4′-TCB + 2,5,2′,5′-TCB or to cyclophosphamide. See text for details. Steel and Torrie's χ-square test for additivity (21) was used to examine an additive or greater than additive result. The conclusions of this test are given in the text. The bars above the columns indicate the standard error of the mean for analysis (1/rat in duplicate). The numbers of rats/group may be obtained from Table I.

Liver analysis

Number of preneoplastic foci. There was no statistical increase in the ratio of residual liver wt to body wt with any of the TCB treatments, but there was a significant increase in the PB and DEN + PB groups (Figure 6). A single dose of 0.1 p.p.m. 3,4,3′,4′-TCB and 10 p.p.m. 2,5,2′,5′-TCB did not increase the

Table I. Histopathologic changes in livers of rats on protocols depicted in Figure 1[a]

Group no.	Treatment	Portal damage[b]	Bile duct proliferation	Neoplastic nodules/rat	Cellular atypia/ neoplastic nodule/rat[c]	HCC/rat
1	Control	–	2/8	–	–	1/8
2	DEN	0/8	2/8	1/8	1/8	1/8
3	2,5,2′,5′-TCB (10 p.p.m.)	0/14	2/14	2/14	0/14	0/14
4	DEN + 10 p.p.m. 2,5,2′,5′-TCB	2/12	1/12	4/12	1/12	1/12
5	3,4,3′,4′-TCB (0.1 p.p.m.)	0/14	5/14	3/14	0/14	0/14
6	DEN + 0.1 p.p.m. 3,4,3′,4′-TCB	0/12	4/12	4/12	0/12	0/12
7	3,4,3′,4′-TCB + 2,5,2′,5′-TCB	9/12	9/12	1/12	1/12	0/12
8	DEN + 3,4,3′,4′-TCB + 2,5,2′,5′-TCB	9/11	11/11	11/11	9/11	2/11
10	DEN + 100 p.p.m. 2,5,2′,5′-TCB	3/5	2/5			
12	DEN + PB	2/11	11/11	11/11	11/11	9/11

[a]Data are presented as the number of rats exhibiting the pathologic process/total number of rats examined.
[b]Includes fibrosis, chronic inflammation and/or hydopic change of periportal hepatocytes. Control animals receiving control diets showed only occasional minimal portal damage and bile duct proliferation. The histopathology of livers of rats in groups 9, 11 and 13 (Figure 1) was no different from that seen in groups 1, 3 and 5.
[c]Cellular atypia is defined as morphological and cytological changes, usually focal, seen in neoplastic nodules, such changes being histologically compatible with one or more patterns of well-differentiated hepatocellular carcinomas (43−45).

total number of AHF or the volume fraction of the regenerated liver occupied by AHF.

Treatment with TCBs caused a predominance of AHF that were scored by the presence of PGST ($PGST^+$) and ATP deficiency as preneoplastic markers (Figure 7), whereas $PGST^+$, ATP deficiency and GGT^+ markers were equally distributed in AHF after DEN + PB (Figure 8). TCB treatment alone did not elevate the number of AHF when compared with the control livers; however, treatment with both TCBs increased the number of AHF to a level that was greater than that of the untreated control and statistically the same as the DEN control (groups 2, 3 and 5 in Figure 1; see also Figure 9). The numbers of preneoplastic foci per liver in the DEN + 10 p.p.m. 2,5,2′,5′-TCB group (group 4) or the DEN + 0.1 p.p.m. 3,4,3′,4′-TCB group (group 6 in Figure 1) were not significantly different from the DEN group (group 2, Figure 1). When rats were treated with DEN followed by both TCBs, the number of AHF was dramatically greater than additive (Figure 9) ($P < 0.001$). Treatment with DEN + 100 p.p.m. 2,5,2′,5′-TCB (group 10) did not cause a significant increase in the number of AHF when compared with DEN (Figure 9). Rats treated with the standard DEN + PB protocol had a significant increase in the number of AHF ($P < 0.001$, Figure 9).

Volume fraction of preneoplastic foci. When the volume fraction of AHF was analyzed, rats intitated with DEN and fed 10 p.p.m. 2,5,2′,5′-TCB (group 4) exhibited statistically the same volume percentage AHF as the DEN group (group 2 in Figure 10); however, the volume of AHF in the DEN + 3,4,3′,4′-TCB group (group 6) was slightly increased over that in the regenerated livers of animals receiving DEN only (group 2, Figure 10). The combination of DEN + both TCBs (group 8 in Figure 1) greatly increased the volume of the residual liver occupied by preneoplastic foci to a level that was much greater than would be expected by an additive model ($P < 0.001$; Figure 10). The group given a 10-fold greater level of 2,5,2′,5′-TCB (group 10) exhibited a significant increase in the volume of the regenerated liver occupied by AHF to 7% of the liver (Figure 10). This level was statistically greater than that of rats given DEN alone but not as great as the DEN plus both TCBs group. When the livers of rats given DEN followed by 0.05% PB in the diet were examined, there was a significant increase in the volume fraction of preneoplastic foci to 20% of the total regenerated liver (group 12 in Figure 1; see Figure 10).

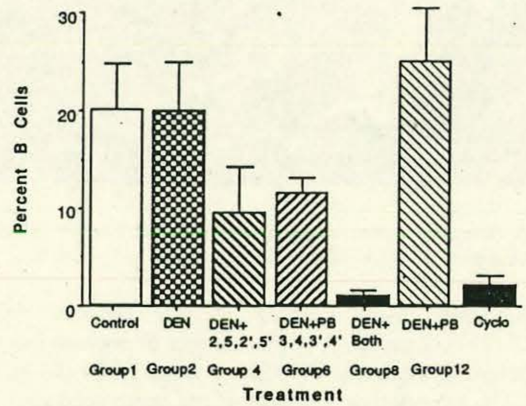


Fig. 3. Percentage of B-cells in the peripheral blood after 10 mg DEN/kg and 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB, 10 p.p.m. 2,5,2′,5′-TCB, or a combination of 3,4,3′,4′-TCB + 2,5,2′,5′-TCB or to cyclophosphamide. See text and legend to Figure 2 for details and statistical conclusions. Steel and Torrie's χ-square test for additivity was used to assess significance. $P < 0.05$.

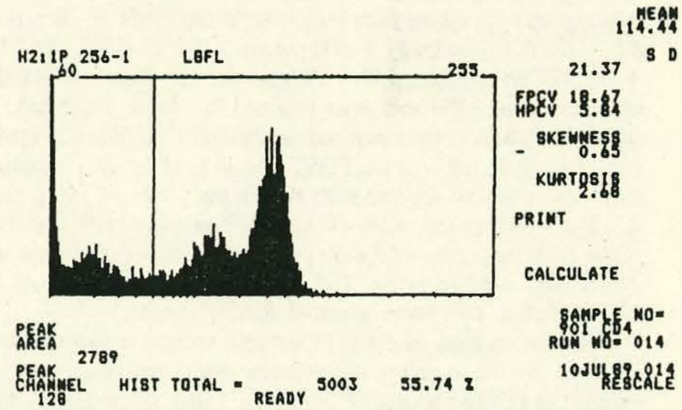


Fig. 4. Histogram of the fluorescence of T-helper cells following 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB. Antibodies conjugated with fluorescence and generated to the CD-4 protein were used to identify the T-helper cells. See text for experimental details.

Cytochrome P450 b/e was found in 10 ± 7% of the preneoplastic foci marked by PGST or ATP of the DEN + 10 p.p.m. 2,5,2′,5′-TCB, but 68 ± 10% of the AHF expressed the

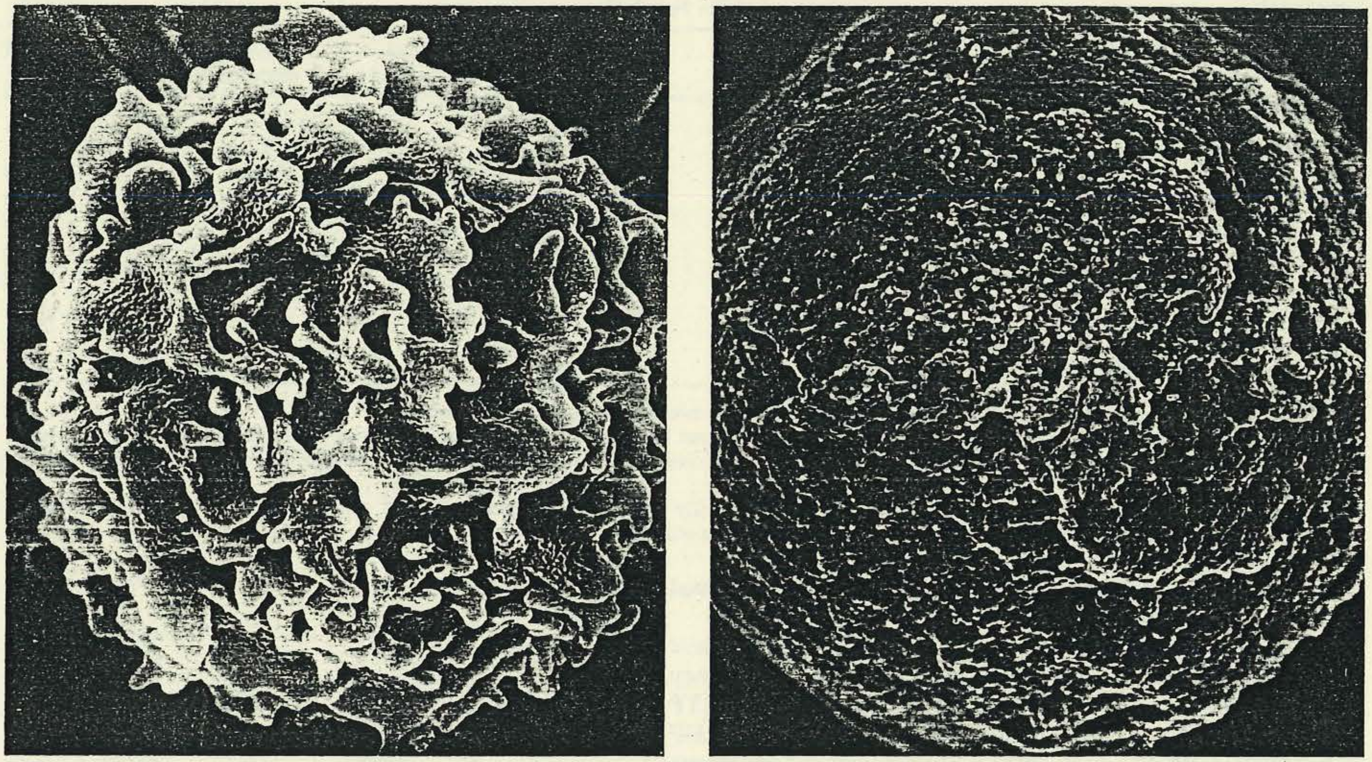


Fig. 5. Scanning electron micrograph of a normal T-helper cell (**left**) and an abnormal T-helper cell (**right**) isolated from the peripheral blood of an animal fed 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB for 1 year (×5000). See text for details.

cytochrome P450 marker in the DEN + 100 p.p.m. 2,5,2′.5′-TCB group. A larger number of positive foci was found in the group treated with DEN + both TCBs (60 ± 5%) than would be expected on the basis of the result seen with 10 p.p.m. 2,5,2′,5′-TCB alone. The number of P450 b/e positive foci found in the DEN + PB group was as large as that of the group given DEN + both TCBs (65 ± 5%) (Table II).

The expression of P450 c/d was localized to the centrolobular and midzonal region of the regenerated liver in the DEN + 3,4,3′,4′-TCB group, the DEN + both TCBs group, and the TCBs group (groups 6, 8 and 9). Centrilobular to midzonal staining was also seen with P450 b/e in the DEN + 10 p.p.m. 2,5,2′,5′-TCB, the DEN + 100 p.p.m. 2,5,2′,5′-TCB, the DEN + both TCBs and the DEN + PB groups. This degree of staining indicates that P450 c/d was induced by these regimens. In addition, P450 b/e was examined; in the DEN + PB group (group 12 in Figure 1), 76% of the PGST and 32% of the ATP-deficient foci were positive for this enzyme. In the DEN + 100 p.p.m. 2,5,2′,5′-TCB group, 22% of the PGST-positive AHF and 41% of the ATP-negative AHF were positive for P450 b/e. When both TCBs were administered, 40% of the PGST and 40% of the ATP-deficient foci were positive for P450 b/e.

The combination of both TCBs also caused a superadditive increase in the number of animals with neoplastic nodules exhibiting cellular atypia ($P < 0.05$, Table I); however, only two of the animals treated with DEN + both TCBs developed hepatocellular carcinoma (HCC). Treatment with DEN + PB for 1 year caused 80% of the animals to develop HCC.

Discussion

The planar congener, 3,4,3′,4′-TCB, and its non-planar isomer, 2,5,2′,5′-TCB, which are found in the major Aroclor mixtures 1254, 1242 and 1248, induced a greater than additive toxicity

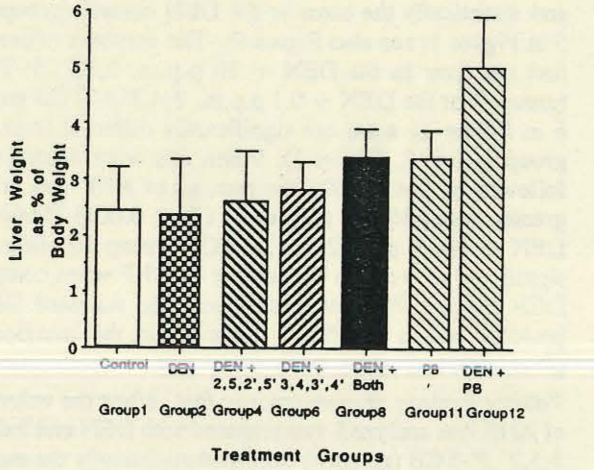


Fig. 6. Histogram of the ratio of the regenerated liver to body wt following 10 mg DEN/kg and 1 year of exposure to TCBs or to PB. The group numbers below each bar refer to the groups listed in Figure 1. The group designated PB is group 11 of Figure 1. Groups seen in Figure 1 not shown in this figure exhibited no significant change from the group 1 control.

in the two major target cell types of PCB toxicity, hepatocytes and lymphocytes, in the studies described here. Our results demonstrated that low doses of the planar 3,4,3′,4′-TCB were more toxic to lymphocytes than a 100-fold higher dose of the non-planar 2,5,2′,5′-TCB congener. The 3,4,3′,4′-TCB congener caused a reduction in the number of B-cells. A similar reduction of B-cells has been noted after acute exposure to 3,4,3′,4′-TCB (10). The combination of the two TCBs caused a greater than additive decrease in the number of circulating B-cells as well as the appearance of an abnormal subpopulation of T-helper cells. The esterase test verified that this abnormal population of

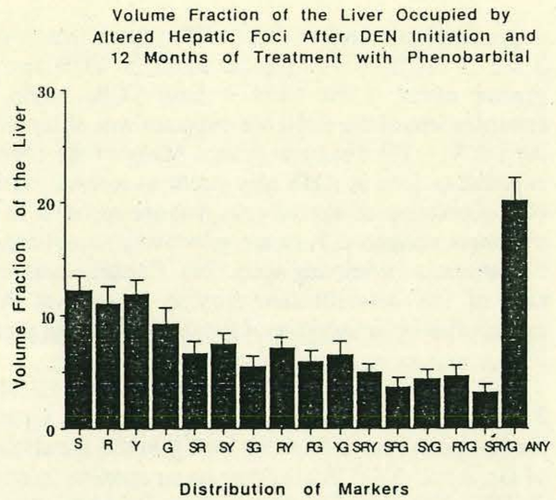


Fig. 7. Distribution of the volume fraction of AHF scored by multiple markers for AHF following initiation with 10 mg DEN/kg and 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB and 10 p.p.m. 2,5,2′,5′-TCB (group 8, Figure 1). Abbreviations: S, glutathione S-transferase-positive volume fraction; R, GGT-positive volume. Y, ATPase-negative volume; G, G6Pase-negative volume; SR, S and R combined; SY, S and Y combined. SG, S and G combined; RY, R and Y combined; RG, R and G combined; YG, Y and G combined; SYG, S and Y and G combined; SRY, S and R and Y combined. See ref. 19 for further details.

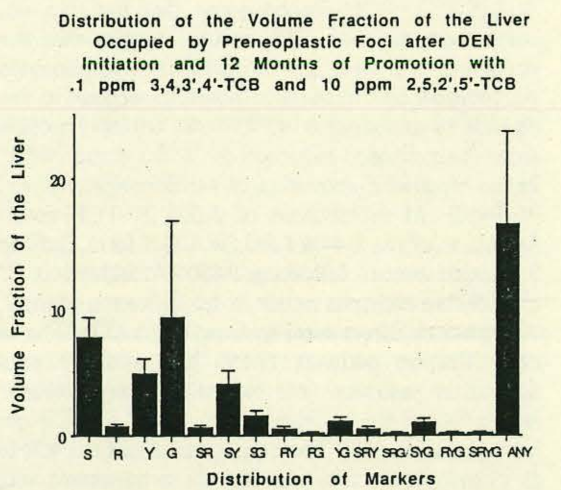


Fig. 8. Histogram of the distribution of the volume fraction of AHF scored by multiple markers for AHF following initiation with 10 mg DEN/kg and 1 year of exposure to 0.05% PB (group 12, Figure 1). See legend to Figure 7 for marker designation.

light-staining CD-4 cells was not a monocyte population, but was a new population of CD-4 cells exhibiting an abnormal surface membrane configuration.

The results from this research also demonstrated that the planar congener had more potent effects in liver cells than the non-planar TCB. The low dose of 3,4,3′,4′-TCB chosen for this study produced a moderate increase in the volume of preneoplastic foci as well as an increase in chromosome damage (L.Sargent and H.C.Pitot, unpublished observations). The relative potency of promoting agents has been expressed by the following relationship:

$$\text{promotion index} = V_f/V_c \times 1/\text{mmol per week}$$

where V_f is the total volume fraction (%) occupied by AHF in the livers of rats treated with the promoting agent, V_c is the total

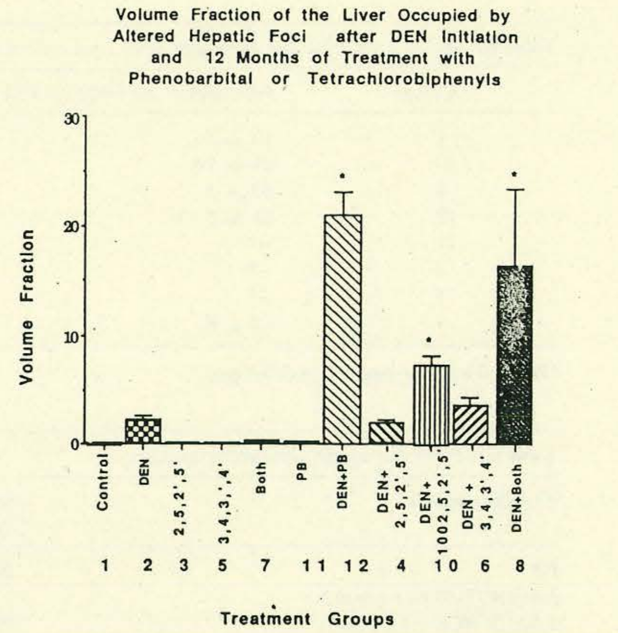


Fig. 9. Number of AHF per liver after initiation with 10 mg DEN/kg and/or 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB (groups 6 and 5), 10 p.p.m. 2,5,2′,5′-TCB (groups 4 and 3), 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB (groups 8 and 7) or to 0.05% PB in the diet for 1 year (groups 12 and 11). Eleven animals per group were killed after each treatment. The bars above the columns indicate the standard error of the mean from 11 animals. See Figure 1 for details of each group designated by number under the columns. *$P < 0.001$ by Student's t-test.

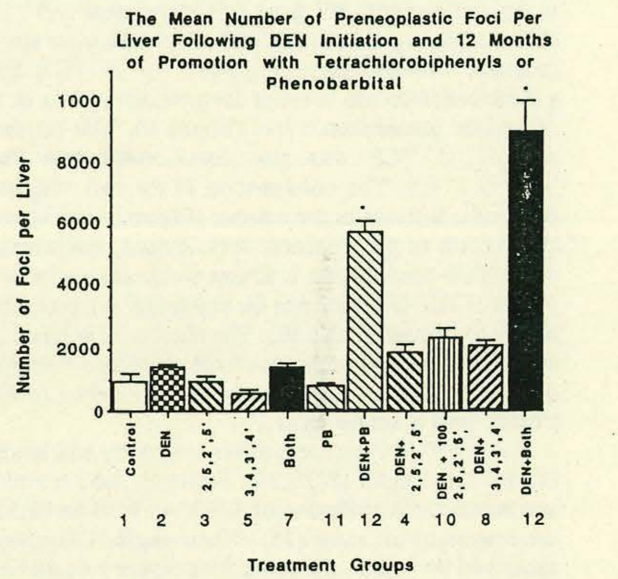


Fig. 10. Volume fraction (%) of AHF following initiation with 10 mg DEN/kg and/or 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB (groups 6 and 5), 10 p.p.m. 2,5,2′,5′-TCB (groups 4 and 3), 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB (groups 8 and 7) or to 0.05% PB (groups 12 and 11) in the diet for 1 year. Each group had 11 animals. See legend to Figure 9 for further details.

volume of AHF in control animals that have only been initiated and not treated with the promoting agent, and mmol is the number of millimoles of the promoting agent.

The promotion index (22) is based on the total number of altered cells within all AHF, thus giving a measure of tumor promotion. Table III shows the relative promotion indices of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB as well as their combination

Table II. AHF-positive P450 b/e expression after 1 year of treatment (%)

Groups	Foci positive for P450 b/e (%)
4	10 ± 7
10	68 ± 10
8	60 ± 5
12	65 ± 5
11	–[a]
3	–[a]
5	–[a]
9	40 ± 6

[a]Too few AHF to report significant data.

Table III. Promoting agents and promotion index

Promoting agents	Promotion index[a]
PB	100
3,4,3′,4′-TCB (0.1 p.p.m.)	1.5×10^4
2,5,2′,5′-TCB (10 p.p.m.)	200
2,5,2′,5′-TCB (100 p.p.m.)	250
2,5,2′,5′-TCB (10 p.p.m.) and 3,4,3′,4′-TCB (0.1 p.p.m.)	8×10^5
2,3,7,8-TCDD[b]	2.8×10^7

[a]See text for details of calculations. Promotion indices were determined in animals that had been initiated with DEN (10 mg/kg) following a 70% partial hepatectomy (see text for details).
[b]Ref. 22.

in comparison with PB from this experiment and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) from an earlier study (22). By contrast, a 10-fold higher dose of 2,5,2′,5′-TCB did not cause a significant increase in either the promotion index or the number of hepatic preneoplastic foci (Figure 9). The promotion index of 2,5,2′,5′-TCB was also considerably less than that of 3,4,3′,4′-TCB. The combination of the two congeners caused a dramatic increase in the number (Figure 9) and volume fraction (Figure 10) of preneoplastic foci. Indeed, the promotion index of the TCB combination is almost within one order of magnitude of that of TCDD, which has the highest known promotion potency of any compound (Table III). The number of animals treated with both TCBs that had numerous large neoplastic nodules exhibiting cellular atypia was also greater than that seen in either group treated with a single TCB.

The two TCB congeners differ in toxicity and binding affinity for the Ah receptor (8,23,24); however, the systemic clearance and volume of distribution of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB are essentially the same (15). When single PCB congeners were examined by others, the promotion potency could be correlated with the affinity for the Ah receptor (23). Our results also demonstrated that the strong Ah receptor ligand, 3,4,3′,4′-TCB, was a strong promoter of AHF, but the non-planar congener was a weak promoter relative to 3,4,3′,4′-TCB and TCDD. Furthermore, previous results have shown that TCDD, which has a 500-fold greater affinity for the Ah receptor than TCBs, was a stronger promoter than 3,4,3′,4′-TCB (24). The non-planar congeners, 2,4,5,2′,4′,5′-TCB (23), 2,4,2′,4′-TCB and 2,5,2′,5′-TCB, have been reported to exhibit promoting activity for hepatic preneoplastic foci (14). The presence of chlorine substitution in the *para* position correlated with an enhancement of promoting potency, but all the non-planar congeners were less potent than the planar 3,4,3′,4′-TCB.

An enhancement of the amount of P450 b/e enzymes was seen in preneoplastic hepatic foci (AHF) of rats receiving 10 p.p.m. 2,5,2′,5′-TCB or 100 p.p.m. 2,5,2′,5′-TCB and to an even greater extent in the DEN + both TCBs group. This same enhancement of the P450 b/e enzymes was observed in AHF of the DEN + PB treatment group. Many of the changes in gene expression seen in AHF may occur as a result of the selection of a population of altered cells that are resistant to the specific treatment utilized (25) or are selectively stimulated to grow by the particular promoting agent (26). Enhancement of the expression of this detoxification enzyme in cells of AHF is also exemplified by an increase of P450 b/e following promotion with PB as well as hexachlorocyclohexane (27,28).

The greater than additive toxicity of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB that was seen *in vivo* in hepatocytes and lymphocytes may have been owing to the metabolic activation of the 2,5,2′,5′-TCB congener to an epoxide intermediate (14, 29,30). This epoxide intermediate is more toxic and more chromosome damaging than the parent compound (31) and has been shown to bind to DNA (29,32). PCB congeners that have both the *meta* and *para* sites available for oxidation can be metabolized through an epoxide intermediate. These intermediates can bind to DNA and have been found to be mutagenic (25,31). Examination of the dose−response curves of previous *in vitro* studies of chromosome damage in human lymphocytes (33) caused by 3,4,3′,4′-TCB and a combination of 3,4,3′,4′-TCB + 2,5,2′,5′-TCB demonstrated that the two dose−response curves are parallel. This would suggest that the two events occurred by a common mechanism. Lymphocytes express the Ah receptor and have been shown to respond to the Ah receptor ligands by an increase in P450 c/d. Metabolic changes resulting from the combined induction of P450 c/d and P450 b/e can result in the metabolic activation of 4-chlorobiphenyl (34). Inhibition of P450 c/d metabolism of 2,5,2′,5′-TCB results in greater formation of the 3,4-diol and the 4-OH form, indicating that more 3,4-oxide occurs following P450 c/d induction. The induction of P450 b/e enzymes results in detoxification of the 2,5,2′,5′-TCB congener by direct *meta*-hydroxylation (32). The absence of the detoxification pathway (P450 b/e) and the presence of the activation pathway (c/d induction) may explain the greater sensitivity of the lymphocytes to 2,5,2′,5′-TCB observed in the *in vivo* studies (35). The enhancement of the P450 b/e expression in preneoplastic foci resulting from treatment with both TCBs and with DEN + 2,5,2′,5′-TCB as well as with DEN + PB may result in a selective reduced toxicity to 2,5,2′,5′-TCB conferred to these cells by this gene expression.

Although centrilobular to midzonal staining for P450 b/e was observed by Buchman *et al.* (36) after DEN initiation and promotion with 3,4,5,3′,4′,5′-hexachlorobiphenyl (HCB) or with 2,4,5,2′,4′,5′-HCB, no increased staining for the P450 b/e isozyme occurred in AHF with this protocol. The 2,4,5,2′,4′,5′-HCB congener is an inducer of the P450 b/e isozyme; however, this congener is not known to be metabolized by this form or any other form of P450. Increased expression of a detoxification enzyme in cells of AHF has been observed as an increase of P450 b/e after promotion with PB as well as with hexachlorocyclohexane (36). Cells of AHF resulting from *N*-hydroxy ethylnitrosamine treatment exhibit reduced levels of P450 b/e and P450 c/d forms and an increase in glutathione S-transferase and expoxide hydrolase (23). Chronic treatment of rats with 2-acetylaminofluorene, which is metabolized by multiple forms of P450 (36), causes the proliferation of focal areas of preneoplastic hepatocytes; this may significantly lower the expression of many P450 genes as well as increase the conjugating enzymes that

detoxify the reactive intermediate (37). When PB administration followed AAF treatment, however, the level of P450 b/e was induced in AHF that had previously been negative for the enzyme (38). Thus, as a result of the alteration of drug-metabolizing enzymes, cells of AHF may have a selective advantage in a toxic environment. Since the growth of normal cells is suppressed by the cytotoxic effects of these treatments, the preneoplastic cells have an additional proliferative advantage.

The centrilobular to midzonal staining for P450 b/e that was evident in the livers of rats treated with DEN + PB or DEN + both TCBs indicates that enzyme induction occurred in response to these compounds in hepatocytes in these zones. Centrilobular staining with P450 c/d after treatment with DEN + 3,4,3',4'-TCB or DEN + both TCBs indicates that induction of this isozyme also occurred. The dose of 3,4,3',4'-TCB was 0.3% of the 6-day chronic dose used for maximal induction by Clevenger (14), and 0.003% of the acute dose used by Parkinson (6). The dose of 2,5,2',5'-TCB utilized in our studies was 33% of the maximal chronic dose and 3% of the maximal acute dose used in other studies (13,23,24).

The greater than additive effect of the mixture of 3,4,3',4'-TCB and 2,5,2',5'-TCB reported in this study may be the result of one or more of three possible mechanisms: (i) Ah receptor gene expression (1,4,5); (ii) the PB-type of cytochrome P450 response (24,39); (iii) the metabolic activation of PCBs to epoxides (29,30). Glutathione conjugation is the major phase II detoxification pathway for the 3,4-oxide of 2,5,2'-TCB. Several different mechanisms can contribute to the toxic effects of 2,5,2',5'-TCB. Although the mechanism of glutathione depletion may be different in hepatocytes and lymphocytes, continuous exposure to the TCB combination may have resulted in depletion of the glutathione levels in both cell types. Depletion of glutathione would prevent a major part of the detoxification of the 3,4-oxide of 2,5,2',5'-TCB (32).

Our results demonstrate an interaction of low doses of two PCBs *in vivo* in the two major target organs of PCB toxicity, the liver and the immune system, at doses that are relevant to human exposure levels (40). The observation of immune depression and promotion of AHF with very low PCB concentrations suggests that the biological effects of a complex Aroclor mixture in two different target cell populations of PCB toxicity may not be owing simply to the summed effects of each of the constituent chemicals or to the individual concentrations of the most toxic congeners, but rather largely to the effects of only a few constituents interacting at low concentrations.

This study also represents the first report of the appearance of an abnormal population of CD-4 lymphocytes in the peripheral blood after PCB exposure. This may be an important finding not only for rodent exposure, but also for human exposure, because this same PCB combination was very genotoxic to cultured human lymphocytes. The abnormal population of CD-4 cells in the peripheral blood may be the result of a genetic change that occurred in these cells. The aneuploidy of many hepatocytes (L.M.Sargent, G.Sattler, C.A.Sattler, B.Roloff, Y.Xu and H.C.Pitot, in preparation) and numerous large neoplastic nodules exhibiting cellular atypia in the liver are indications that the combination of 3,4,3',4'-TCB and 2,5,2',5'-TCB induces the stage of progression of hepatocarcinogenesis (41,42). Confirmation of this hypothesis will require further testing because the percentage of animals with hepatocellular carcinoma was not elevated after 1 year of treatment in this experiment. The numerous large neoplastic nodules with cellular atypia probably represent rapidly growing populations of abnormal cells. If this protocol had been allowed to continue further, it is possible that there would have been an increase in the frequency of hepatocellular carcinoma in the livers of rats receiving the combination compared with those administered each TCB alone.

Acknowledgements

We would like to thank Dr Colin Jefcoate for supplying the P450 antibodies. We would like to extend our gratitude to Dr James A.Miller for the gift of 2,5,2',5'-TCB. We also thank Dr David Auerbach and the State Laboratory of Hygiene for their help in performing the flow cytometry. The expert histotechnology of Ms Jane Weeks and Mrs Jennifer Potter is also gratefully acknowledged, as well as the expert technical typing of Mrs Mary Jo Markham. The authors are grateful to Dr Ilse Riegel for technical editing and comments on the manuscript. The experiments described in this document were funded in part by grants from the National Cancer Institute (CA-07175, CA-2284 and CA-45700) and by a training grant from the National Institute of Environmental Health Sciences (ES-07015).

References

1. Safe,S. (1989) Polychlorinated biphenyls (PCBs): mutagenicity and carcinogenicity. *Mutat. Res.*, **220**, 31–47.
2. Passivirta,J. and Linko,R. (1980) Environmental toxins in Finnish wildlife. A study of trends of residue contents in fish during 1973–1978. *Chemosphere*, **9**, 643.
3. Jacobs,L.W., Chou,S.F. and Tiedje,J.M. (1978) Field concentrations and persistence of polybrominated biphenyls in soils and solubility of polybrominated biphenyls in natural waters. *Environ. Health Perspect.*, **23**, 1.
4. Safe,S., Bandiera,S., Sawyer,T., Robertson,L.W., Safe,L., Parkinson,A., Thomas,P.E., Ryan,D.E., Reik,L.M., Levin,W., Denomme,M.A. and Fujita,T. (1985) PCBs: structure–function relationships and mechanisms of action. *Environ. Health Perspect.*, **60**, 47–56.
5. Poland,A. and Knutson,J.C. (1982) 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin and related halogenated aromatic hydrocarbons: examination of the mechanism of toxicity. *Annu. Rev. Pharmacol. Toxicol.*, **22**, 517–554.
6. Parkinson,A., Robertson,L., Safe,L. and Safe,S. (1981) Polychlorinated biphenyls as inducers of hepatic microsomal enzymes: structure–activity rules. *Chem.-Biol. Interactions*, **35**, 1–2.
7. McKinney,J.D. and Singh,P. (1981) Structure–activity relationships in halogenated biphenyls: unifying hypothesis for structural specificity. *Chem.-Biol. Interactions*, **333**, 271–283.
8. Yoshimura,H., Yoshihara,S., Ozawa,N. and Miki,M. (1979) Possible correlation between induction modes of hepatic enzymes by PCBs and their toxicity in rats. *Ann. NY Acad. Sci.*, **320**, 179–192.
9. Silkworth,J.B. and Grabstein,E.M. (1982) Polychlorinated biphenyl immunotoxicity: dependence on isomer planarity and the *Ah* gene complex. *Toxicol. Appl. Pharmacol.*, **65**, 109–119.
10. Greenlee,W.F. and Irons,R.E. (1981) Modulation of benzene-induced lymphocytopenia in the rat by 2,4,5,2',4',5'-hexachlorobiphenyl and 3,4,4',5'-tetrachlorobiphenyl. *Chem.-Biol. Interactions*, **33**, 345–360.
11. Wölfle,D., Münzel,P., Fischer,G. and Bock,K.-W. (1988) Altered growth control of rat hepatocytes after treatment with 3,4,3',4'-tetrachlorobiphenyl *in vivo* and *in vitro*. *Carcinogenesis*, **9**, 919–924.
12. Osterele,D. and Deml,E. (1981) Promotion effect of various PCBs and DDT on enzyme altered islands in rat liver. *Nauyn-Schmiedberg's Arch. Pharmacol. Suppl. R*, **16**, 316.
13. Preston,B.D., Miller,E.C. and Miller,J.A. (1985) The activities of 2,2',5,5'-tetrachlorobiphenyl, its 3,4-oxide metabolite and 2,2',5,5'-tetrachlorobiphenyl in tumor induction and promotion assays. *Carcinogenesis*, **6**, 451–453.
14. Clevenger,M.A., Roberts,S.M., Sattin,D.L., Harbison,R.D. and James,R.C. (1989) The pharmacokinetics of 2,2',5,5'-tetrachlorobiphenyl and 3,3',4,4'-tetrachlorobiphenyl and its relationship to toxicity. *Toxicol. Appl. Pharmacol.*, **100**, 315–327.
15. Pitot,H.C., Campbell,H.A., Maronpot,R., Nimrat,B., Rizvi,T.A., Xu,Y.-H., Sargent,L.M., Dragan,Y. and Pyron,M. (1989) Critical parameters in the quantitation of the stages of initiation, promotion, and progression in one model of hepatocarcinogenesis in the rat. *Toxicol. Pathol.*, **17**, 594–612.
16. Pitot,H.C., Barsness,L., Goldsworthy,T. and Kitagawa,T. (1978) Biochemical characterization of stages of hepatocarcinogenesis after a single dose of diethylnitrosamine. *Nature*, **271**, 456–458.
17. Yam,L.T., Li,C. and CrosbyW.H. (1971) Cytochemical identification of monocytes and granulocytes. *Am. J. Clin. Pathol.*, **55**, 283–290.
18. Braylan,R.C. (1983) Attributes and applications of flow cytometry. *Ann. Clin. Lab. Sci.*, **13**, 379–384.

19. Xu,Y.-H., Campbell,H.A., Sattler,G.L., Hendrich,S., Maronpot,R., Sato,K. and Pitot,H.C. (1990) Quantitative stereological analysis of the effects of age and sex on multistage hepatocarcinogenesis in the rat by use of four cytochemical markers. *Cancer Res.*, **50**, 472–479.
20. Campbell,H.A., Xu,Y.-H., Hanigan,M.H. and Pitot,H.C. (1986) Application of quantitative stereology to the evaluation of phenotypically heterogeneous enzyme-altered foci in the rat liver. *J. Natl. Cancer Inst.*, **76**, 751–767.
21. Steel,R.G.D. and Torrie,J.H. (1980) Enumeration data II: contingency tables, some uses of χ-square. In *Principles and Procedures of Statistics, a Biometrical Approach*. McGraw-Hill Book Company, New York, pp. 469–520.
22. Pitot,H.C., Goldsworthy,T.L., Moran,S., Kennan,W., Glauert,H.P., Maronpot,R.R. and Campbell,H.A. (1987) A method to quantitate the relative initiating and promoting potencies of hepatocarcinogenic agents in their dose–response relationships to altered hepatic foci. *Carcinogenesis*, **8**, 1491–1499.
23. Safe,S. (1983) Polychlorinated biphenyls (PCBs) and polybrominated biphenyls: biochemistry, toxicology and mechanisms. *CRC Rev. Toxicol.*, **13**, 319–325.
24. Silberhorn,E.M., Glauert,H.P. and Robertson,L.W. (1990) Carcinogenicity of polyhalogenated biphenyls: PCBs and PBBs. *Crit. Rev. Toxicol.*, **20**, 439–496.
25. Eriksson,L., Ahluwalia,M., Spiewak,J., Lee,G., Sarma,D.S.R., Roomi,M.J. and Farber,E. (1983) Distinctive biochemical pattern associated with resistance to hepatocytes in hepatocyte nodules during liver carcinogenesis. *Environ. Health Perspect.*, **49**, 171–174.
26. Dragan,Y.P., Xu,Y.-H., Hully,J.R., Bawa,N., Rizvi,T., Campbell,H.A., Maronpot,R.R. and Pitot,H.C. (19??) An initiation-promotion assay in rat liver as a potential complement to the two-year carcinogenesis bioassay. *Fund. Appl. Toxicol.*, in press.
27. Schulte-Hermann,R., Roome,N., Timmermann-Trosiener,I. and Schuppler,J. (1984) Immunocytochemical demonstration of a phenobarbital-induced cytochrome P450 in putative preneoplastic foci of rat liver. *Carcinogenesis*, **5**, 149–153.
28. Schwarz,M., Peres,G., Buchmann,A., Friedberg,T., Waxman,D.J. and Kunz,W. (1987) Phenobarbital induction of cytochrome P450 in normal and preneoplastic rat liver: comparison of enzyme and mRNA expression as detected by immunohistochemistry and *in situ* hybridization. *Carcinogenesis*, **8**, 1355–1357.
29. Forgue,S.T., Preston,B.D., Hargraves,W.A., Reich,I.L. and Allen,J.R. (1979) Direct evidence that an aerene oxide is a metabolic intermediate of 2,5,2′,5′-tetrachlorobiphenyl. *Biochem. Biophys. Res. Commun.*, **91**, 475–483.
30. Forgue,S.T. and Allen,J.R. (1982) Identification of an aerene oxide metabolite of 2,5,2′,5′-tetrachlorobiphenyl by gas chromatography–mass spectroscopy. *Chem.-Biol. Interactions*, **40**, 233–245.
31. Stadnicki,S.S., Francis,S.D.L. and Allen,J.R. (1979) DNA strand breaks caused by 2,5,2′,5′-tetrachlorobiphenyl and its metabolites. *Res. Commun. Chem. Pathol. Pharmacol.*, **24**, 313–325.
32. Preston,B.D., Miller,J.A. and Miller,E.C. (1984) Reactions of 2,2′,5,5′-tetrachlorobiphenyl 3,4-oxide with methionine, cysteine and glutathione in relation to the formation of methylthio-metabolites of 2,2′,5,5′-tetrachlorobiphenyl in the rat and mouse. *Chem.-Biol. Interactions*, **50**, 289–312.
33. Sargent,L.M., Roloff,B.D. and Meisner,L.F. (1989) *In vitro* chromosome damage due to PCB interactions. *Mutat. Res.*, **224**, 79–88.
34. Wyndhman,C., Devenish,J. and Safe.S. (1978) The *in vitro* metabolism, macromolecular binding and bacterial mutagenicity of 4-chlorobiphenyl, a model PCB substrate. *Res. Commun. Chem. Pathol. Pharmacol.*, **15**, 563–570.
35. Kawabata,T.T. and White,K.L., Jr (1989) Benzo[*a*]pyrene metabolism by murine spleen microsomes. *Cancer Res.*, **49**, 5816–5822.
36. Buchmann,A., Kunz,W., Wolf,C.R., Oesch,F. and Robertson,L.W. (1986) Polychlorinated biphenyls, classified as either phenobarbital- or 3-methylcholanthrene-type inducers of cytochrome P450, are both hepatic tumor promoters in diethylnitrosamine-initiated rats. *Cancer Lett.*, **32**, 243–253.
37. Roomi,M.W., Ho,R.K., Sarma,D.S.R. and Farber,E. (1985) A common biochemical pattern in preneoplastic hepatocyte nodules generated in four different models in the rat. *Cancer Res.*, **45**, 564–571.
38. Ghoshal,A., Gurtoo,H.L., Faletto,M.B., Koo,P., Nagi,M. and Farber,E. (1990) Molecular basis for the constitutive decrease in cytochromes P450 in putative preneoplastic hepatocytes. *Proc. Am. Assoc. Cancer Res.*, **31**, 136.
39. Goldstein,J.A., Hickman,P., Bergman,H., McKinney,J.D. and Walker, M.P.(1977) Separation of pure polychlorinated biphenyl isomers into two types of inducers on the basis of induction of P450 or P448. *Chem.-Biol. Interactions*, **17**, 69–87.
40. Cordle,F., Corneliussen,P., Jelinek,C., Hackley,B., Lehman,R., McLaughlin,J., Rhoden,R. and Shapiro,R. (1978) Human exposure to polychlorinated biphenyls and polybrominated biphenyls. *Environ. Health Perspect.*, **24**, 157–172.
41. Sherer,E., Feringa,A.W. and Emmelot,P.(1984) Initiation–promotion–initiation induction of neoplastic foci within islands of precancerous liver cells in the rat. In Börzxönyi,M., Lapi,K., Day,N. and Yamasaki,H. (eds), *Models, Mechanisms and Etiology of Tumour Promotion*. IARC Scient. Pub. 56, Lyon, pp. 57–66.
42. Pitot,H.C. (1989) Progression: the terminal stages in carcinogenesis. *Jpn. J. Cancer Res.*, **80**, 599–607.
43. Schauer,A. and Kunze,E. (1976) Tumours of the liver. In Turusov,V.S. (ed.), *Pathology of Tumours in Laboratory Animals. Vol. 1. Tumours of the Rat, Part 2*. IARC, Lyon, pp. 41–72.
44. Squire,R.A. and Levitt,M.H. (1975) Report of a workshop on classification of specific hepatocellular lesions in rats. *Cancer Res.*, **35**, 3214–3223.
45. National Research Council (1980) Histologic typing of liver tumors in the rat. *J. Natl. Cancer Inst.*, **64**, 179–206.

Received on August 20, 1990; revised on January 17, 1991; accepted on January 25, 1991

Attachment 6

CANCER MORTALITY IN WORKERS EXPOSED TO 2,3,7,8-TETRACHLORODIBENZO-*p*-DIOXIN

MARILYN A. FINGERHUT, PH.D., WILLIAM E. HALPERIN, M.D., DAVID A. MARLOW, B.S., LAURIE A. PIACITELLI, M.S., PATRICIA A. HONCHAR, PH.D., MARIE H. SWEENEY, PH.D., ALICE L. GREIFE, PH.D., PATRICIA A. DILL, A.B., KYLE STEENLAND, PH.D., AND ANTHONY J. SURUDA, M.D.

Abstract *Background.* In both animal and epidemiologic studies, exposure to dioxin (2,3,7,8-tetrachlorodibenzo-*p*-dioxin, or TCDD) has been associated with an increased risk of cancer.

Methods. We conducted a retrospective cohort study of mortality among the 5172 workers at 12 plants in the United States that produced chemicals contaminated with TCDD. Occupational exposure was documented by reviewing job descriptions and by measuring TCDD in serum from a sample of 253 workers. Causes of death were taken from death certificates.

Results. Mortality from several cancers previously associated with TCDD (stomach, liver, and nasal cancers, Hodgkin's disease, and non-Hodgkin's lymphoma) was not significantly elevated in this cohort. Mortality from soft-tissue sarcoma was increased, but not significantly (4 deaths; standardized mortality ratio [SMR], 338; 95 percent confidence interval, 92 to 865). In the subcohort of 1520 workers with ≥1 year of exposure and ≥20 years of latency, however, mortality was significantly increased for soft-tissue sarcoma (3 deaths; SMR, 922; 95 percent confidence interval, 190 to 2695) and for cancers of the respiratory system (SMR, 142; 95 percent confidence interval, 103 to 192). Mortality from all cancers combined was slightly but significantly elevated in the overall cohort (SMR, 115; 95 percent confidence interval, 102 to 130) and was higher in the subcohort with ≥1 year of exposure and ≥20 years of latency (SMR, 146; 95 percent confidence interval, 121 to 176).

Conclusions. This study of mortality among workers with occupational exposure to TCDD does not confirm the high relative risks reported for many cancers in previous studies. Conclusions about an increase in the risk of soft-tissue sarcoma are limited by small numbers and misclassification on death certificates. Excess mortality from all cancers combined, cancers of the respiratory tract, and soft-tissue sarcoma may result from exposure to TCDD, although we cannot exclude the possible contribution of factors such as smoking and occupational exposure to other chemicals. (N Engl J Med 1991; 324:212-8.)

SEVERAL epidemiologic and toxicologic studies have suggested an association between 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), or the chemicals it contaminates, and soft-tissue sarcoma,[1-4] Hodgkin's disease,[5] non-Hodgkin's lymphoma,[6-8] stomach cancer,[9,10] nasal cancer,[11] and cancer of the liver.[12,13] In other studies of these cancers, no significant associations with TCDD exposure were found.[14-19] The carcinogenicity of TCDD has been demonstrated in studies of rats, mice, and hamsters; histiocytic lymphomas, fibrosarcomas, and tumors of liver, skin, lung, thyroid, tongue, hard palate, and nasal turbinates have been found.[12,13,20] TCDD acts as a promoter[21,22] and may also initiate carcinogenesis.[12,13,20] To evaluate the effect of occupational exposure to TCDD, particularly with respect to the cancers listed above, we conducted a retrospective cohort study of mortality among U.S. chemical workers assigned to the production of substances contaminated with TCDD.

METHODS

Identification of Companies

In 1978 the National Institute for Occupational Safety and Health began an effort that would eventually identify the exposed workers at all U.S. chemical companies that had made TCDD-contaminated products between 1942 and 1984. TCDD was generated as a contaminant in the production of 2,4,5-trichlorophenol and was carried into subsequent production processes.[23] One derivative, 2,4,5-trichlorophenoxyacetic acid, was widely used in the United States to kill brush and was a constituent of defoliants such as Agent Orange. Other derivatives included the herbicides 2-(2,4,5-trichlorophenoxy)propionic acid (Silvex) and 2-(2,4,5-trichlorophenoxy)-ethyl 2,2-dichloropropionate (Erbon), the insecticide *O,O*-dimethyl *O*-(2,4,5-trichlorophenyl)phosphorothioate (Ronnel), and the bactericide 2,2′-methylene-bis[3,4,6-trichlorophenol] (hexachlorophene).

Identification of Exposed Workers

Workers from 12 companies were included in the study cohort if a personnel or payroll record documented that they had been assigned to a production or maintenance job in a process involving TCDD contamination (n = 5000), or if they had been identified in a previously published study on the basis of exposure to TCDD (n = 172).[24] Personnel records for 202 workers did not reveal the duration of their assignment to processes involving TCDD contamination; they were therefore included in the analysis of overall mortality but excluded from analyses according to duration of exposure. Sixty-seven women are not included in this report; there were 10 deaths among them, including a single death from cancer (lung cancer).

At each plant, we made a thorough review of operating conditions, job duties, and records of TCDD levels in industrial-hygiene samples, intermediate reactants, products, and wastes. This review provided clear evidence of potential daily exposure to TCDD. The production of TCDD-contaminated substances at the various plants involved similar raw materials, processes, and job duties.[25] However, there were differences between jobs and between plants in the extent of TCDD exposures. Occupational exposure to substances contaminated with TCDD was confirmed by measuring serum TCDD levels, as adjusted for lipids, in 253 surviving members of the study cohort from two plants who were also participants in a related cross-sectional medical study.[26]

Life-Table Analysis

Vital status was determined as of December 31, 1987, from records of the Social Security Administration or Internal Revenue Service, or from the National Death Index. All death certificates

From the Industrywide Studies Branch, Division of Surveillance, Hazard Evaluations, and Field Studies, National Institute for Occupational Safety and Health, Centers for Disease Control, 4676 Columbia Pky., Cincinnati, OH 45226, where reprint requests should be addressed to Dr. Fingerhut.

Supported in part by the Agency for Toxic Substances and Disease Registry.

were independently classified by two nosologists according to the rules of the revision of the *International Classification of Diseases* (ICD) in effect at the date of death.[27]

Life-table analysis was used to evaluate mortality in the cohort.[28] At each plant, the number of person-years at risk was calculated as the interval between the first systematically documented assignment to a process involving TCDD contamination and the date of death or December 31, 1987, whichever occurred first. Those whose vital status was unknown were assumed to be alive at the end of the study. Standardized mortality ratios (SMRs) were computed by dividing the observed number of deaths by the expected number and multiplying by 100, after stratification to adjust for the confounding effects of age, race, and year of death. Two-sided 95 percent confidence intervals were computed for each cause-specific SMR, with use of the Byar approximation for eight deaths or more and Fisher's exact method for fewer than eight deaths.[29] The U.S. population was used as the reference group, because the 12 plants were located in 11 states throughout the country.

Analyses According to Duration of Exposure and Employment

Duration of exposure was defined as the number of years the worker was employed in processes involving TCDD contamination and was calculated with data from personnel records. We used duration of exposure as a surrogate for cumulative exposure to TCDD on the basis of the high correlation of the logarithm of serum TCDD levels with the logarithm of the number of years assigned to processes involving TCDD contamination in our sample of 253 workers (Pearson's product-moment coefficient $r = 0.72$) (Fig. 1), and on the assumption that the production processes were similar in the 12 plants.[25]

Because of the concentration of person-years in the short-duration categories, duration of exposure was stratified before analysis into categories of <1, 1 to <5, 5 to <15, and ≥15 years (Table 1). Mortality was also examined according to time since first exposure (latency) in periods of 0 to <10, 10 to <20, and ≥20 years since first exposure. To examine mortality in a subgroup with substantial exposure and adequate time for cancer to develop, we identified a group of workers who had 1 year or more of exposure to processes involving TCDD contamination and at least 20 years of latency. One year was chosen as a cutoff point for this high-exposure subcohort because in the sample of workers whose serum TCDD levels were measured, 100 percent of those exposed for more than one year had serum TCDD levels higher than the mean level in the unexposed reference group (7 pg per gram of lipid). For this subcohort, the number of person-years at risk was calculated from the date the person attained both 20 years of latency and 1 year of exposure.

Most of the 12 plants were large U.S. chemical manufacturing sites that produced thousands of chemicals. Complete documentation of each worker's exposures was impossible. A separate measure called "duration of employment," defined as the total time that each worker was employed at a study plant, was therefore used. Because of the long total employment at the plants, analyses according to duration of employment were stratified into periods of <5, 5 to <10, 10 to <15, 15 to <20, 20 to <25, 25 to <30, and ≥30 years (Table 1). For these analyses, latency was defined as time since first employment.

When the SMRs showed an apparent trend associated with duration of exposure or employment and when the observed numbers of deaths were sufficiently large, we conducted internal comparisons using directly standardized rate ratios and tests for trend.[30] For the standardized rate ratios, the cause-specific mortality rate in each of the categories of longer duration was compared with the rate in the category of shortest duration, after stratification of the rates for the potential confounding effects of age, race, and calendar time.

Results

The cohort of 5172 male workers from 12 plants had 116,748 person-years of observation. Table 1 describes the vital status, race, latency, and duration of exposure and employment of the workers. Overall mortality for all causes of death was similar to national rates in the United States (1052 deaths; SMR, 99; 95 percent confidence interval, 93 to 105). Mortality from heart disease was also similar to national rates

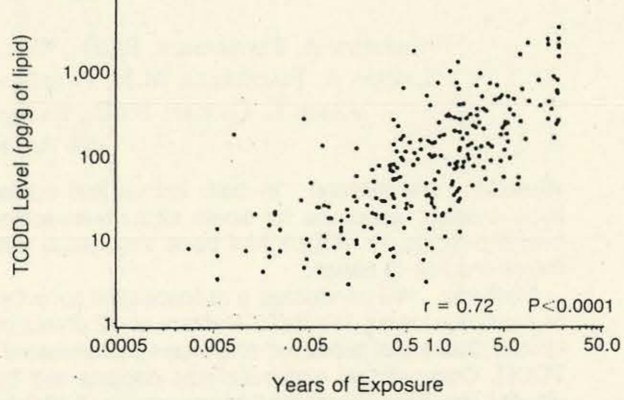


Figure 1. Serum Levels of TCDD, as Adjusted for Lipids, in 253 Workers, According to Years of Exposure.

Table 1. Vital Status and Demographic and Employment Characteristics of the Study Cohort.

Variable	Number (Percent)
Vital status*	
Alive	4043 (78)
Dead	1052 (20)
Unknown	77 (2)
Total	5172 (100)
Deaths*	
White men	985 (94)
Nonwhite men	67 (6)
Total	1052 (100)
Death certificates obtained	1037 (99)
Race	
White	4590 (89)
Nonwhite	385 (7)
Unknown	197 (4)
Total	5172 (100)
Duration of exposure (yr)†	
<1	2697 (54)
1 to <5	1427 (29)
5 to <15	639 (13)
≥15	207 (4)
Total	4970 (100)
Duration of employment (yr)†	
<5	2125 (43)
5 to <10	501 (10)
10 to <15	605 (12)
15 to <20	403 (8)
20 to <25	391 (8)
25 to <30	415 (8)
≥30	530 (11)
Total	4970 (100)
Years since first exposure (latency)†	
<10	271 (5)
10 to <20	1663 (33)
≥20	3036 (61)
Total	4970 (100)
Years since last exposure†	
<10	453 (9)
10 to <20	1789 (36)
≥20	2728 (55)
Total	4970 (100)

*As of December 31, 1987.

†Excludes 202 workers for whom duration of assignment to processes involving TCDD contamination was not available from work records.

(393 deaths; SMR, 96; 95 percent confidence interval, 87 to 106). There were significant reductions in the mortality rates for diseases of the circulatory system (67 deaths; SMR, 77; 95 percent confidence interval, 60 to 98), primarily because of fewer deaths from stroke, and for diseases of the digestive system (38 deaths; SMR, 70; 95 percent confidence interval, 49 to 96), primarily because of fewer deaths from cirrhosis. There were also significantly fewer deaths from alcoholism and personality disorders (2 deaths; SMR, 23; 95 percent confidence interval, 3 to 87). The low mortality from circulatory disease may be a reflection of the "healthy worker" effect — cohorts of workers die at lower rates than the general population, particularly of causes other than cancer.[31] The reduced number of deaths from cirrhosis and alcoholism implies that this cohort consumed less alcohol than the general population. Reduction may also have occurred simply by chance, since numerous comparisons were made between the cohort and the U.S. population. Fatal injuries were significantly more frequent in the cohort (106 deaths; SMR, 128; 95 percent confidence interval, 104 to 154), but they did not appear to be associated particularly with exposure to TCDD. Mortality from all cancers combined (265 deaths; SMR, 115; 95 percent confidence interval, 102 to 130) was significantly elevated in the cohort.

Cancers of a Priori Interest

The term "soft-tissue sarcoma" describes the group of rare malignant neoplasms arising from supporting tissue other than bone.[32] We restricted our analysis of mortality due to soft-tissue sarcoma to cases of soft-tissue sarcoma listed as the underlying cause of death

Table 2. Cancer Mortality in the Entire Cohort and in Workers with More Than 20 Years of Latency.

Site of Cancer	ICD Code*	Entire Cohort (N = 5172)†			Subcohort with ≥20 Yr of Latency (N = 3036)‡					
					<1 yr of exposure (N = 1516)§			≥1 yr of exposure (N = 1520)¶		
		deaths observed	deaths expected	SMR‖	deaths observed	deaths expected	SMR‖	deaths observed	deaths expected	SMR‖
All cancers	140–208	265	229.9	115 (102–130)**	48	46.8	102 (76–136)	114	78.0	146 (121–176)**
Buccal and pharynx	140–149	5	7.0	70 (23–166)	2	1.4	145 (18–524)	2	2.2	90 (11–325)
Pharynx	146–149	3	3.4	88 (18–259)	2	0.7	298 (36–1080)	0	1.2	0 (—)
Other parts	142–145	2	1.9	105 (13–379)	0	0.4	0 (—)	2	0.6	329 (40–1190)
Digestive organs	150–159	67	59.7	112 (87–143)	13	11.8	111 (59–189)	28	20.1	140 (93–202)
Esophagus	150	9	5.9	152 (70–290)	2	1.2	165 (20–602)	4	2.0	200 (55–513)
Stomach	151	10	9.7	103 (50–190)	3	1.7	178 (37–521)	4	2.9	138 (38–353)
Small intestine and colon	152–153	25	20.4	122 (79–181)	5	4.3	117 (38–274)	13	7.3	178 (95–304)
Rectum	154	5	5.6	89 (29–209)	1	1.0	100 (3–557)	2	1.7	115 (14–415)
Liver and biliary	155, 156	6	5.2	116 (42–252)	1	1.0	100 (3–557)	1	1.7	59 (1–327)
Pancreas	157	10	11.9	84 (40–155)	1	2.4	41 (1–232)	4	4.0	100 (27–253)
Peritoneum and unspecified	158, 159	2	1.1	184 (22–666)	0	0.2	0 (—)	0	0.4	0 (—)
Respiratory system	160–165	96	84.5	113 (92–139)	19	18.4	103 (62–161)	43	30.2	142 (103–192)
Larynx	161	7	3.3	211 (84–434)	2	0.7	297 (36–1074)	3	1.1	268 (55–783)
Trachea, bronchus, and lung	162	89	80.1	111 (89–137)	17	17.5	96 (56–155)	40	28.8	139 (99–189)
Male genital organs	185–187	17	15.3	111 (65–177)	2	3.2	63 (8–229)	9	6.0	149 (68–283)
Prostate	185	17	13.9	122 (71–195)	2	3.0	67 (8–237)	9	5.9	152 (70–290)
Urinary organs	188–189	17	11.4	148 (86–238)	3	2.4	128 (26–373)	6	4.0	149 (55–324)
Kidney	189.0–189.2	8	5.7	140 (60–275)	3	1.2	253 (52–742)	2	1.9	106 (13–384)
Bladder and other	188, 189.3–189.9	9	5.7	157 (72–298)	0	1.2	0 (—)	4	2.2	186 (51–476)
Lymphatic and hematopoietic tissue	200–208	24	22.1	109 (70–162)	4	3.9	102 (28–260)	8	6.4	125 (54–247)
Hodgkin's disease	201	3	2.5	119 (25–349)	0	0.2	0 (—)	1	0.4	276 (7–1534)
Non-Hodgkin's lymphoma††	200, 202	10	7.3	137 (66–254)	2	1.5	135 (16–488)	2	2.1	93 (11–337)
Lymphosarcoma and reticulosarcoma††	200	5	3.5	142 (46–332)	0	0.6	0 (—)	1	0.9	107 (3–594)
Other lymphatic††	202	5	3.7	133 (43–313)	2	0.9	215 (26–779)	1	1.4	71 (2–385)
Multiple myeloma††	203	5	3.0	164 (53–385)	0	0.6	0 (—)	3	1.1	262 (54–766)
Leukemia and aleukemia	204–208	6	8.9	67 (24–146)	2	1.6	126 (15–457)	2	2.6	77 (9–277)
Other sites	170–173, 190–199	39	29.6	131 (94–180)	5	5.8	87 (28–202)	18	9.0	201 (118–316)**
Skin	172, 173	4	4.9	82 (22–211)	0	0.9	0 (—)	2	1.3	155 (19–559)
Brain and nervous system	191, 192	5	7.3	68 (22–160)	0	1.3	0 (—)	2	1.9	106 (13–384)
Bone	170	2	0.9	227 (27–819)	0	0.1	0 (—)	1	0.2	521 (13–2903)
Connective tissue and soft tissue	171	4	1.2	338 (92–865)	0	0.2	0 (—)	3	0.3	922 (190–2695)**
Other and unspecified	194–199	24	14.8	162 (104–241)**	5	3.1	159 (52–372)	10	5.1	196 (94–361)

*From the *International Classification of Diseases*, 9th revision.

†Mean number of years exposed, 2.7; mean number of years employed, 12.6.

‡Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records.

§Mean number of years exposed, 0.3; mean number of years employed, 10.7; 12,299 person-years at risk.

¶Mean number of years exposed, 6.8; mean number of years employed, 19.2; 15,136 person-years at risk.

‖SMR equals deaths observed divided by deaths expected and multiplied by 100. Slight differences are due to rounding. Values in parentheses are 95 percent confidence intervals.

**P<0.05.

††Person-years at risk and observed deaths are computed from 1960; no deaths occurred before that year.

on death certificates and assigned to the ICD category "malignant neoplasms of connective and other soft tissue." In the cohort, mortality from soft-tissue sarcoma was nonsignificantly higher than in the reference population (four deaths; SMR, 338; 95 percent confidence interval, 92 to 865) (Table 2). The deaths occurred at 2 of the 12 plants, with a significant increase at 1 plant (two deaths; SMR, 1512; 95 percent confidence interval, 183 to 5462). A review of tissue specimens from the four men whose deaths were attributed to soft-tissue sarcoma showed that only two were in fact soft-tissue sarcomas (Cases 1 and 4, Table 3).[33] Mortality from soft-tissue sarcomas was increased significantly in the subcohort of 1520 workers with 1 year or more of exposure and at least 20 years of latency (the high-exposure subcohort) (three deaths; SMR, 922; 95 percent confidence interval, 190 to 2695). Two other deaths in the cohort (Cases 5 and 6) were attributed to soft-tissue sarcoma according to hospital records, and one of them (Case 5) was confirmed by review of a tissue specimen. These two deaths did not contribute to mortality due to soft-tissue sarcoma in our life-table analysis, because the deaths were assigned other ICD codes. We are aware of a seventh death from soft-tissue sarcoma, which occurred in a group of 139 workers with chloracne who were excluded from the cohort because they did not meet the entry criteria.

In the cohort, the SMRs for the other cancers of a priori interest were nonsignificantly increased (Table 2). There were no deaths from nasal cancer, although approximately one was expected. In the high-exposure subcohort, the SMRs were nonsignificantly higher for Hodgkin's disease and stomach cancer and lower for non-Hodgkin's lymphoma and cancer of the liver, biliary passages, and gallbladder (Table 2).

A Posteriori Findings

A small but significant increase in mortality due to all cancers combined was observed in the entire cohort (SMR, 115; 95 percent confidence interval, 102 to 130). In the high-exposure subcohort the SMR was 146 (95 percent confidence interval, 121 to 176) (Table 2). At 9 of the 12 plants, mortality from all cancers combined was increased; at one of these plants the increase was statistically significant. Mortality was significantly higher than expected in the category of cancers of unspecified sites, which included those of rare sites not included in a category of the life-table analysis and those for which no primary site was listed on the death certificate. Hospital records, which were obtained for 96 percent of these cancers, revealed no particular clustering according to site.

The cohort had a nonsignificant increase in mortality from cancers of the trachea, bronchus, and lung (ICD code 162; SMR, 111; 95 percent confidence interval, 89 to 137). Mortality from cancers of the respiratory system (ICD codes 160 to 165) was significantly higher than expected in the high-exposure subcohort (SMR, 142; 95 percent confidence interval, 103 to 192) (Table 2). To estimate the effect of smoking on the increase in lung cancer, the expected number of lung cancers was adjusted according to the smoking prevalence found in lifetime histories obtained in 1987 by interviewing 223 workers from two plants.[25] This adjustment increased the expected number of lung cancers in the overall cohort by 5 percent and in the high-exposure subcohort by 1 percent, which reduced the SMR in the full cohort to 105 (95 percent confidence interval, 85 to 130) and in the high-exposure subcohort to 137 (95 percent confidence interval, 98 to 187).

Analyses According to Duration of Exposure and Employment

The study cohort worked a mean of 2.7 years in processes involving TCDD contamination and 12.6 years at the plants. The high-exposure subcohort worked a mean of 6.8 years in processes involving TCDD contamination and a mean of 19.2 years in total employment at the plants.

The numbers of deaths due to the rare cancers of

Table 3. Deaths from Soft-Tissue Sarcoma among Workers in the Cohort.*

Case No.	Years Employed	Type of Exposure	Year First Exposed	Years Exposed	Year of Death	Latency (yr)†	Cause of Death: Death Certificate	Cause of Death: Hospital Records	Cause of Death: Tissue Review‡
1	1946–1978	TCP and 2,4,5-T	1950	8.8	1978	28	MFH	MFH	MFH
2	1946–1972	TCP and 2,4,5-T	1948	7.1	1972	24	Liposarcoma	Liposarcoma	Carcinoma, poorly differentiated§
3	1950–1975	TCP	1963	1.2	1975	12	Fibrosarcoma	Fibrosarcoma	Renal carcinoma§
4	1951–1982	TCP	1951	14.9	1983	32	MFH	MFH	MFH
5¶	1943–1975	TCP or 2,4,5-T	Intermittent	Unknown	1980	Unknown	Carcinomatosis§	Myxoid neurogennic sarcoma	Leiomyosarcoma
6¶	1941–1964	TCP	1949	Unknown	1965	16	Metastatic osteosarcoma§	Fibrosarcoma	Not available

*Cases 1 through 5 have been previously described.[33] For other previously described cases, records of exposure to TCDD were not available, and the cases were not included in this cohort study. Some information differs slightly from that reported earlier, since additional records were reviewed. Few details about exposure were available for Cases 5 and 6. TCP denotes 2,4,5-trichlorophenol; 2,4,5-T, 2,4,5-trichlorophenoxyacetic acid; and MFH, malignant fibrous histiocytoma.

†Time from first exposure to death.

‡Conducted at the Armed Forces Institute of Pathology.

§Not a soft-tissue sarcoma.

¶Death was not attributed to soft-tissue sarcoma in the life-table analysis.

Table 4. Mortality from All Cancers and from Cancers of the Trachea, Bronchus, and Lung, According to Latency Period and Duration of Exposure to Processes Involving TCDD Contamination.*

Cause/Latency Period	Duration of Exposure (yr)										Test for Trend
	<1		1 to <5		5 to <15		≥15		Overall		
	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	
All cancers											
<10 Yr	10	68	8	71	3	71	0	0	21	70	
10 to <20 Yr	28	109	16	87	18	122	7	340†	69	113	
≥20 Yr	48	102	59	165‡	37	138	18	115	162	129‡	
Total	86	98	83	127†	58	126	25	141	252	116†	
SRR		100		127		123		129			0.3
Trachea, bronchus, and lung											
<10 Yr	3	77	3	95	1	79	0	0	7	84	
10 to <20 Yr	6	69	5	79	9	180	1	137	21	101	
≥20 Yr	17	96	17	126	14	146	9	156	57	123	
Total	26	86	25	109	24	151	10	154	85	112	
SRR		100		109		166		136			0.2

*Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records. The number of observed deaths and the SMRs therefore differ slightly from those in Table 2. SRR denotes standardized rate ratio.

†P<0.05.

‡P<0.01.

a priori interest were too small to permit meaningful analyses according to duration. For all cancers combined and for cancers of the trachea, bronchus, and lung, Table 4 shows the distribution of mortality with increasing duration of exposure to products contaminated with TCDD. The standardized rate ratios were increased in the strata of longer duration for both these categories, but significant linear trends were not found. Mortality increased with increasing latency for both these categories of cancer. Table 5 shows the distribution of mortality for the same categories with increasing duration of employment. Significant linear trends were not observed for either category with increasing length of employment, although standardized rate ratios were higher than expected in several strata of employment ≥20 years. Mortality increased with increasing latency for both categories of cancer.

Serum Levels of TCDD

The mean serum TCDD level, as adjusted for lipids, in the sample of 253 workers from two plants was 233 pg per gram of lipid (range, 2 to 3400) (Fig. 1). A mean level of 7 pg per gram was found in the comparison group of 79 unexposed persons, all of whose levels were under 20, a range found in other unexposed populations.[34] The mean for 119 workers with one year or more of exposure was 418 pg per gram. All the workers had received their last occupational exposures 15 to 37 years earlier.

Discussion

TCDD, widely known as dioxin, has acquired the reputation of a potent carcinogen. Our study, although limited in its ability to detect increased numbers of rare cancers, found little increase in mortality from the cancers associated with TCDD in previous studies in humans. The exception was an increase in soft-tissue sarcoma. The difficulties of evaluating soft-tissue sarcomas in a cohort study of mortality have been described.[33] These include variability in pathological diagnosis and misclassification on death certificates. Consequently, the interpretation of the increased mortality from soft-tissue sarcoma in our study is limited by the small number of cases and the fact that the cause of death was sometimes misclassified on the death certificates of the workers (Table 3) and in the U.S. comparison population.[35]

Several case–control studies have found significant fourfold increases in non-Hodgkin's lymphoma in persons reporting exposure to phenoxy herbicides or chlorophenols, some of which contained TCDD.[6,8] The magnitude of the increase in mortality in the cohort described here (SMR, 137; 95 percent confidence interval, 66 to 254) suggests a smaller increase in this risk, or no increase at all. Mortality was not significantly higher than expected for other cancers of a priori interest — liver and stomach cancers and Hodgkin's disease. No deaths from nasal cancer were observed. The inconsistency between the results reported here and those of earlier epidemiologic studies is accentuated by the longer and probably greater exposure of this cohort to phenoxy herbicides and chlorophenols contaminated with TCDD.

Mortality from cancers of the trachea, bronchus, and lung was nonsignificantly higher in the cohort. Among the workers with 20 years or more of latency, mortality from respiratory cancer was significantly increased in the high-exposure subcohort, which had 1 year or more of exposure (SMR, 142; 95 percent confidence interval, 103 to 192) but not in the subcohort with less than 1 year of exposure (SMR, 103; 95 percent confidence interval, 62 to 161) (Table 2). SMRs for lung cancer are known to be somewhat higher in blue-collar groups than in the general U.S. population because of more cigarette smoking in the blue-collar groups.[36] However, the increased number of lung cancers in the high-exposure subcohort was probably not due to confounding by smoking, for several reasons. First, other diseases related to smoking were not more common than expected in this subco-

Table 5. Mortality from All Cancers and from Cancers of the Trachea, Bronchus, and Lung, According to Latency Period and Duration of Employment at the Study Plants.*

CAUSE/LATENCY PERIOD	DURATION OF EMPLOYMENT (YR)																TEST FOR TREND
	<5		5 TO <10		10 TO <15		15 TO <20		20 TO <25		25 TO <30		≥30		OVERALL		
	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	
All cancers																	
<10 Yr	10	85	1	18	0	0	0	0	0	0	0	0	0	0	11	64	
10 to <20 Yr	21	114	5	126	12	103	8	80	0	0	0	0	0	0	46	105	
≥20 Yr	40	138	15	140	6	70	15	98	34	134	31	116	54	135†	195	125‡	
Total	71	120	21	104	18	89	23	91	34	134	31	116	54	135†	252	116	
SRR		100		99		61		76		128		84		115			0.9
Trachea, bronchus, and lung																	
<10 Yr	3	103	1	74	0	0	0	0	0	0	0	0	0	0	4	94	
10 to <20 Yr	5	82	0	0	5	139	4	122	0	0	0	0	0	0	14	98	
≥20 Yr	11	102	2	51	2	65	3	55	12	133	18	180†	19	126	67	117	
Total	19	96	3	46	7	105	7	81	12	133	18	180†	19	126	85	112	
SRR		100		65		91		89		171		147		98			0.6

*Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records. SRR denotes standardized rate ratio.

†P<0.05. ‡P<0.01.

hort; mortality from nonmalignant respiratory disease (ICD codes 470 to 478 and 490 to 519), which is often associated with smoking, was lower than expected (15 deaths; SMR, 96; 95 percent confidence interval, 54 to 158). Second, in the exposed population with 20 years of latency, whose members presumably shared similar smoking habits, the increase was confined to the high-exposure subcohort. Third, on the basis of empirical evidence from other studies, Siemiatycki et al.[36] have shown that between a blue-collar population and the general U.S. population, confounding by smoking is unlikely to account for an excess risk of more than 10 to 20 percent. Finally, a limited adjustment in the risk of lung cancer,[37,38] based on the smoking prevalence of surviving workers at only two plants, did not substantially change our results.[25] Although confounding by smoking is unlikely to explain the higher rate of respiratory cancer in the high-exposure subcohort, it remains possible that the increase was due to confounding by occupational exposures other than TCDD. For example, asbestos may have contributed to mortality from lung cancer in the cohort, since two deaths were due to mesotheliomas.

An unexpected finding was the small but significant increase in mortality from all cancers combined. The observed increase is consistent with a carcinogenic effect of TCDD. For all cancers combined, mortality was significantly higher than expected in the entire cohort, more pronounced in the high-exposure subcohort, and increased at 9 of 12 plants. With mortality from cancers of the trachea, bronchus, and lung excluded, mortality from all remaining cancers combined was still higher than expected in the overall cohort (SMR, 117; 95 percent confidence interval, 100 to 136) and in the high-exposure subcohort (SMR, 150; 95 percent confidence interval, 118 to 189). Consequently, the increased risk for all cancers combined is not explained by smoking or by increased mortality due to cancer of the trachea, bronchus, and lung. The generation of tumors in a number of organs in animals exposed to TCDD[12,13] and the demonstration that TCDD promoted tumors in two organs[21,22] make it biologically plausible that TCDD may produce tumors in more than one organ in humans. Moreover, a significantly increased SMR for all cancers combined is unusual in occupational studies of chemical workers. Results similar to ours were observed in a study of German workers exposed to TCDD after a 2,4,5-trichlorophenol reactor accident in 1953. A subgroup of workers with chloracne (used as a surrogate for exposure) and at least 20 years of latency had an SMR of 201 (90 percent confidence interval, 122 to 315) for all cancers combined, based on 14 deaths.[39] This is the only other industrial cohort with both substantial exposure to TCDD and a long period of latency during which mortality was examined. Workers from U.S. production cohorts described in previous studies were included in the current study if they met our entry criteria.[40-42]

Two observations argue against a carcinogenic effect of TCDD. First, there was not a significant linear trend of increasing mortality with increasing duration of exposure to products contaminated with TCDD (Table 4). However, our use of duration of exposure may have misclassified the cumulative dose of some workers. In addition, a dose–response relation is generally viewed as strong evidence for an association when it is present, but as fairly weak evidence against an association when it is absent.[43] Second, our study did not directly assess the effect of exposure to TCDD alone. The workers were exposed concurrently to the chlorophenols and phenoxy herbicides that were contaminated with TCDD. In addition, they may have been exposed to numerous other chemicals while employed at the plants.

Because the exposure of our cohort was substantially higher than that of most nonoccupational populations, the estimates of effect in this study may provide an upper level of risk to be anticipated in humans. For several types of cancer previously associated with

TCDD, we found no increases above expected levels. Soft-tissue sarcoma was an exception; a ninefold increase was found among workers who were exposed for 1 year or more and who had at least 20 years of latency. Interpretation of the increased SMR is limited, however, by the small number of cases and because this cause of death was sometimes misclassified on the death certificates of the workers and in the national comparison population. Continued surveillance of the cohort may provide a firmer estimate of risk.

Mortality from all cancers combined was 15 percent higher than expected in the overall cohort. The subcohort with 1 year or more of exposure and 20 years or more of latency had a 46 percent increase in all cancers combined and a 42 percent increase in cancers of the respiratory tract. Although the study could not completely exclude the possible contribution of other occupational carcinogens or smoking, the increased mortality, especially in the subcohort with one year or more of exposure, is consistent with the status of TCDD as a carcinogen.

We are indebted to the National Institute for Occupational Safety and Health statistical clerks, Steve Green, Joyce Godfrey, and others, for their technical contributions; to representatives of the companies and unions for assistance in gathering the data for the study; to our colleagues at the Center for Environmental Health and Injury Control, Centers for Disease Control, for analysis of the serum samples; and to Lawrence Fine, David Brown, and the members of our blue-ribbon review panel for their helpful advice.

References

1. Hardell L, Sandstrom A. Case-control study: soft-tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. Br J Cancer 1979; 39:711-7.
2. Eriksson M, Hardell L, Adami HO. Exposure to dioxins as a risk factor for soft tissue sarcoma: a population-based case-control study. J Natl Cancer Inst 1990; 82:486-90.
3. Eriksson M, Hardell L, Berg N, Moller T, Axelson O. Soft-tissue sarcomas and exposure to chemical substances: a case-referent study. Br J Ind Med 1981; 38:27-33.
4. Hardell L, Eriksson M. The association between soft tissue sarcomas and exposure to phenoxyacetic acids: a new case-referent study. Cancer 1988; 62:652-6.
5. Hardell L, Bengtsson NO. Epidemiologic study of socioeconomic factors and clinical findings in Hodgkin's disease, and reanalysis of previous data regarding chemical exposure. Br J Cancer 1983; 48:217-25.
6. Hardell L, Eriksson M, Lenner P, Lundgren E. Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols and phenoxy acids: a case-control study. Br J Cancer 1981; 43:169-76.
7. Woods JS, Polissar L, Severson RK, Heuser LS, Kulander BG. Soft tissue sarcoma and non-Hodgkin's lymphoma in relation to phenoxyherbicide and chlorinated phenol exposure in western Washington. J Natl Cancer Inst 1987; 78:899-910.
8. Persson B, Dahlander A, Fredriksson M, Brage HN, Ohlson CG, Axelson O. Malignant lymphomas and occupational exposures. Br J Ind Med 1989; 46:516-20.
9. Axelson O, Sundell L, Andersson K, Edling C, Hogstedt C, Kling H. Herbicide exposure and tumor mortality: an updated epidemiologic investigation on Swedish railroad car workers. Scand J Work Environ Health 1980; 6:73-9.
10. Thiess AM, Frentzel-Beyme R, Link R. Mortality study of persons exposed to dioxin in a trichlorophenol-process accident that occurred in the BASF AG on November 17, 1953. Am J Ind Med 1982; 3:179-89.
11. Hardell L, Johansson B, Axelson O. Epidemiological study of nasal and nasopharyngeal cancer and their relation to phenoxy acid or chlorophenol exposure. Am J Ind Med 1982; 3:247-57.
12. Kociba R, Keyes D, Beyer J, et al. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. Toxicol Appl Pharmacol 1978; 46:279-303.
13. National Toxicology Program (NTP). Carcinogenesis bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin (CAS No. 1746-01-6) in Osborne-Mendel rats and B6C3F1 mice (gavage study) 1982. Washington, D.C.: Government Printing Office, 1982. (DHHS publication no. (NIH) 82-1765.)
14. Smith AH, Pearce NE, Fisher DO, Giles HJ, Teague CA, Howard JK. Soft tissue sarcoma and exposure to phenoxyherbicides and chlorophenols in New Zealand. J Natl Cancer Inst 1984; 73:1111-7.
15. Wiklund K, Holm L. Soft tissue sarcoma risk in Swedish agricultural and forestry workers. J Natl Cancer Inst 1986; 76:229-34.
16. Pearce NE, Sheppard RA, Smith AH, Teague CA. Non-Hodgkin's lymphoma and farming: an expanded case-control study. Int J Cancer 1987; 39:155-61.
17. Wiklund K, Dich J, Holm LE. Risk of malignant lymphoma in Swedish pesticide appliers. Br J Cancer 1987; 56:505-8.
18. Olsen JH, Jensen OM. Nasal cancer and chlorophenols. Lancet 1984; 2:47-8.
19. Hardell L, Bengtsson N, Jonsson V, Ericksson S, Larsson L. Aetiological aspects on primary liver cancer with special regard to alcohol, organic solvents and acute intermittent porphyria — an epidemiological investigation. Br J Cancer 1984; 50:389-97.
20. Rao MS, Subbarao V, Prasad JD, Scarpelli DG. Carcinogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the Syrian golden hamster. Carcinogenesis 1988; 9:1677-9.
21. Poland A, Palen D, Glover E. Tumour promotion by TCDD in skin of HRS/J hairless mice. Nature 1982; 300:271-3.
22. Pitot HC, Goldsworthy T, Campbell HA, Poland A. Quantitative evaluation of the promotion by 2,3,7,8-tetrachlorodibenzo-p-dioxin of hepatocarcinogenesis from diethylnitrosamine. Cancer Res 1980; 40:3616-20.
23. Esposito M, Tiernan T, Dryden F. Dioxins. 1980. Cincinnati: Industrial Environmental Research Laboratory, 1980. (EPA publication 600/2-80-197.)
24. Suskind RR, Hertzberg VS. Human health effects of 2,4,5-T and its toxic contaminants. JAMA 1984; 251:2372-80.
25. Fingerhut M, Halperin W, Marlow D, et al. Mortality among U.S. workers employed in the production of chemicals contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). NIOSH Final Report PB91125971. Springfield, Va.: National Technical Information Service, 1990.
26. Sweeney MH, Fingerhut MA, Connally LB, et al. Progress of the NIOSH cross-sectional medical study of workers occupationally exposed to chemicals contaminated with 2,3,7,8-TCDD. Chemosphere 1989; 19:973-7.
27. World Health Organization. International classification of diseases: manual of the international statistical classification of diseases, injuries, and causes of death. Geneva: World Health Organization, 1977.
28. Steenland K, Beaumont J, Spaeth S, et al. New developments in the NIOSH lifetable analysis system. J Occup Med 1990; 32:1091-8.
29. Rothman K, Boice J. Epidemiologic analysis with a programmable calculator. Washington, D.C.: Government Printing Office, 1979:30-1. (DHEW publication no. (NIH) 79-1649.)
30. Rothman KJ. Modern epidemiology. Boston: Little, Brown, 1986:229, 338-9.
31. Fox AJ, Collier PF. Low mortality rates in industrial cohort studies due to selection for work and survival in the industry. Br J Prev Soc Med 1976; 30:225-30.
32. Suit HD. Sarcoma of soft tissue. CA 1978; 28:284-95.
33. Fingerhut MA, Halperin WE, Honchar PA, Smith AB, Groth DH, Russell WO. An evaluation of reports of dioxin exposure and soft tissue sarcoma pathology among chemical workers in the United States. Scand J Work Environ Health 1984; 10:299-303.
34. Patterson DG Jr, Fingerhut MA, Roberts DR, et al. Levels of polychlorinated dibenzo-p-dioxins and dibenzofurans in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Am J Ind Med 1989; 16:135-46.
35. Percy C, Stanek E III, Gloekler L. Accuracy of cancer death certificates and its effect on cancer mortality statistics. Am J Public Health 1981; 71:242-50.
36. Siemiatycki J, Wacholder S, Dewar R, Cardis E, Greenwood C, Richardson L. Degree of confounding bias related to smoking, ethnic group, and socioeconomic status in estimates of the association between occupation and cancer. J Occup Med 1988; 30:617-25.
37. Axelson O. Aspects on confounding in occupational health epidemiology. Scand J Work Environ Health 1978; 4:98-102.
38. Steenland K, Beaumont J, Halperin W. Methods of control for smoking in occupational cohort mortality studies. Scand J Work Environ Health 1984; 10:143-9.
39. Zober A, Messerer P, Huber P. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. Int Arch Occup Environ Health 1990; 62:139-57.
40. Zack JA, Suskind R. The mortality experience of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident. J Occup Med 1980; 22:11-4.
41. Zack JA, Gaffey WR. A mortality study of workers employed at the Monsanto Company plant in Nitro, West Virginia. Environ Sci Res 1983; 26:575-91.
42. Ott MG, Olson RA, Cook RR, Bond GG. Cohort mortality study of chemical workers with potential exposure to the higher chlorinated dioxins. J Occup Med 1987; 29:422-9.
43. Monson RA. Occupational epidemiology. Boca Raton, Fla.: CRC Press, 1990:100.

750 30# 1012082 22:60 01/20 Attachment 7

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE 4 February 1987

SUBJECT 2,3,7,8-TCDD in Aquatic Environments

FROM Philip M. Cook, Ph.D. PMC
Chief, Hazardous Waste Research Branch, ERL-Duluth

TO Jim Cummings
Office of the Assistant Administrator
for Solid Waste and Emergency Response

This memorandum is provided in response to your request for an update on the state of knowledge concerning 2,3,7,8-TCDD in aquatic environments. A considerable amount of new information is being generated and much will be reported during 1987. Most of the information I can provide results from our own research. I believe you have already received reprints for research results already published.

I reported bioconcentration factor (BCF) determinations for 2,3,7,8-TCDD, 1,2,3,4-TCDD, 1,3,6,8-TCDD and 1,3,7,9-TCDD at the Society for Environmental Toxicology and Chemistry meeting last November. A journal publication is in preparation. The EPA Water Quality Criteria Document presently uses a value of 5000 for the 2,3,7,8-TCDD BCF. We determined a value of 66,000 for carp and 97,000 and 159,000 for fathead minnows at two different exposure concentrations. Our BCF data for the four TCDD isomers is summarized in the attached table. We concluded from this study that ---

1. BCFs for different TCDD isomers vary greatly as expected from field monitoring data.

2. TCDD isomers other than 2,3,7,8-TCDD have lower BCFs than predicted on the basis of structure or log Kow due to more rapid rates of elimination.

3. Differences in rates of metabolism probably explain differences in TCDD rates of elimination and thus BCFs.

4. The gill uptake efficiencies for the four TCDD isomers studied appear to be similar despite structural differences and different uptake rate measurements attributed to large differences in elimination rates.

5. Approximately 90% of the TCDD in the fish exposure water was associated with particulate and dissolved organic matter. Thus, BCFs calculated on the basis of organic carbon free TCDD in the water would be ten times greater.

EPA Form 1320-6 (Rev. 3-76)

6. The Water Quality Criteria Document BCF value for 2,3,7,8-TCDD is very low because previously reported BCF determinations were made on the basis of very short exposure periods, inadequate depuration data, static exposure conditions, overestimates of water exposure concentrations, and other factors which lower the estimate of equilibrium fish concentrations with respect to actual water concentrations.

7. 2,3,7,8-TCDD is so toxic to fish that BCF determinations have not yet been made over long exposure periods without toxic effects and mortality occurring. No-effect levels are likely to be less than 10 ppq total 2,3,7,8-TCDD in water and possibly less than 1 ppq if only "dissolved" 2,3,7,8-TCDD is considered in the bioaccumulatable and toxic component.

8. 2,3,7,8-TCDD was lethal to carp at an accumulated dose of 2 ug/Kg. Rainbow trout appear to be a little more sensitive. This toxicity is comparable to the 1 ug/Kg LD50 found for the guinea pig, the most sensitive mammalian species known. Fathead minnows appear to be at least five times less sensitive than carp or rainbow trout.

It is likely that fish bioaccumulation of PCDDs and PCDFs is greatly influenced by food chain links to contaminated sediments and contact time of fish with sediment. Field monitoring data generally supports this premise. For example, fish collected from field surveys when analyzed for all TCDD isomers generally only have detectable amounts of 2,3,7,8-TCDD despite the presence of greater amounts of other TCDD isomers in contaminated sediments. Many of the TCDD isomers have relatively low bioaccumulation potential as seen from our BCF measurements for 1,2,3,4-TCDD and 1,3,7,9-TCDD and thus are not likely to be detected. 1,3,6,8-TCDD, however, would be expected in the fish in detectable levels if uptake from water was the major route for bioaccumulation. The lack of 1,3,6,8-TCDD in the fish is consistent with a kinetic effect involving decreasing amounts of 1,3,6,8-TCDD with respect to 2,3,7,8-TCDD in each step along the food chain to a fish and the absence of significant uptake from water.

For higher chlorinated PCDD and PCDF congeners, differences in elimination rates from fish and their food chain organisms create similar preferential bioaccumulation of 2,3,7,8-substituted planar molecules which are likely to be metabolized at a slower rate. In addition, as molecular weight and size increase with increasing degree of chlorination, it is apparent that the rate uptake from water across the gills decreases. Absorption efficiency from ingested material is also probably less for higher chlorinated congeners.

The net result of the above considerations is that many PCDDs and PCDFs found in sediments are not detectable in fish. The attached table on "Congener Dependent Bioavailability of PCDDs and PCDFs"

demonstrates how this same effect occurs for laboratory exposure of fish to municipal incinerator fly ash. The effect is more extreme when the "food chain chromatography" effect is present and longer exposure times are involved (much longer time required to reach steady state) as with the fish exposed to sediment in a reservoir. The compounds included in the table are all members of the "biosignificant fraction of PCDDs and PCDFs in that they do appear to bioaccumulate, are all 2,3,7,8-substituted and thus all have significant toxic potential. We developed a simple expression called the "bioavailability index" (BI) for comparing relative bioaccumulation tendencies for different chemicals associated with different solid wastes on sediments. The BI is simply the ratio of chemicals accumulated per gram of fish lipid to the amount present per gram of organic carbon in the solid material the fish are exposed to. The BI can be normalized to a value of 1.0 for 2,3,7,8-TCDD in order to make comparison of the other PCDD and PCDF congener's BIs easier. Although the magnitudes of the fly ash and sediment BIs cannot be directly compared due to great differences in the fish exposures, the normalized BIs for both fly ash and sediment show the same trends. For both PCDDs and PCDFs the normalized BIs decrease as the degree of chlorination increases. There also appears to be a tendency for 2,3,7,8-TCDF to be less bioaccumulable than 2,3,7,8-TCDD. The penta-CDD and -CDF results for the sediment seem divergent and will be rechecked before this data is published in this form. We will soon have much more of this kind of data when results are obtained for Lake Ontario sediments and paper mill sludges.

EPA is frequently faced with the question of what fish TCDD contamination levels will result from known or projected environmental contamination levels. The use of a BCF value, no matter how accurate, for predicting fish residues has a major limitation in that environmental TCDD water concentrations can never be detected even with the most sensitive techniques. Even if water measurements could be made, it would be difficult to determine what fraction of TCDD in water is not associated with dissolved or particulate organic carbon so that a laboratory derived BCF could be applied. An alternative approach is to use expected equilibrium partitioning relationships for sediment and fish to predict maximum levels of fish contamination and rely on site-specific sediment to fish TCDD ratios to determine more realistic "approach to steady-state" relationships likely to exist between sediments and fish. This should be done on the basis of partitioning between organic carbon in sediment and lipid in fish. In theory there should be a simple 1:1 equilibrium relationship between sediment organic carbon and lipid concentrations for very hydrophobic organic compounds such as 2,3,7,8-TCDD which are very slowly metabolized and eliminated from the organism. There are data for compounds such as PCBs which indicate approximately a four-fold preference of these compounds for lipids over organic carbon in sediment. Our 2,3,7,8-TCDD BI value of .27 for sediment is 4X less than the theoretical partitioning value of 1.0 and ~~8X~~ 16X less than the lipid preference value of 4.0 at least in part because steady-state conditions were not reached when the fish were exposed to the sediment.

In many environmental situations expected steady-state relationships between fish bioaccumulation levels and sediment contamination levels will

44

not be reached. Kinetic models and appropriate rate constants are needed to accurately predict fish bioaccumulation levels. When an aquatic ecosystem has a constant input of TCDD so that surface sediment concentrations are relatively constant, fish concentrations will approach a steady-state level dependent on rates of uptake from water, food and contact with sediment. For Lake Ontario we are investigating sediment to fish TCDD ratios under present conditions so that remedial actions for Superfund sites and other sources of TCDD can be evaluated with respect to changes in fish residues which will result in the future. That is, if sediment TCDD levels are decreased or increased in the future through man's activities, we should be able to predict eventual changes in fish contamination levels when a new "approach to steady-state" system results. In Lake Ontario our preliminary data indicates that fish lipids have only about 5% of the TCDD concentration found in the organic carbon fraction of the surface sediments. An extensive survey of sediment and fish TCDD levels throughout Lake Ontario is scheduled for this summer.

CONGENER DEPENDENT BIOAVAILABILITY OF PCDDs AND PCDFs IN FLY ASH AND SEDIMENT

Compound	Fly Ash pg/g Carbon	Fish pg/g Lipid	BI	Normalized BI	Sediment pg/g Carbon	Fish pg/g Lipid	BI	Normalized BI
2,3,7,8-TCDD	1.3×10^5	93	7.4×10^{-4}	1.00	5430	1500	.27	1.00
2,3,4,8-TCDF	1.7×10^5	95	5.7×10^{-4}	.77	5870	300	.06	.22
1,2,3,7,8-PeCDD	1.2×10^6	540	4.3×10^{-4}	.58	1000	60	.06	.22
2,3,4,7,8-PeCDF	7.3×10^5	180	2.5×10^{-4}	.34	190	55	.28	1.04
1,2,3,6,7,8-; 1,2,3,4,7,8-H_xCDD	5.0×10^6	1300	2.6×10^{-4}	.35	5800	200	.04	.15
1,2,3,6,7,8-H_xCDF	8.2×10^5	290	3.5×10^{-4}	.47	560	~~200~~ 12	.04	.14
1,2,3,4,6,7,8-H_pCDD	1.6×10^7	1300	7.8×10^{-5}	.11	71000	340	.005	.018
1,2,3,4,6,7,8-H_pCDF	3.7×10^6	340	9.2×10^{-5}	.12	9400	31	.003	.012

Attachment 8

Environmental Toxicology and Chemistry, Vol. 7, pp. 47-62, 1988
Printed in the USA. Pergamon Journals Ltd.

555

TOXICITY AND BIOCONCENTRATION OF 2,3,7,8-TETRACHLORODIBENZODIOXIN AND 2,3,7,8-TETRACHLORODIBENZOFURAN IN RAINBOW TROUT

PAUL M. MEHRLE,* DENNY R. BUCKLER, EDWARD E. LITTLE, LARRY M. SMITH, JIM D. PETTY, PAUL H. PETERMAN and DAVID L. STALLING
National Fisheries Contaminant Research Center, U.S. Fish and Wildlife Service, Columbia, Missouri 65201

G. M. DE GRAEVE and JAMES J. COYLE
Battelle Laboratories – Columbus, Columbus, Ohio 43201

WILLIAM J. ADAMS
Monsanto, St. Louis, Missouri 63167

(*Received* 25 *March* 1987; *Accepted* 14 *July* 1987)

Abstract – Among the most toxic isomers of polychlorinated dibenzodioxins and polychlorinated dibenzofurans, two groups of toxic aromatic compounds, are 2,3,7,8-tetrachlorodibenzodioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF). We examined the chronic toxicity of these compounds to rainbow trout (*Salmo gairdneri*). The fish (0.38 ± 0.09 g) were continuously exposed in an intermittent-flow proportional diluter for 28 d to 0, 38, 79, 176, 382, and 789 pg TCDD/L (parts per quadrillion) or to 0, 0.41, 0.90, 1.79, 3.93, and 8.78 ng TCDF/L (parts per trillion); exposures to each chemical were followed by a 28-d depuration phase. TCDD had significant effects on survival, growth, and behavior during the exposure and depuration phases. The no observed effect concentration was lower than the lowest exposure concentration of 38 pg/L. The average measured BCF at 28 days was 26,707. The estimated bioconcentration factor at steady-state equilibrium was 39,000 in the lowest exposure concentration where fish were least affected. TCDF, like TCDD, induced similar effects on survival, growth and behavior. The no observed effect concentration, based on survival, was 1.79 ng/L; that based on growth was 0.41 ng/L. The measured bioconcentration factor was 6,049 in fish exposed to 0.41 ng/L, and 2,455 in fish exposed to 3.93 ng/L for 28 d.

Keywords – Dioxin Furan 2,3,7,8-tetrachlorodibenzodioxin (TCDD) Rainbow trout 2,3,7,8-tetrachlorodibenzofuran (TCDF)

INTRODUCTION

Polychlorinated dibenzofurans (PCDFs) and polychlorinated dibenzo-*p*-dioxins (PCDDs) are two groups of toxic compounds composed of 135 and 75 individual isomers, respectively. Certain of these isomers are extremely toxic, particularly those with chlorine substituents in the 2,3,7,8-positions of the aromatic rings. PCDFs occur as trace contaminants in polychlorinated biphenyls (PCBs) and are sometimes formed in significant quantities from pyrolysis or incomplete combustion of PCBs [1]. Isomer specific PCDFs and PCDDs also occur as contaminants in the manufacture and pyrolysis of certain chlorinated phenols [2]. During combustion of these formulations, PCDDs are formed primarily from thermal dimerization and conversion of chlorinated phenoxyphenols, whereas PCDFs are formed from chlorinated diphenyl ethers. PCDDs and PCDFs have also been found in fly ash of municipal waste incinerators [3].

The isomers 2,3,7,8-tetrachlorodibenzodioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF) have been reported as contaminants in fish and sediment. Both have been detected in fish from the Great Lakes [4–6], and residues have been found in resident and migratory fish, crustaceans and sediment in the Chesapeake Bay area [7] and in industrialized and heavily populated areas of the northeastern United States [8]. The concentrations of these compounds in fish vary widely from low pg/g to ng/g quantities, and those of

*To whom correspondence may be addressed.

TCDF are usually higher than those of TCDD. In certain areas of the Great Lakes and the northeastern United States (Newark Bay, Passaic River), TCDD residues in fish and crustaceans exceed the U.S. Food and Drug Administration (FDA) "levels of concern" of 25 pg/g and 50 pg/g, respectively [8,9].

The chronic toxicity and bioconcentration of TCDD and TCDF in aquatic species have not been elucidated. Helder [10,11] reported that exposing fertilized eggs of rainbow trout (*Salmo gairdneri*) for 96 h to TCDD concentrations of 0.1 ng/L significantly decreased the growth of the resulting fry, and that exposing rainbow trout fry for 96 h to 10 and 100 ng/L TCDD retarded growth, caused histological changes in tissues and delayed mortality. Miller et al. [12] reported the toxicity and pathologic changes induced by short-term exposures of guppies (*Poecilia reticulata*) and coho salmon (*Oncorhyncus kisutch*) to TCDD. Coho salmon exposed to 56 pg/L and 1,000 ng/L for 24 h exhibited delayed mortality. Cooper et al. [13] observed delayed development and decreased survival in Japanese medaka (*Oryzias latipes*) exposed to TCDD concentrations of 6 to 500 ng/L. The oral toxicity and metabolism of TCDD in rainbow trout and yellow perch (*Perca flavescens*) were recently reported by Kleeman et al. [14,15]. In rainbow trout exposed for 6 h to 107 ng/L TCDD, followed by a 139-d depuration period, Branson et al. [16] estimated the bioconcentration factor (BCF) to be 9,270 and the elimination half-life to be 58 d. Significant delayed effects were similar to those reported by Miller et al. [12]. No similar studies have been conducted to characterize the toxicity and bioconcentration of TCDF in aquatic species.

Because of the lack of chronic toxicity data involving continuous low-level exposures of fish to TCDD and TCDF, we attempted to measure the chronic toxicity of these two compounds to rainbow trout. Their effects on survival, growth, and behavior were evaluated during a 28-d continuous exposure followed by a 28-d depuration phase. Uptake and depuration kinetics and BCFs for TCDD and TCDF were also evaluated.

METHODS

Test organisms

Eyed eggs of rainbow trout obtained from the Erwin (Tennessee) National Fish Hatchery came from two-year-old spawners of the "Fish Lake" strain; they were transferred to the National Fisheries Contaminant Research Center (NFCRC), Columbia, Missouri, where they hatched on 11 April 1985. About 2,000 swim-up fry produced from the eggs were shipped by air to Battelle Laboratories, Columbus, Ohio, on 2 May 1985. Mortality associated with shipping was less than 5%.

The fish were maintained in reconstituted water in 1,200-liter fiberglass tanks until the study was begun. The fish were held at a temperature of 11°C (±1°C), and were fed Tetramin floating flake food ad libitum. Analysis of the food showed no detectable quantities of TCDD (detection limit, less than 0.06 ng/g), TCDF (detection limit, less than 0.04 ng/g) or other organochlorine compounds.

Experimental approach

A flow-through diluter was used to continuously expose rainbow trout for 28 d to five duplicated concentrations each of [^{3}H]TCDD and TCDF plus duplicated controls. After the exposure period, toxicant input to the exposure chambers was terminated and the fish were held in laboratory water under flow-through conditions in the same test chambers during the 28-d depuration period. The fish were fed Tetramin floating flake food ad libitum throughout the study.

Fifty fish (0.38 ± 0.09 g each) were stocked in each aquarium. Samples of fish for residue analyses were taken on days 7, 14, 21, and 28 of the exposure phase and on day 28 of the depuration phase. To determine initial background concentrations of TCDD and TCDF, 30 fry with no previous TCDD and TCDF exposure history were weighed, measured, frozen, and analyzed for TCDD and TCDF. Fish collected for residue analyses were frozen until the time of analysis.

Daily survival records were maintained throughout the study. In addition, we recorded daily observations of swimming behavior, feeding behavior, location and position in the exposure tank, external lesions, and deformities.

Diluter and toxicant exposure system

The diluter system used in the study was constructed at NFCRC and installed in the West Jefferson Environmental Research Laboratory, Battelle Laboratories, Columbus, Ohio. The system consisted of two separate proportional flow-through diluters in a temperature-controlled waterbath. Both the diluter and waterbath were enclosed in a vented Plexiglas structure to reduce environmental exposures resulting from volatilization of the compounds. Each diluter delivered five concentrations (50% dilutions) of each compound (plus water for controls) into duplicate tanks containing

15 liters of water. Over the course of the study the diluter cycle rate varied between 2.4 and 3.0 cycles per hour; the replacement volume was 500 ml per replicate tank per cycle. The approximate water turnover rate in the exposure tanks was 2.4 times per day. The maximum fish loading in each test tank throughout the study was about 1.3 g/L and the maximum fish loading was 0.5 g/L of water passing through the tank in 24 h. Excess food and fecal matter were removed daily. Daily records of diluter operations were maintained throughout the studies. Nominal exposure concentrations (ng/L) were 0 (control), 0.115, 0.231, 0.463, 0.925, and 1.85 for TCDD; and 0 (control), 1.3, 2.7, 5.3, 10.6, and 21.3 for TCDF. Water temperature in the exposure tanks was maintained at 12 ± 1°C.

The combined effluents from the diluter system were recycled through two columns containing activated charcoal to remove TCDD and TCDF from solution. GC-MS and radiometric analyses were used to monitor the effluent for TCDD and TCDF.

Toxicants

Monsanto Company (St. Louis, MO) supplied the TCDD and TCDF used in the studies. The [^{3}H]TCDD (99+% pure; 22% unlabeled, 42% monotritiated and 36% ditritiated) used had a specific activity of 2.81×10^5 dpm/ng (0.128 μCi/ng) as determined by radiometric and GC-MS analyses. The TCDF provided by Monsanto was originally obtained from KOR, Inc. (Cambridge, MA), and was 98+% pure as determined by GC-MS.

Preparation of stock solutions

All glassware used to prepare stock solutions was rinsed several times with reagent-grade solvents. Carrier solvent for the compounds was acetone (Baker-analyzed). The [^{3}H]TCDD was diluted with acetone to a concentration of 36 ng/L. The stock solution was analyzed by GC-MS and by liquid scintillation radiometric analysis. Toxicants were delivered by an automatic pipetting system (Micromedic) that provided 0.05 ml/L or less of acetone to each exposure concentration. The TCDF was diluted with acetone to a measured concentration of 407 ng/L. This stock solution was used throughout the study and was delivered to exposure tanks by Micromedic pipetting systems. The acetone concentration delivered to each tank was 0.05 ml/L or less.

Water chemistry

In an effort to reduce the number of instruments coming in contact with the toxicants, we performed routine water chemistry only on the control chambers of both compounds, and only once during the exposure phase and once during the depuration phase. Alkalinity was measured by potentiometric titration with 0.02 N H_2SO_4 to pH 4.5, and hardness was titrated with EDTA according to standard methods [17]. We used an Orion

Table 1. Concentration of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in exposure water as measured by radiometric and GC-MS analyses

		TCDD nominal concentration (pg/L)					
Day	Measurement	0	115	231	463	925	1,850
1	pg/L (^{3}H)[a]	1.2	31	62	130	280	527
	pg/L (GC-MS)	—[b]					—[b]
7	pg/L (^{3}H)[a]	1.4	41	78	169	359	705
	pg/L (GC-MS)	<25[c]					840
14	pg/L (^{3}H)[a]	1.1	34	69	146	298	606
	pg/L (GC-MS)	<15[c]					730
21	dpg/L (^{3}H)[a]	0.7	41	87	200	466	970
	pg/L (GC-MS)	<15[c]					1,220
28	pg/L (^{3}H)[a]	1.3	44	99	234	507	1,135
	pg/L (GC-MS)	<20[c]					1,400
$\bar{x}$ pg/L (^{3}H) ± SD		1.1	38 ± 5	79 ± 15	176 ± 42	382 ± 101	789 ± 256
$\bar{x}$ pg/L (GC-MS) ± SD		<15[c]					1,048 ± 315

[a]Measured by radiometric analyses for [^{3}H]TCDD. Conversion of dpm/L to pg/L (^{3}H) based on specific activity of 2.81×10^5 dpm ^{3}H/ng TCDD.
[b]Not determined.
[c]None detected (less than minimal detectable limits).

digital pH meter to measure pH, a Sybron/Barnstead Model pM-70CB conductivity bridge to measure conductivity and a Varian Model 3700 gas chromatograph to measure ammonia. Water chemistry determinations were as follows: hardness, 153 ppm; alkalinity, 88 ppm; pH, 7.7; conductivity, 215 μohms; un-ionized ammonia, 0.0013 mg/L; and dissolved oxygen, 65 to 85% saturation.

Analyses of exposure water

During the exposure phase of the study, samples for GC-MS analysis were extracted from the TCDD control and highest exposure concentrations and from all TCDF exposure concentrations on days 0, 7, 14, 21, and 28. On each day immediately following the date of sample collection for GC-MS, we took samples for radiometric TCDD analyses from all exposure chambers. Radiometric analyses of all water extracts were conducted at Battelle Laboratories. Water from replicate *A* was sampled on days 0, 7 and 21, and water from replicate *B* on days 1, 14, and 28. On day 7 of the depuration period, the TCDD control and highest concentrations were measured radiometrically, and the TCDF control and highest concentrations were sampled for GC-MS analysis. On day 7 of the depuration phase, only 92 pg/L TCDD was measured in water from the highest TCDD exposure chamber, and 0.56 ng/L TCDF in the highest TCDF exposure chamber. The TCDD and TCDF exposure concentrations measured throughout the exposures are shown in Tables 1 and 2.

Water samples of a volume necessary to provide an adequate amount of analyte were collected from the diluter tanks with solvent-washed glassware and transferred directly to a glass separatory funnel. The water sample was then spiked with the appropriate internal standard solution containing $[^{13}C_{12}]$2,3,7,8-TCDD and $[^{13}C_{12}]$2,3,7,8-TCDF at 4.0 pg/μl in acetonitrile. The water sample was extracted three times with 50-ml portions of methylene chloride (CH_2Cl_2) and the extracts were passed through a column (about 2 × 6 cm) of anhydrous, granular sodium sulfate to break emulsions and remove suspended water. The extract was then rotary-evaporated to a low volume and transferred with three or four portions of CH_2Cl_2 to a glass ampoule, blown to dryness with nitrogen and flame-sealed.

The sample was removed from the opened ampoule with four 1.5-ml portions of 20% CH_2Cl_2 in hexane onto a dual column arrangement of 2 × 0.5 cm 40% H_2SO_4 on silica gel (SA-SG) in the first column and 15 mg Amoco PX-21 activated carbon dispersed in 150-mg glass fibers (CGF) [18]. The efficiency of transfer of $[^3H]$TCDD from these ampoules in the presence of solid residues was determined to exceed 99%. The SA-SG column was then discarded and the CGF column slightly pressurized to move the sample entirely onto the carbon adsorbent. We applied 15 ml CH_2Cl_2 to the CGF column at about 2 ml/min under pressure, and discarded the eluate.

The analyte, either $[^3H]$TCDD or TCDF, was recovered from the CGF by back-flushing with 15 ml toluene. The toluene was removed by rotary evaporation in a waterbath at 65 to 70°C under a 9.8-cm vacuum (sample taken just to dryness).

At this point, we added 2-(4-biphenyl)-6-phenylbenzoxazole (PBBO) to perform radiometric analyses on each sample or aliquots thereof containing $[^3H]$TCDD. The quench curve for counting efficiency was determined by the sealed tritium standard (HAV3612), corrected for decay, as the reference point, and replicate analyses of samples of $[^3H]$TCDD at various quench values. We used the equation, dpm = cpm/0.85 × S, where dpm is disintegrations per minute, cpm is counts per minute and S is the quench value.

Table 2. Concentration (ng/L) of 2,3,7,8-tetrachlorodibenzofuran (TCDF) as measured by GC-MS in exposure water during a 28-d chronic toxicity study with rainbow trout

Day	TCDF nominal concentration (ng/L)					
	0	1.3	2.7	5.3	10.6	21.3
1	0.02	0.38	0.70	1.40	3.20	6.60
7	<0.06	0.33	0.91	1.98	3.84	9.04
14	<0.029	0.44	0.86	1.56	3.82	7.97
21	<0.025	0.37	0.93	1.93	4.19	10.4
28	0.017	0.52	1.10	2.10	4.60	9.9
$\bar{x}$ ± SD	<0.02	0.41 ± 0.07	0.90 ± 0.14	1.79 ± 0.30	3.93 ± 0.52	8.78 ± 1.53

We applied the sample to alumina (Bio-Rad AG4 acid alumina, 3.5 ml = 3.65 g activated at 190°C) packed in a 5-ml graduated pipet with solvent reservoir using multiple washings of hexane totaling 5.0 ml. The column was then washed with 10 ml 5% CH_2Cl_2 in hexane (discarded) and the analyte recovered with 10 ml 20% CH_2Cl_2/hexane. The sample was evaporated just to dryness by rotary evaporation and transferred with three 1-ml portions of CH_2Cl_2 to a conical vial. The solvent was gently removed under a stream of nitrogen. The sample was then dissolved in a minimum of 5 μl *o*-xylene in preparation for GC-MS analysis.

We carried out the GC-MS analysis on a Finnigan 4023 quadrupole mass spectrometer (EI mode at 35 eV), using a 30 m × 0.25 mm DB-5 (0.25 μm) column (J&W Scientific, Inc., Rancho Cordova, CA) and helium carrier gas at about 35 cm/s. The temperature program was 120°C, hold 1 min, increase 20°C/min to 210°C, 5°C/min to 270°C and 4.5°C/min to 300°C. Selected ions monitored were m/z 304, 306, and 308 summed for 2,3,7,8-TCDF; m/z 316, 318 and 320 summed for $[^{13}C_{12}]$2,3,7,8-TCDF; m/z 320, 322, 324 and 326 summed for $[^3H]$2,3,7,8-TCDD; and m/z 332, 334, and 336 summed for $[^{13}C_{12}]$2,3,7,8-TCDD. We calibrated the internal standard solutions by preparing calibration mixtures of these standards with quantitative standards of native 2,3,7,8-TCDD and 2,3,7,8-TCDF prepared at the NFCRC and 2,3,7,8-TCDD solution as a U.S. Environmental Protection Agency (EPA) quality assurance material (Ref. No. 20603; EPA, Las Vegas, NV). We assumed equal integrated GC-MS responses for the molecular ions of native and $[^3H]$2,3,7,8-TCDD. The level of tritiation of the $[^3H]$2,3,7,8-TCDD computed from the molecular ion abundances measured by GC-MS gave a mole fraction of tritium of 27.3% and a specific activity of 2.15×10^5 dpm/ng. We calculated the specific activity, using the GC-MS–determined concentration and measured activity, to be $2.81 \pm 0.07 \times 10^5$ dpm/ng (triplicate analyses).

Collection of fish for residue analyses

Fish for whole-body TCDD and TCDF residue analyses were collected during the exposure period on days 0 (prior to exposure), 7, 14, 21, and 28, and on day 56 (after 28 d of depuration). When we removed fish from the exposure tanks for residue analyses on day 7, we removed unequal numbers from different tanks to reduce the number of fish remaining in all tanks to 42, and thus reduce the biomass and avoid potential overloading in the exposure tanks.

Fish for residue analyses were collected randomly from the exposure tanks for each toxicant. Individual weights and lengths were measured for fish collected on day 7 of the exposure and on day 28 of the depuration phase. Fish collected on other sampling days were weighed but not measured for length. All fish were blotted dry before they were weighed and were then wrapped in hexane-rinsed aluminum foil, placed in labeled screw-topped glass vials and stored at −10°C until residue analyses were begun.

GC-MS determinations of TCDD and TCDF in fish

Analyses of fish samples were performed by the method of Smith et al. [19]. The GC-MS conditions and spiking procedures were as described above for the analysis of the water samples.

Sample extracts that required radiometric analysis for $[^3H]$TCDD were rotary-evaporated and brought to 10.0-ml volumes; an appropriate aliquot (usually 1.00 ml) was then taken for scintillation counting. The quench values for the aliquots of the fish extracts were uniformly near the minimum (*S* values of 0.65), as observed for analytical standards. Negative and positive control samples were routinely included in the radiometric determinations of $[^3H]$TCDD and established so that there was no procedural background contribution in these determinations.

The internal standard procedure for GC-MS determinations of both $[^3H]$TCDD and TCDF provided internal quality control for overall accuracy of quantitation. In all reported determinations of these analytes, the criteria attained were relative GC retention time (±1 scan number in 1,160 or ±0.001 relative retention units) and correct ion abundances of the three or four molecular ion cluster members (±10% of theoretical value). The limit of quantitation was five times the signal-to-noise ratio and the limit of detection was three times the signal-to-noise ratio. The molecular ion cluster for $[^3H]$TCDD was significantly distorted from that produced by the native populations of ^{35}Cl and ^{37}Cl. Relative ion abundances of m/z 320, 324, and 326 were 24, 75, 100 and 70%, respectively. This pattern remained constant throughout the study, indicating no significant exchange of hydrogen for tritium in TCDD during the exposure. This observation also demonstrated no significant background of native 2,3,7,8-TCDD in any of the samples, because the presence of

native dioxin would have had an easily discernible effect on this pattern. Procedural background controls showed no 2,3,7,8-TCDD (limit of quantitation, less than 0.006 ng/g) by radiometric analysis and no TCDF (limit of quantitation, less than 0.06 ng/g) by GC-MS. The limit of quantitation for [^{3}H]TCDD was also less than 0.06 ng/g by GC-MS.

Analyses of fish food were carried out by the same procedure used for fish samples, and analyses of [^{3}H]TCDD and TCDF stock solutions were performed by direct dilution before analysis.

We computed percent recoveries of [^{13}C]TCDD and [^{13}C]TCDF internal standards by the less precise external standard technique, using the responses of the [^{13}C]TCDD and [^{13}C]TCDF internal standards; the recoveries of [^{13}C]TCDF and [^{13}C]TCDD, respectively, are listed here according to the various matrices: stock solutions, 71 ± 30% and 71 ± 33%; exposure water, 134 ± 55% and 109 ± 52%; fish, 101 ± 37% and 117 ± 46%; all matrices combined, 112 ± 51% and 105 ± 47%.

Determination of total concentration of [^{3}H]TCDD species in fish by biological material oxidation procedure

Determinations of total body burden of [^{3}H]TCDD residues in fish, as opposed to extractable residue, were made on homogenate aliquots of individual fish by the method of total burn, followed by liquid scintillation radiometric analysis of the combustion products. A Harvey Biological Materials Oxidizer (Model OX-100, R. J. Harvey Instrument Corp., Hillsdale, NJ) and a Harvey tritium cocktail (lot No. DC02) were used in the procedure. The combustion/trapping efficiency was 84% with triplicate analyses of a [^{14}C]PCB standard. Cryogenic traps and dry ice and methanol were used to trap the tritiated water produced in the combustion. The combustion/trapping efficiency observed for a standard of [^{3}H]TCDD was 89 ± 3% for spiked fish tissue. The scintillation counting efficiency when the tritium cocktail was used was 37%, and radioactivity was calculated from scintillation analysis using the equation, dpm = cpm/0.64 × S, after subtraction of 50 cpm background.

Samples that had previously been weighed, wrapped in filter paper and aluminum foil and stored in the freezer were transferred along with the approximately 1-cm^2 pieces of filter paper to the quartz combustion boats. Before combustion of samples, we ran a series of blanks and spikes to ensure that performance was satisfactory. Each sample was combusted twice into the cryogenic trap, which contained about 0.5 ml residual methanol. The glass elbow connecting the trap and oxidation chamber was heated with a hot air gun during the procedure to prevent loss by condensation. The condensed residue was transferred from the trap to a scintillation vial with three 5-ml portions of the cocktail. We then washed the trap thoroughly three times with methanol, leaving about 0.5 ml to aid in the next trapping. Because previous tests had indicated that carryover between sample combustions was a potential problem, blank combustions were performed after each sample and control. Scintillation analysis of the blanks showed that carryover was negligible.

Observation of fish for behavioral responses

The behavioral responses of rainbow trout were assessed daily during the TCDD and TCDF exposures. A checklist of behavioral reactions modified from Drummond et al. [20] was used to systematically document and characterize abnormal responses. The responses included coloration, activity (hyperactive, lethargic), excitability by external stimuli (hyperactive, unresponsive), location in aquaria, mode of swimming (head-up, frequent sinking and rising, swimming on side, swimming on back, free swimming), feeding, and morphological observations (bent spine, fin erosion). Observations were made each day by the same observer at the time of feeding.

An aberrant behavioral reaction was recorded when at least one fish in a given treatment responded in a manner that obviously differed from that of controls. Although no attempt was made to quantify the number of fish responding abnormally, an overall measure of the onset, duration and sequence of behavioral changes was made from the systematic daily observations.

Statistical analyses

Daily mortality was analyzed by one-way analysis of variance on the arc-sin transformed values. Differences among means were determined using Fisher's least significant difference (LSD) procedure [21].

Growth as measured by weight or length was analyzed by analysis of variance, including the effects of treatment, replicate within treatment, day, treatment × day, and replicate (treatment × day). Since the replicates, not the individual fish, were the experimental unit, replicate within treatments was used as the error term for testing the effect of treatment, and replicate (treatment × day) was used as the error term for testing the effects of day and treatment × day. We deter-

mined differences among means by calculating a t statistic, using the standard error of the difference for a split-plot design. For growth of TCDD-exposed fish during the depuration phase, we tested the control and lowest exposure concentration groups for equal population means, using a two-sample t test adjusted for unequal variance where appropriate [21].

The cumulative number of days on which fish showed abnormal behavior, from the time of induction to the day of depuration, was analyzed by simple regression against concentration, to provide an estimate of the behavioral responses to chemical exposure.

The BIOFAC computer program [22] was used to estimate the bioconcentration kinetics for TCDD and TCDF. Data from only the exposure phase in each study were used to estimate the kinetics because the number of fish residue samples available during the depuration phase was not adequate. In addition, the fish were held in their original exposure test tanks during the depuration phase, which resulted in the presence of the toxicants in the water because they desorbed from the glass aquaria. Because water concentration measurements and sufficient fish to sample during the depuration phase were not available, we were unable to use data from the depuration phase to estimate rate constants for the toxicants.

To estimate the 56-d LC50 value for TCDD, we computed a multiple-regression model to determine the relationship between percent mortality (arc-sin transformation) to concentration and time of exposure. The linear statistical model contained the effects of linear concentration (CL), days of exposure linear (DL), concentration quadratic (CQ), and day of exposure quadratic (DQ): CL * DL, CL * DQ, CQ * DL and CQ * DQ [21]. We used a quadratic function relationship to estimate the concentration of TCDD at a constant mortality (50%) and period of exposure (56 d).

RESULTS AND DISCUSSION

Mortality

TCDD induced significant mortality in rainbow trout within 14 d of exposure in the highest exposure concentration (789 pg/L), and there was a trend toward increased mortality in fish exposed to 176 and 382 pg/L (Table 3). After 28 d of exposure, significant mortality was evident in the three highest exposure concentrations; the no observed effect concentration (NOEC) was 79 pg/L. Although no mortality was observed, fish in the 38 and 79 pg/L exposure groups were obviously stressed, as judged by reduced growth and behavioral responses. Only rainbow trout in the control group and the three lowest exposure concentrations were observed during the 28-d depuration phase of the study; fish in the two highest exposure concentrations were excluded because the survivors were few and obviously stressed. Significant mortality continued to occur throughout the depuration period in fish previously exposed to 38, 79, and 176 pg/L. There was no apparent recovery in the fish during the 28-d depuration period in clean

Table 3. Cumulative mortality (%) in rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzodioxin (TCDD) for 28 d followed by a 28-d depuration period

	Mean TCDD exposure concentration (pg/L)						
Phase and day	0	38	79	176	382	789	F value
Exposure							
7	5	0	1	4	6	10	1.79
14	5	1	1	13	17	33[a]	5.48[b]
21	5	3	9	36[a]	46[a]	74[a]	28.02[b]
28	5	6	18	50[a]	73[a]	85[a]	27.51[b]
Depuration							
7	5	12	64[a]	85[a]	—[c]	—[c]	9.33[b]
14	5	22	78[a]	95[a]	—	—	30.49[b]
21	7	33	83[a]	95[a]	—	—	28.63[b]
28	7	45[a]	83[a]	95	—	—	27.72[b]

[a]Significantly different from controls by least-significant-difference multiple means comparison test ($p < 0.05$).

[b]Significant treatment effect (one-way analysis of variance: $p < 0.05$).

[c]Exposure groups not part of depuration phase.

water. The NOEC of TCDD, based on mortality throughout the exposure and depuration phases, was less than the lowest exposure concentration of 38 pg/L (parts per quadrillion).

Further insight into the NOEC was inferred from the background concentration of 1.1 pg/L of TCDD detected by radiometric analyses in the control group throughout the study. This low background was probably due to volatilization of TCDD and translocation within the diluter system. Mortality in the control group was 5% during the exposure phase and most of the depuration phase. We suggest from these observations that the NOEC was between 1.1 and 38 pg/L. However, the minimal detectable limits for TCDD in water by GC-MS were not adequate to confirm the 1.1 pg/L detected by radiometric analyses.

A 56-d LC50 of 46 pg/L was calculated from the combined mortality data for the exposure and depuration phases. The surface response curve describing the relation among daily mortality, time and exposure concentrations is shown in Figure 1. The quadratic equation describing this relation was used to derive the 56-d LC50.

Significant mortality was induced by TCDF in rainbow trout within 14 d at exposure concentrations of 3.93 and 8.78 ng/L (Table 4). No additional significant mortality occurred throughout the 28-d exposure phase. During the depuration phase, additional mortality occurred only in fish exposed to 8.78 ng/L. The NOEC throughout the exposure and depuration phases was 1.79 ng/L.

Growth

Growth as measured by the weight of the fish was significantly decreased by all TCDD concentrations after 28 d of exposure (Table 5). There were trends of decreased growth within 14 d of exposure, but significant effects in all concentrations were not observed until 28 d of exposure. During the 28-d depuration phase, growth was measured in fish from only the control and the lowest exposure concentration because of the excessive mortality in the higher TCDD exposure concentrations. There was a significant decrease in growth in the fish exposed to 38 pg/L after the 28-d depuration phase. Fish exposed to 38 pg/L TCDD did not grow during the depuration phase, whereas the weight of fish in the control group exhibited an 80% increase. The NOEC of TCDD on growth during the exposure and depuration phases was less than the lowest exposure concentration of 38 pg/L.

TCDF exposure concentrations of 1.79, 3.93 and 8.78 ng/L significantly decreased the growth of rainbow trout within 28 d of exposure (Table 6). There were trends toward decreased growth

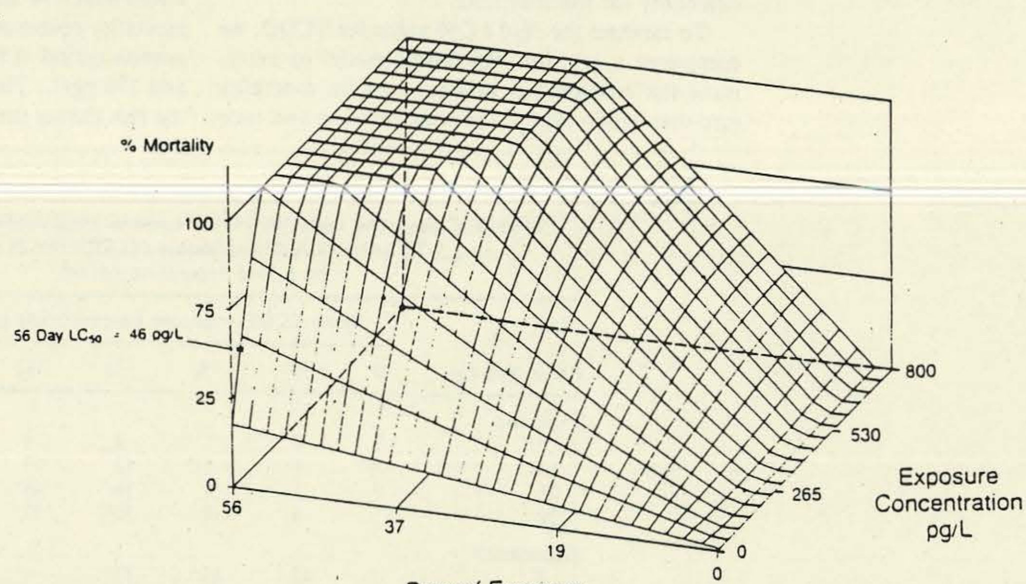


Fig. 1. Surface response describing the relation among daily mortality, time of exposure during the 28-d exposure and 28-d depuration phases, and TCDD exposure concentrations. The quadratic relation was used to derive a 56-d LC50 value of 46 pg/L TCDD for rainbow trout.

Table 4. Cumulative mortality (%) in rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d followed by a 28-d depuration period

	Mean TCDF exposure concentration (ng/L)						
Phase and day	0	0.41	0.90	1.79	3.93	8.78	F value
Exposure							
7	0	1	1	2	2	12	2.54
14	0	1	3	3	16[a]	22[a]	4.51[b]
21	0	2	5	3	18[a]	23[a]	3.73[b]
28	0	2	6	3	18[a]	28[a]	4.49[b]
Depuration							
7	0	2	6	3	20[a]	37[a]	6.53[b]
14	0	2	6	3	22[a]	46[a]	8.56[b]
21	0	2	6	3	22[a]	46[a]	8.56[b]
28	0	2	6	3	22[a]	46[a]	8.56[b]

[a]Significantly different from controls by least-significant-difference multiple means comparison test ($p < 0.05$).
[b]Significant treatment effect (one-way analysis of variance; $p < 0.05$).

Table 5. Weight (g) of rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzodioxin (TCDD) for 28 d followed by a 28-d depuration period

	Mean TCDD exposure concentration (pg/L)					
Phase and day	0	38	79	176	382	789
Exposure[a]						
7	0.37	0.36	0.38	0.33	0.36	0.33
14	0.41	0.39	0.42	0.33	0.35	0.40
21	0.48	0.35[b]	0.40	0.39	0.39	0.44
28	0.61	0.53[b]	0.47[b]	0.49[b]	0.45[b]	0.42[b]
Depuration[c]						
28	1.1	0.54[b]	—[d]	—[d]	—[d]	—[d]

Weights are expressed as the mean of 7 to 22 observations.
[a]Analysis of variance used for testing the effects of exposure concentration and time; $F = 2.43$ (time × exposure), $p < 0.03$.
[b]Significantly different from control group (t test; $p < 0.05$).
[c]Fish weight in depuration phase analyzed by t test adjusted for unequal variances.
[d]No measurements made.

after 21 d of exposure but the decrease observed was significant only in the group exposed to 3.93 ng/L. Decreased growth was evident in fish exposed to 0.90 ng/L or more after the 28-d depuration phase. The NOEC for TCDF based on growth during the exposure and depuration phases was 0.41 ng/L. This was the most sensitive response to TCDF.

Behavioral responses

Exposure to TCDD and TCDF induced behavioral impairments that became progressively worse over time and with increasing concentration. The two highest concentrations of TCDD caused behavioral changes within two weeks of exposure that included lethargic swimming, feeding inhibition, and lack of response to external stimuli, for example, waving of hand above aquaria (Fig. 2). Similar changes were evident in all groups exposed to TCDD by the end of the 28-d exposure, whereas the behavior of the controls remained normal. Although significant mortality did not occur in the two lowest exposure concentrations during 28 d of exposure, the fish were seriously stressed, as evidenced by an abnormal head-up swimming posture and confinement to the bottom of the aquar-

Table 6. Weight (g) of rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d followed by a 28-d depuration period

	Mean TCDF exposure concentration (ng/L)					
Phase and day	0	0.41	0.90	1.79	3.93	8.78
Exposure[a]						
7	0.33	0.35	0.37	0.36	0.35	0.32
14	0.39	0.40	0.43	0.42	0.31	0.41
21	0.55	0.47	0.45	0.50	0.39[b]	0.44
28	0.59	0.59	0.53	0.48[b]	0.50[b]	0.46[b]
Depuration[c]						
28	1.1	0.91	0.85[b]	0.80[b]	0.79[b]	0.71[b]

Weights represent the mean of 8 to 24 observations.

[a]Analysis of variance used for testing the effects of exposure concentration and time; $F = 4.37$ (time × exposure), $p < 0.05$.

[b]Significantly different from controls (t test; $p < 0.05$).

[c]Analysis of variance used for testing the effect of exposure concentration; $F = 5.73$ (exposure), $p < 0.03$.

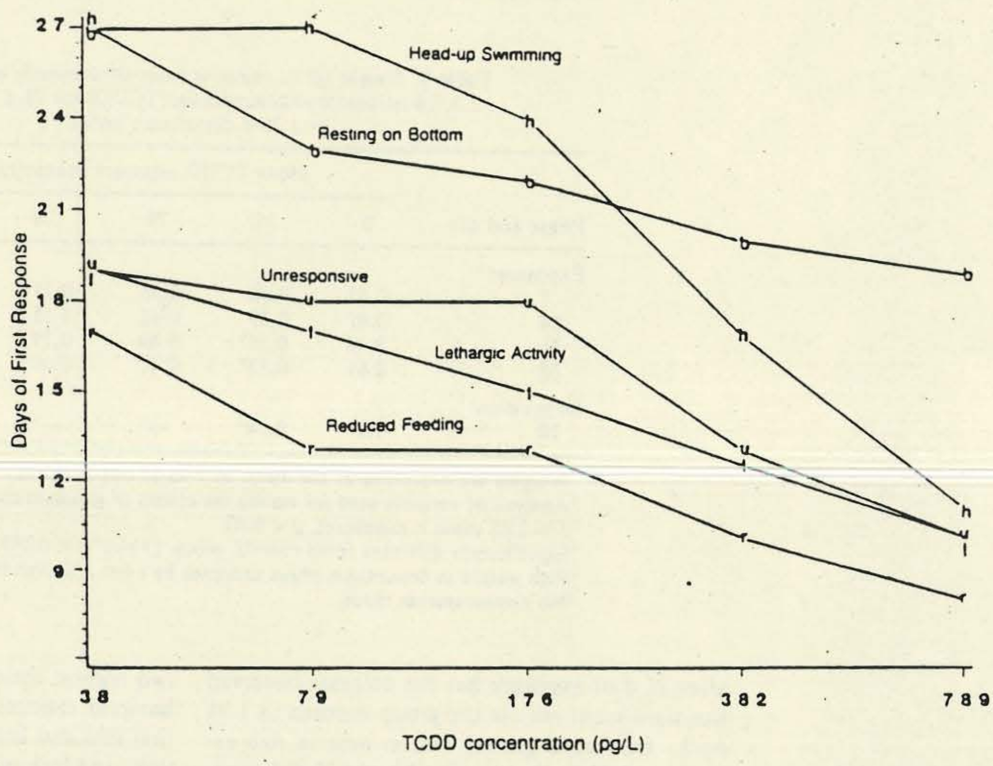


Fig. 2. Days of TCDD exposure required to induce behavioral changes in rainbow trout during a 28-d exposure.

ia. The feeding inhibition and other behavioral changes were not reversed during the 28-d depuration period.

Behavioral reactions similar to those observed in the TCDD exposure were observed in fish exposed to TCDF; however, the responses were of lesser magnitude (Fig. 3). Lethargy, unresponsiveness to external stimuli and diminished feeding

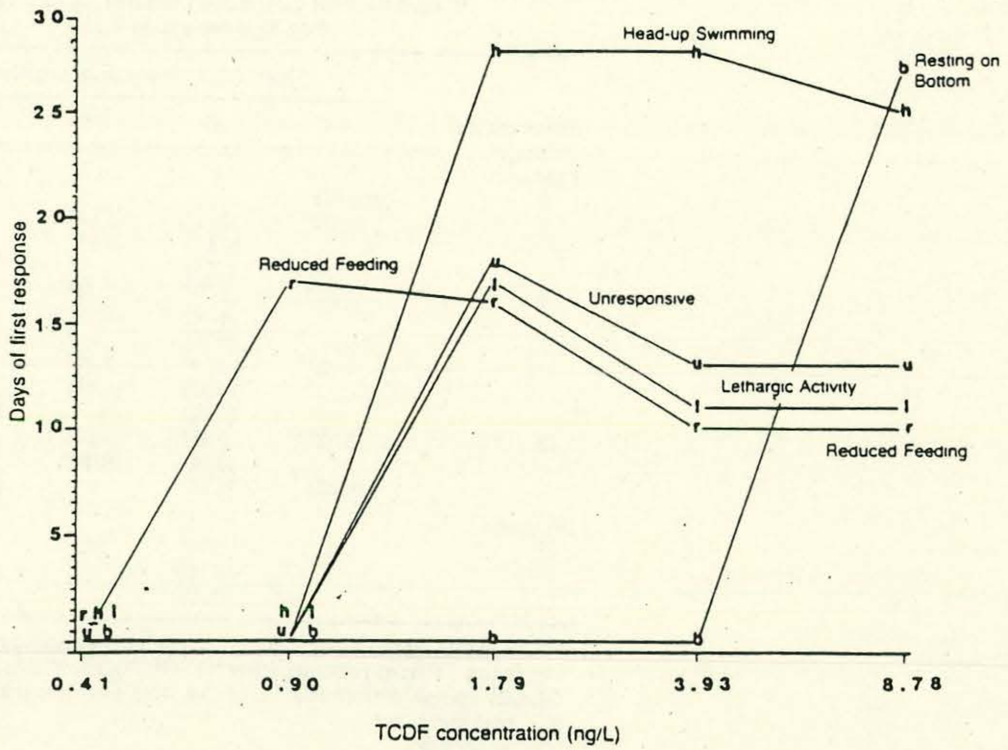


Fig. 3. Days of TCDF exposure required to induce behavioral changes in rainbow trout during a 28-d exposure.

reactions increased significantly in the three highest exposure groups. Recovery of behavioral function was evident in all but the two highest treatment groups by the end of the 28-d depuration period.

Neither TCDD nor TCDF induced observable responses in coloration or morphological characteristics such as scoliosis or lordosis; however, fin erosion was observed in fish in the lowest TCDD exposure concentration at the end of the depuration phase. In addition, exposure to both TCDD and TCDF induced observable, unique characteristics in fecal appearance. The two highest exposure concentrations of each toxicant induced long, stringy faces within the last several days of the 28-d exposure phase.

Bioconcentration

The BCFs for TCDD and TCDF differed greatly during the 28 d of continuous exposure. Whole-body residues throughout the exposure phase were in the low end of a 0.41 to 15.41 ng/g range for TCDD (Table 7). The greater the exposure concentration, the higher were the whole-body residues of TCDD during the 28-d exposures. The measured BCF for TCDD ranged from 8,558 to 28,664 during the exposure and did not appear to reach steady-state equilibrium in any of the exposure concentrations during the 28-d exposure (Table 8). The GC-MS analyses for whole-body TCDD levels agreed closely with the whole-body radiometric determinations for [^{3}H]TCDD. This similarity suggests that the ^{3}H label on the TCDD molecule was not being exchanged, and that the ^{3}H detected in the fish tissue was associated with the parent TCDD molecule. This similarity also indicates that organic extracted [^{3}H]TCDD was not being appreciably metabolized during the exposure and depuration phases. However, as judged by the results of total combustion of fish samples, it appears that about 30% of the ^{3}H label was associated with polar compounds that could have been TCDD metabolites.

Since it was apparent that a steady-state equilibrium for TCDD bioconcentration had not been reached after 28 d of exposure, we used the BIOFAC computer program [22] to estimate the bioconcentration kinetics for TCDD based only on data from the exposure phase. The estimated BCF at steady-state equilibrium was relatively consistent in fish from different exposure concentrations; the

Table 7. Whole-body residues of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout continuously exposed for 28 d followed by a 28-d depuration phase

	Mean TCDD exposure concentration (pg/L)				
Phase and day	0	38	176	382	789
Exposure					
0	[<0.02][a]				
7	0.012[a]	0.41[b] (0.05) [0.38]	1.68[b] (0.15)	3.44[b] (0.20)	6.75[b] (0.37) [6.78]
14	0.022[c]	0.77[b] (0.06) [0.71]	2.81[b] (0.18)	6.22[b] (0.67)	11.67[b] (0.68) [12.3]
21	0.023[d]	0.99[e] (0.03) [0.96]	3.87[b] (0.14)	10.10[e] (1.42) [11.3]	15.41[e] (0.86) [17.6]
28	0.027[a] [<0.02]	0.98[b] (0.05) [0.93]	4.52 (0.41)	10.95[b] (0.87) [10.8]	ND
Depuration					
28	0.22[a]	0.74[b] (0.11) [0.78]	ND	ND	ND

Values (ng/g) represent the mean (with standard deviation in parentheses) of individual fish analyzed radiometrically for [^{3}H]TCDD. Values in brackets represent GC-MS analyses performed on a pooled sample of fish, expressed as ng/g.
ND, not determined.
[a]One observation.
[b]Six observations.
[c]Two observations.
[d]Four observations.
[e]Eight observations.

Table 8. Measured bioconcentration factor (BCF)[a] for 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout exposed continuously for 28 d

	Measured TCDD exposure concentration (pg/L)			
Days of exposure	38	176	382	789
7	10,736	9,551	9,005	8,558
14	20,131	15,966	16,282	14,790
21	25,947	21,977	26,439	19,510
28	25,789	25,670	28,664	ND

[a]BCF = $(C_t/C_w) \times 1{,}000$. ND, not determined.

estimated BCF at 90% steady-state equilibrium ranged from about 37,000 to 86,000 (Table 9). Fish exposed to 382 pg/L showed somewhat different kinetics in that the estimated BCF, time to reach steady-state equilibrium and half-life were greater than in the other exposure concentrations. The relatively low K_2 value, compared with K_2 values from other exposure groups, suggested that metabolic effects may have been reducing the elimination of TCDD.

Ideally, the BCF should be estimated in fish not showing toxicity-induced responses. Inasmuch as the fish exposed to the lowest TCDD concentration of 38 pg/L showed the least toxic responses during the 28-d exposure, we suggest that the predicted BCF of 39,000 is probably the most reliable

Table 9. Estimated bioconcentration kinetics[a] of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout exposed to TCDD for 28 d

Kinetic parameter	TCDD exposure concentrations (pg/L)			
	38	176	382	702[b]
K_1, uptake rate constant (d^{-1})	1,852 (132)[c]	1,543 (69)	1,337 (61)	1,591 (53)
K_2, depuration rate constant (d^{-1})	0.047 (0.01)	0.041 (0.005)	0.015 (0.005)	0.043 (0.005)
BCF-K_B	39,000 (9,400)	37,560 (5,032)	86,000 (25,000)	36,637 (4,290)
Time to reach 90% steady state (d)	49 (11)	56 (7)	149 (43)	53 (6)
Elimination half-life, $t_{1/2}$ (d)	15 (3)	17 (2)	48 (13)	16 (2)

[a]Estimated kinetics using BIOFAC [22].
[b]Mean of TCDD measurements at days 1, 7, 14 and 21.
[c]Values in parentheses represent standard deviations.

estimate. The range in BCF we observed was substantially greater than the BCF of 7,000 to 9,270 previously reported in the literature [16,23,24]. Results from our study were perhaps better estimates of the equilibrium BCF because we used a continuous exposure in flowing water for a longer period at lower exposure concentrations. Based on the water solubility of 7.9 ng/L for TCDD [25], the predicted BCF would be about 467,000 if the regression equation, $\log BCF = 2.791 - 0.564 \log S$ [26], were used; it would be about 1,000,000 if the regression equation, $\log BCF = 3.41 - 0.508 \log S$ [27], were used.

We suggest from our experimental data that the overall bioconcentration from water to fish is probably much less than the theoretical estimation. The obvious toxicity-induced effects of TCDD, as well as potential influences on membrane transport and other metabolic functions, could account for the observed BCF being less than the theoretical predictions.

The estimated elimination half-life ($t_{1/2}$) from the BIOFAC ranged from 15 to 17 d among exposure concentrations, except for the estimated half-life of 48 d in fish exposed to 382 pg/L. Adams et al. [24] reported an elimination half-life of 15 d, and Branson et al. [16] reported a half-life of 58 d. In the fish exposed to 38 pg/L for 28 d and then held during the 28-d depuration phase, the whole-body residues did not decrease sufficiently to support an estimated half-life in the range of 15 to 17 d (Table 7). The whole-body residues decreased from 0.93 (±0.05) to 0.74 (±0.11) ng/g during the 28-d depuration phase. Excessive mortality in the other TCDD exposure concentrations precluded our obtaining experimental data on elimination in fish exposed to higher concentrations.

The uptake and depuration of TCDF were measured in fish exposed to 0.41 and 3.93 ng/L. In contrast to TCDD kinetics, TCDF uptake reached an apparent steady-state equilibrium after only 7 d of exposure (Table 10). Whole-body residues of TCDF did not increase after 7 d of exposure in fish exposed to 0.41 and 3.93 ng/L. In fish exposed for 28 d, the measured BCF was 6,049 at 0.41 ng/L and 2,455 at 3.93 ng/L (Table 11). The estimated bioconcentration kinetics of TCDF are shown in Table 12. Rainbow trout apparently were able to readily eliminate or metabolize TCDF. The whole-body residues in fish held during the 28-d depuration phase suggested a very short elimination half-life for this compound. Although TCDD and TCDF are structurally very similar, their bioconcentration kinetics and toxicities were found to be very different.

Table 10. Whole-body residues of 2,3,7,8-tetrachlorodibenzofuran (TCDF) in rainbow trout continuously exposed for 28 d followed by a 28-d depuration phase

Phase and day	Mean TCDF exposure concentration (ng/L)		
	0	0.41	3.93
Exposure			
0	<0.06		
7	0.17	1.63 (0.89)	11.9 (2.88)
14	0.12	1.80 (0.62)	9.30 (2.26)
21	0.19	1.05 (0.44)	10.7 (2.24)
28	0.22	2.48 (1.32)	9.65 (1.30)
Depuration			
28	<0.06	0.09 (0.06)	0.54 (0.08)

Values represent the mean (with standard deviation in parentheses) of four observations performed on individual fish, expressed as ng/g wet weight.

Table 11. Measured bioconcentration factors (BCF)[a] for 2,3,7,8-tetrachlorodibenzofuran (TCDF) in rainbow trout exposed continuously for 28 d

Days of exposure	TCDF exposure concentration (ng/L)	
	0.41	3.93
7	3,976	3,028
14	4,390	2,366
21	2,561	2,730
28	6,049	2,455

[a] $BCF = (C_f/C_w) \times 1{,}000$.

CONCLUSIONS

We conclude that TCDD and TCDF—especially TCDD—are extremely toxic to rainbow trout. A relative comparison of TCDD and TCDF chronic toxicities with those of several other organochlorine compounds demonstrated that TCDD is more than 10,000 times as toxic to fish as either endrin or toxaphene, and that TCDF is about 1,000 times more toxic than either of these insecticides (Table 13). Results from previous toxicity studies with fish by Helder [10,11], Miller et al. [12] and Adams et al. [24] demonstrated the toxicity of TCDD to be in the low ng/L range. However, we have shown that our lowest TCDD exposure concentration of 38 pg/L induced significant adverse effects on survival, growth, and behavioral responses. Results from our studies are perhaps more adequate estimates of TCDD toxicity because we used continuous exposure techniques for a longer time than had been used in previous studies. For similar reasons, we believe the BCF for TCDD derived from our studies is a more accurate estimate of the bioconcentration potential than are the estimates reported by Branson et al. [16] and Adams et al. [24]. Although we showed that TCDD was ex-

Table 12. Estimated bioconcentration kinetics[a] for TCDF in rainbow trout exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d

Kinetic parameter	TCDF exposure concentration (ng/L)	
	0.41	3.93
K_1 uptake rate constant (d^{-1})	1,228 (1,191)	6,852 (8,037)
K_2 depuration rate constant (d^{-1})	0.28 (0.30)	2.60 (3.04)
BCF-K_{II}	4,449 (6,481)	2,640 (4,379)
Time to reach 90% steady state (d)	8 (9)	0.90 (1.04)
Elimination half-life, $t_{1/2}$ (d)	3 (3)	0.27 (3.1)

Values in parentheses represent standard deviations.
[a] Estimated kinetics using BIOFAC [22].

Table 13. Chronic no effect concentrations ($\mu g/L$) for growth and survival of freshwater fish exposed to various organochlorine chemicals

Chemical and fish species	Days of exposure	Survival	Growth[a]	Source
Aroclor 1254, brook trout	118	9.0	9.0	[28]
Chlorodecone, fathead minnows	120	>0.31	>0.31	[29]
Pentachlorophenol (ultrapure), fathead minnows	90	>139	>139	[30]
Toxaphene, brook trout	90	>0.50	0.38	[31]
Toxaphene, channel catfish	90	0.096	0.20	[32]
Endrin, bluntnose minnows	30	0.1	0.1	[33]
TCDD, rainbow trout	56	<0.000038	<0.000038	This study
TCDF, rainbow trout	56	0.00179	0.00041	This study

[a] Change in weight of fish.

tremely toxic to rainbow trout, even our lowest exposure concentration was too high to derive a NOEC.

Acknowledgement – We are grateful to the many people from the Fish and Wildlife Service (FWS), Battelle and Monsanto who assisted in conducting these studies. We especially thank Mr. Dave Zumwalt for his efforts in designing the specialized diluter exposure system, and Mr. Zumwalt and Mr. George Holroyd for their outstanding efforts in constructing and calibrating the system. We appreciate the excellent advice and assistance of Dr. Mark Ellersieck and Ms. Linda Sappington in analyzing the data, and the technical assistance of Mr. Rick Archeski in analyzing the behavioral data. We give special thanks to Dr. Paul Eschmeyer, Editorial Section, Office of Information Transfer, FWS, Fort Collins, Colorado, for his review of the manuscript and for editorial advice.

REFERENCES

1. **Olie, K., M.v.d. Berg** and **O. Hutzinger.** 1983. Formation and fate of PCDD and PCDF from combustion processes. *Chemosphere* 12:627–636.
2. **Firestone, D.** 1972. Determination of polychlorodibenzo-*p*-dioxins and related compounds in commercial chlorophenols. *J. A.O.A.C.* 55:85–92.
3. **Ballschmiter, K., W. Zoller, C. Scholz** and **A. Nottrodt.** 1983. Occurrence and absence of polychlorodibenzofurans and polychlorodibenzodioxins in fly ash from municipal incinerators. *Chemosphere* 12: 585–594.
4. **Petty, J.D., D.L. Stalling, L.M. Smith** and **J.L. Johnson.** 1983. Occurrence and potential impact of PCDF's and PCDD's in aquatic ecosystems. In D.D. Hemphill, ed., *Trace Substances in Environmental Health* – XVII. University of Missouri Press, Columbia, MO, pp. 96–102.
5. **Crummett, W.B.** 1982. Environmental chlorinated dioxins from combustion: The trace chemistries of fire hypothesis. In O. Hutzinger, R.W. Frei, E. Merian and F. Pocchiari, eds., *Chlorinated Dioxins and Related Compounds Impact on the Environment.* Pergamon Press, Elmsford, NY, p. 261.
6. **Ryan, J.J., P.-Y. Lan, J.C. Pilon** and **D. Lewis.** 1983. 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and 2,3,7, 8-tetrachlorodibenzofuran residues in Great Lakes commercial and sport fish. In G. Choudhary, L.H. Keith and C. Rappe, eds., *Chlorinated Dioxins and Dibenzofurans in the Total Environment.* Butterworth, Boston, MA, pp. 87–97.
7. **Columbia National Fisheries Research Laboratory.** 1983. Impacts of contaminants on early life stages of striped bass. In P.M. Mehrle and J.L. Ludke, eds., *Progress Report.* U.S. Fish and Wildlife Service, Columbia, MO.
8. **Belton, T.J., R. Hazen, B.E. Ruppel, K. Lockwood, R. Mueller, E. Stevenson** and **J.J. Post.** 1985. A study of dioxin contamination in select finfish, crustaceans, and sediments of New Jersey Waterways. Office of Science and Research, New Jersey Department of Environmental Protection, Trenton, NJ.
9. **U.S. Food and Drug Administration.** 1981. Correspondence from FDA Commissioner Dr. Arthur Hall Hayes, Jr., to Governor Milliken of Michigan concerning the public health significance of TCDD contaminant "levels of concern" for finfish in Great Lakes. 26 August.
10. **Helder, T.** 1980. Effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on early life stages of the pike (*Esox lucius* L.). *Sci. Total Environ.* 14:255–264.
11. **Helder, T.** 1981. Effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on early life stages of rainbow trout (*Salmo gairdneri*, Richardson). *Toxicology* 19: 101–112.
12. **Miller, R.A., A.N. Logan** and **C.L. Hawkes.** 1979. Toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in aquatic organisms. *Environ. Health Perspect.* 5: 177–186.
13. **Cooper, K.R., J. Schell, P. Kahn** and **M. Gallo.** 1986. The effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on the development and survival of the Japanese medaka (*Oryzias latipes*). *Toxicologist* 6:27 (Abstract).
14. **Kleeman, J.M., J.R. Olson, S.M. Chen** and **R.E. Peterson.** 1986. Metabolism and disposition of 2,3, 7,8-tetrachlorodibenzodioxin in rainbow trout. *Toxicol. Appl. Pharmacol.* 83:391–401.
15. **Kleeman, J.M., J.R. Olson, S.M. Chen** and **R.E. Peterson.** 1986. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin metabolism and disposition in yellow perch. *Toxicol. Appl. Pharmacol.* 83:402–411.
16. **Branson, D.R., I.T. Takahashi, W.M. Parker** and **G.E. Blau.** 1985. Bioconcentration kinetics of 2,3,7, 8-tetrachlorodibenzo-*p*-dioxin in rainbow trout. *Environ. Toxicol. Chem.* 4:779–788.
17. **American Public Health Association, American Water Works Association** and **Water Pollution Control Federation.** 1980. *Standard Methods for the Examination of Water and Wastewater,* 15th ed. American Public Health Association, Washington, DC.
18. **Smith, L.M.** 1981. Carbon dispersed in glass fibers as an adsorbent for contaminant enrichment and fractionation. *Anal. Chem.* 53:2152–2154.
19. **Smith, L.M., D.L. Stalling** and **J.L. Johnson.** 1984. Determination of part-per-trillion levels of dibenzofurans and dioxins in environmental samples. *Anal. Chem.* 56:1830–1842.
20. **Drummond, R.A., C.L. Russom, D.L. Geiger** and **D.L. DeFoe.** 1986. Behavioral and morphological changes in fathead minnow, *Pimephales promelas,* as diagnostic endpoints for screening chemicals according to mode of action. In *Aquatic Toxicology and Hazard Assessment: Ninth Symposium.* American Society for Testing and Materials, Philadelphia, PA, pp. 415–435.
21. **Snedecor, G.W.** and **W.C. Cochran.** 1967. *Statistical Methods,* 6th ed. Iowa State University Press, Ames, IA.
22. **Blau, G.E., W.B. Neely** and **D.R. Branson.** 1975. Ecokinetics: A study of the fate and distribution of chemicals in laboratory ecosystems. *AIChE J.* 21: 854–861.

23. **Isensee, A.R.** 1978. Bioaccumulation of 2,3,7,8-tetrachlorodibenzo-para-dioxin. *Ecol. Bull.* 27:255–262.
24. **Adams, W.J., G.M. DeGraeve, T.D. Sabourin, J.D. Cooney** and **G.M. Mosher.** 1986. Toxicity and bioconcentration of 2,3,7,8-TCDD to fathead minnows (*Pimephales promelas*). *Chemosphere* 15:1503–1511.
25. **Adams, W.J.** and **K.M. Blaine.** 1986. A water solubility determination of 2,3,7,8-TCDD. *Chemosphere* 15:1397–1400.
26. **Kenaga, E.E.** and **C.A.I. Goring.** 1980. Relationship between water solubility, soil sorption, octanol-water partitioning, and concentration of chemicals in biota. In J.G. Eaton, P.R. Parrish and A.C. Hendricks, eds., *Aquatic Toxicology.* STP 707. American Society for Testing and Materials, Philadelphia, PA, pp. 78–115.
27. **Chiou, C.T., V.H. Freed, D.H. Schmedding** and **R.L. Kohnert.** 1977. Partition coefficients and bioaccumulation of selected organic chemicals. *Environ. Sci. Technol.* 11:475–478.
28. **Mauck, W.L., P.M. Mehrle** and **F.L. Mayer.** 1978. Effects of the polychlorinated biphenyl Aroclor 1254 on growth, survival, and bone development in brook trout (*Salvelinus fontinalis*). *J. Fish. Res. Board Can.* 35:1084–1088.
29. **Buckler, D.R., A. Witt, Jr., F.L. Mayer** and **J.N. Huckins.** 1981. Acute and chronic effects of Kepone and mirex on the fathead minnow. *Trans. Am. Fish. Soc.* 110:270–280.
30. **Cleveland, L., D.R. Buckler, F.L. Mayer** and **D.R. Branson.** 1982. Toxicity of three preparations of pentachlorophenol to fathead minnows: A comparative study. *Environ. Toxicol. Chem.* 1:205–212.
31. **Mayer, F.L., P.M. Mehrle** and **W.P. Dwyer.** 1975. Toxaphene effects on reproduction, growth, and mortality of brook trout. EPA-600/3-75-013. U.S. Environmental Protection Agency, Duluth, MN.
32. **Mayer, F.L., P.M. Mehrle** and **W.P. Dwyer.** 1977. Toxaphene: Chronic toxicity to fathead minnows and channel catfish, EPA-600/3-77-069. U.S. Environmental Protection Agency, Duluth, MN.
33. **Mount, D.I.** 1962. Chronic effects of endrin on bluntnose minnows and guppies. U.S. Fish and Wildlife Service Research Report No. 58, Washington, DC.

Attachment 9

ASSESSMENT OF THE HUMAN HEALTH RISKS RELATED TO THE PRESENCE OF DIOXINS IN COLUMBIA RIVER FISH

Prepared by:

Russell E. Keenan, Ph.D.
Alan H. Parsons, Ph.D.
Ellen S. Ebert
Pamela D. Boardman, M.P.H.
Steven L. Huntley
Mary M. Sauer, M.S.P.H.

ChemRisk™
A McLaren Company
1685 Congress Street
Stroudwater Crossing
Portland, ME 04102
(207) 774-0012
(207) 774-8263

January 8, 1990

ChemRisk
A McLaren Company

An exposure pathway consists of four necessary elements: a source and mechanism of chemical release into the environment, an environmental transport medium for the released chemical, a point of potential human contact with the environmental medium, and a human exposure route (eg., inhalation, dermal contact, ingestion) at the point contact. Each pathway describes a unique potential mechanism by which a population or an individual may be exposed to a chemical. For each exposure pathway, the environmental fate and persistence of the chemical from the point of discharge to the point of human contact is an important consideration. Many factors such as adsorption onto particulates, sedimentation, and solubility influence the degree of human exposure. These factors are highly variable in the environment. Consequently, a truly valid exposure assessment can only be conducted using site-specific data. To this purpose, a study of the levels of dioxin in the edible portions of Columbia River fish has been conducted. Additionally, the rates of consumption of locally caught fish were estimated.

Columbia River fish sampling

For the purpose of determining accurate species-specific concentrations of dioxin in edible fish fillets, a variety of species of fish were collected from six different sites along the Columbia River system by an independent laboratory and consultant. A total of 680 individual fish were sampled at the six sites. Species collected included top and bottom feeders as well as resident and anadromous populations. Migratory fish sampled included coho salmon, fall chinook salmon (upriver and tule) and summer steelhead trout. Resident species sampled included white sturgeon, largescale sucker, and carp. Results of sampling data are reported below[1].

Fillet TCDD Levels in Columbia River Fish (ppt)

Species	Sampling Site					
	1	2	3	4	5	6
Coho salmon	0.08	0.10	NS	NS	NS	NS
Fall chinook salmon (Upriver)	0.08	0.09	NS	NS	NS	NS
Fall chinook salmon (Tule)	0.31	0.18	NS	NS	NS	NS
Summer steelhead trout	0.07	0.07	NS	NS	NS	NS
White sturgeon	0.09	0.12	1.09	0.88	1.68	0.55
Largescale sucker	0.32	NS	0.39	0.19	0.22	0.26
Carp	0.79	NS	1.06	1.35	1.46	0.76

At Sites 1 and 2, located downstream of NWPPA pulp and paper mills, the geometric mean concentrations of TCDD in salmon ranged from 0.08 to 0.31 parts per trillion (ppt) and steelhead trout averaged 0.07 ppt. Sturgeon, sucker, and carp collected from sites 1, 2, 3, and 4 had fillet TCDD levels averaging

1 Note: 80% of the anadromous and 45% of all species sampled had nondetectable levels of TCDD. Nondetectable samples were assigned a value equal to one half the limit of detection per EPA protocol. This results in a more conservative estimation of tissue TCDD levels because actual values could equal zero.

DRAFT Attachment 10

ANALYSIS OF THE POTENTIAL POPULATIONS AT RISK FROM THE CONSUMPTION OF FRESHWATER FISH CAUGHT NEAR PAPER MILLS

Craig McCormack
Office of Policy Planning and Evaluation

David Cleverly 202-382-7891 (D.C)
Office of Research and Development

April 23, 1990

INTRODUCTION:

OTS, OSW, and OW have conducted a detailed human and ecological risk assessment of environmental loadings of dioxin from bleached pulp and paper mills. In that analysis only maximum lifetime cancer risk and average lifetime cancer risk to the hypothetically exposed individual was estimated for various exposure scenarios. No estimation of potential population risk, especially to sensitive subgroups, was provided in the analysis. Since draft publication of these results, we have identified populations of Asians, and tribal Native Americans that reside along the banks of the Columbia River in Oregon. The State government indicates that there are eight bleached pulp and paper mills that directly discharge to the Columbia River. The State also indicates that freshwater fish caught from the Columbia river are the main source of animal protein for these people. They consume an average of 100 to 150 grams of fish flesh each day over the course of the year. These individuals are much more likely to catch and consume fish that has been contaminated with dioxin from the effluent discharged from the mills than other populations in the area. The Native Americans number about 15,000, and the Asians number about 30,000 people.

In addition to these subpopulations exposed by diet to dioxin, we have estimated that approximately 610,000 people living in the vicinity of pulp and paper mills have family incomes at or below the poverty level. These individuals are also expected to derive a significant portion of animal protein from both subsistence and sports fishing in rivers near paper mills. Subsistence fishermen consume about 100 grams of fish per day/1, and sports fishermen consume about 69 grams fish per day/2.

For purposes of the assessment of potential cancer risk, we have employed monitoring data of dioxin contamination in fresh water fish caught in the vicinity of bleached pulp and paper mills. This was developed by the Environmental Research Laboratory in Duluth Minnesota as part of the National Bioaccumulation Study of freshwater fish in the U.S. The range of detected TCDD equivalent concentration in the edible fish fillet was from 0.1 ppt - 24 ppt. The weighted

average fillet concentration was 6.5 ppt (6.5 pg/gm). For purposes of estimating incremental lifetime cancer risk to the most exposed individual, a fillet concentration of 24 ppt was used. The weighted average dioxin concentration in the fillet of 6.5 ppt was used to derive the approximate average lifetime risk to subsistence and sports fishermen. The average exposure and average lifetime risk was used to estimate the annual cancer incidence in these sensitive subpopulations. In addition a human body weight of 70 kilograms was assumed to compute estimates of excess cancer risk.

CONCLUSIONS:

It is currently not possible to directly measure the association between the chronic dietary intake of dioxin contaminated freshwater fish, and the occurrence of specific forms of cancer in the exposed populations. The epidemiologic studies of these populations with a high dependency for subsistence fishing as a source of dietary animal protein have not been conducted. Therefore we have mathematically estimated lifetime excess cancer risk to the population residing near the Columbia River, as well as to low-income populations living in the vicinity of other mills in the U.S. This analysis is not intended to replace any previous risk assessments involving the human consumption of fish that has been contaminated with dioxin from the effluent discharged from paper mills, but is merely to illustrate that methodologies can be developed to estimate total populations at risk in the U.S.

The following are the results:

	Pop.	MIR(a)	AVG Risk(b)	Cancer Inc.(c)
Native Americans	**15,000. . . .**	**8.6×10^{-3}**	**1.5×10^{-3}**	**0.33**
Asian Americans	**30,000**	**8.6×10^{-3}**	**1.5×10^{-3}**	**0.67**
Total Risk	**45,000**	**8.6×10^{-3}**	**1.5×10^{-3}**	**1.0**
Low income families	**610,000**	**5.4×10^{-3}**	**1.0×10^{-3}**	**9.3**

(a) MIR is the maximum individual risk, and is associated with the highest fish consumption rate and the highest dioxin concentration in fish caught near paper mills.

(b) Average lifetime cancer risk is the excess cancer risk based on the average fish consumption rate for subsistence and sports fishermen, and the weighted average dioxin concentration in fish caught near paper mills.

(c)Cancer incidence is the estimated number of cancer cases per year within the

defined exposed population. This was computed using average lifetime risk.

1/ U.S. Environmental Protection Agency (1988). Risk Assessment for Dioxin Contamination Midland, Michigan. Region 5. EPA-905/4-88-005.

2/Estimated consumption by the U.S. Food and Drug Administration, assuming substitution of average U.S. population daily consumption of red meat with fish.

Calculations of Risk

1. Native Americans

Assumptions:

a. MEI consumes 150 gms fish/day.
b. Average consumption is 100 grms fish/day.
c. 70 kilogram person.
d. Lifetime exposure.
e. Max. dioxin concentration in fish fillet = 24 pg/gm.
f. Weighted average dioxin in fish fillet = 6.5 pg/gm.
g. Population of 15,000.
h. Risk Specific Dose of Dioxin = lifetime cancer risk of one in a million is: 0.006 pg/kg/day.

Max. Daily Dose= (150 gms/day X 24 pg/gm) / 70 kg person
= 51.43 pg dioxin/kg/day

MIR ={(51.43 pg/kg/day) / (0.006 pg/kg/day)} X 10^{-6}
MIR = 8.6 X 10^{-3}

Avg. Daily Dose= (100 gms/day X 6.5 pg/gm)/ 70 kg person
= 9.28 pg dioxin/kg/ day

Avg. lifetime risk = {(9.28 pg/day)/(0.006 pg/kg/day)} X 10-6
= 1.5 X 10^{-3}

Annual Cancer Incidence = (Avg risk * population)/ 70 year lifespan
= (1.5 X 10^{-3} * 15,000)/ 70 yrs
= 0.33

2. Asian Americans

Assumptions are the same as with Native Americans. The population size is

MEI = maximally exposed individual

30,000.

Max. Daily Dose = 51.43 pg dioxin/kg/day.
MIR = 8.6 X 10-3

Avg. Daily Dose = 9.28 pg dioxin/kg/day
Avg. lifetime risk = 1.5 X 10^{-3}

Annual Cancer Incidence = (1.5 X 10^{-3} * 30,000)/70 yr lifespan
= 0.67

3. <u>Low income families.</u>

Assumptions:

a. MEI consumes 100 gms fish/day.
b. Average consumption is 69grms fish/day.
c. 70 kilogram person.
d. Lifetime exposure.
e. Max. dioxin concentration in fish fillet = 24 pg/gm.
f. Weighted average dioxin in fish fillet = 6.5 pg/gm.
g. Population of 610,000.
h. Risk Specific Dose of Dioxin = lifetime cancer risk of one in a million is: 0.006 pg/kg/day.

Max Daily Dose = (100 gms/day) X (24 pg dioxin/gm)/ 70 kg person
= 34.28 pg dioxin/kg/day

MIR = {(34.28 pg/kg/dy)/(0.006 pg/kg/dy)} X 10^{-6}
= 5.7 X 10^{-3}

Avg. Daily Dose = (69 gms/day) X (6.5 pg/gm)/70 kg person
= 6.41 pg dioxin/kg/day

Avg. lifetime risk = { (6.41 pg/kg/dy)/(0.006 pg/kg/dy)} X 10-6
= 1.0 X 10^{-3}

Annual Cancer Incidence ={ (1.0 X 10^{-3}) * (610,000)}/ 70 year lifespan
=9.3

The Bottom Line:

• The "Forest through the trees" is that the environmental loadings of dioxin from the mills may result in high levels of risk to humans.

• The analysis of the regulatory options suggests that this particular industrial source category fits the mold for a regulatory pollution prevention initiative through use of the CWA, TSCA, and RCRA.

* could require substantial reduction in the overall use of chlorine
* BACT seems to be oxygen delignification

DIOXINS, FURANS AND PCBs: THE TRUE STORY

Dioxins, furans and PCBs have become some of the most controversial chemicals of modern society. Dioxin in particular has been labelled the most toxic chemical ever produced by man. More than $1 billion has been spent so far on dioxin research[1], yet at the same time, industry and government officials insist that not enough evidence on the toxicity exists to justify elimination of the sources.

This paper explores some of the myths and facts surrounding these environmentally dangerous chemicals and explains why the scientific debate has become of an increasing political nature.

What Are 'Dioxins'

The term 'dioxins' usually refers to a whole chemical family with 75 individual members, which more correctly should be termed chlorinated dibenzo-p-dioxins. The most toxic member of this family is 2,3,7,8-Tetra-Chloro-Dibenzo-p-Dioxin, often abbreviated as 2,3,7,8-TCDD.

Often, the term 'dioxins' also includes a closely related chemical family called chlorinated dibenzofurans. The most toxic among the 135 known furans is 2,3,7,8-Tetra-Chloro-Dibenzo-Furan (TCDF), which is one tenth as toxic as the corresponding dioxin, TCDD.

Of the 210 dioxins and furans, twelve are extremely toxic and are commonly referred to as the 'Dirty Dozen'. Their individual toxicity is ranked by comparing them to 2,3,7,8-TCDD via internationally agreed upon Toxic Equivalence Factors (TEFs). Box 1 (next page) shows the chemical structures of dioxins and furans, and their toxicity ranking.

PCBs are another chemical family closely related to dioxins. Due to their similar chemical structure, some PCBs can act through exactly the same pathways in organisms as dioxins, but are much less potent. However, due to their chemical nature, PCBs are inevitably contaminated with furans and dioxins, and will form these more toxic chemicals during fires.

How Toxic Are Dioxins [2]

a) Extreme Ability to Kill

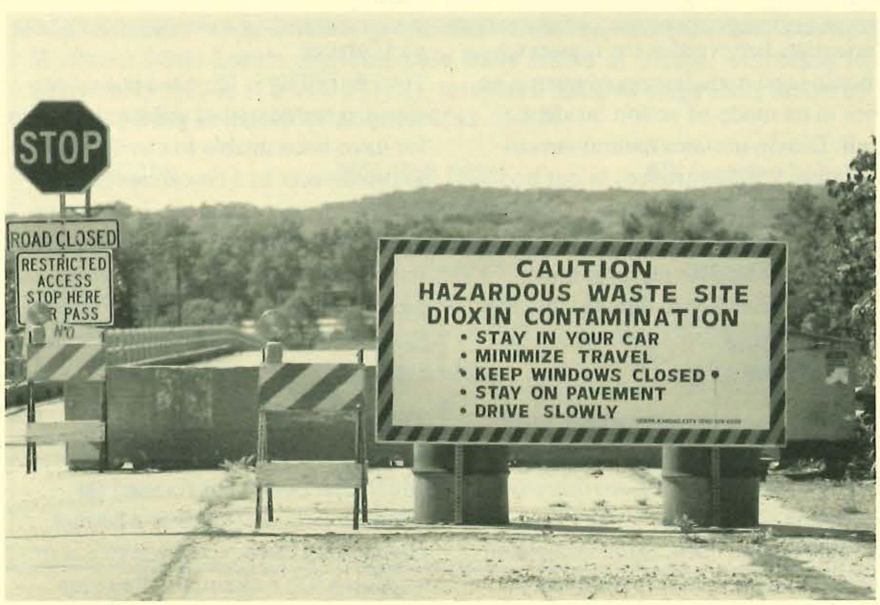
Dioxin TCDD is the most toxic man-made chemical ever tested on laboratory animals. Acutely lethal doses are measured in micro-grams per kilogram animal weight, in the parts per billion range. [2e] Though the lethal dose varies considerably from species to species, dioxin has been found to be extraordinarily toxic to all species tested.

Characteristic of lethal dioxin exposure is the 'wasting syndrome': animals seem to waste away, and eventually die, without displaying any overt pathological symptoms. The exact reason why dioxin can cause death in these minute quantities is not yet known.[2e]

b) Extremely Bio-Accumulative

Dioxins are some of the most persistent and bio-accumulative man-made chemicals released into the environment. While dioxins can be broken down under certain conditions, in particular when exposed to intensive sunlight, they cannot be broken down once absorbed by soil or dust. When they enter the food-chain, they will bio-magnify, often to levels many thousands of times higher than their surroundings.[2d,3]

It is this combination of dioxin's extreme toxicity and its bio-magnification in the environment that makes Greenpeace believe that there can be no safe level of dioxin emissions.



Conclusions and Greenpeace Demands

Enough research exists to prove that dioxin is extremely toxic and persistent, and that levels in our environment and in human milk are increasing. Given that many health effects occur from exposure to even minute quantities over time, and that widespread contamination of our environment and the build-up of these chemicals in the food chain has already led to dangerously high levels in human milk and in marine mammals, all energy must be devoted toward preventing any further releases of dioxins into the environment.

The elimination of man-made dioxin sources would go hand-in-hand with the elimination of a much larger group of environmentally dangerous organochlorines, which would be extremely desirable from an overall environmental point of view. Elimination of all dioxin sources would mark a turning point in our dealings with pollution control, since a holistic approach would have to include the phase-out of an entire class of anthropogenic chemicals presently discharged in large quantities into the environment.

In 1983, after two years of research, the Ministers' Expert Advisory Committee on Dioxins stated that [15]:

"Regardless of arguments about the significance of species differences in sensitivity, the validity of risk assessments, and other uncertainties which may take years to resolve, it is quite clear that dioxins are very unpleasant things to have in our environment and the less we have of them the better. It is, in fact, imperative to reduce dioxin exposure to the absolute possible minimum."

Despite these recommendations, the Canadian government has failed to eliminate even such outstanding dioxin sources as pentachlorophenol, but has instead actually added new dioxin sources to the Canadian environment by building further municipal and hazardous waste incinerators.

Greenpeace demands that the Canadian government follow the leadership provided by forward thinking European governments, and:

establish a five-year plan to eliminate all known industrial dioxin sources,

and in particular:

- **ban import and use of chlorophenols immediately;**
- **establish an indefinite moratorium on construction of new municipal and hazardous waste incinerators;**
- **phase out disposable products made of PVC or PVDC;**
- **phase out PVC coating of copper wire;**
- **phase out chlorinated solvents;**
- **eliminate the use of chlorine in the pulp and paper industry and metallurgical industry;**
- **establish a mass-balance of chlorine and organochlorines in Canada; i.e. determine the amount of chlorine gas and organochlorines produced, and their fate in the environment. This mass balance should extend to other halogens and organohalogens;**
- **commission a feasibility study on phase-out of all production and use of organochlorines.**
- **Fund research to find clean production technologies and alternatives to chlorinated products, as well as safe methods of destroying the existing piles of dioxin and other chlorinated waste.**

This paper was researched and written by Renate Kroesa, M.Sc., Toxic Project Co-ordinator.

REFERENCES

1) Report from Conferences, the 5th Int'l Dioxin Symposium, Bayreuth, 1985; Chemosphere, 1986, 15, N1-2.

2) This entire section is based on the following five overview reports/books published on the toxicology of dioxin. All reports/books give an excellent overview and provide many detailed references to the interested reader.
   a) 'Human Health Aspects of Exposure to PCDDs and PCDFs'; UAREP, Bethesda, Maryland, June 1988 (funded by the American Paper Institute).
   b) 'The Chemical Scythe', by Alistair Hay; Plenum Press 1982.
   c) 'A Cancer Risk-Specific Dose Estimate for 2,3,7,8-TCDD'; US-EPA/600/6-88/007Ab, June 1988, plus Appendices A-F.
   d) 'Dioxins in the Environment' by the UK Dept of the Environment; Pollution Paper No. 27, 1989.
   e) S.A. Skene et al, Human Toxicol, 1989, 8, 173-203.

3) P.M. Mehrle et al, Environmental Toxicology and Chemistry, 1988, 7, 47-62.

4) F. Rohleder, Presentation to the 9th Int'l Dioxin Symposium, Toronto, 1989.

5) T. Sinks, Presentation to the 7th Int'l Symposium on Epidemiology in Occupational Health, Tokyo, 1989.

6) a) R.E. Bowman et al, Neurotoxicology, 1986, 7, 637-650.
   b) J.R. Allen et al, Toxicology and Applied Pharmacology, 1979, 48, A180.
   c) J.R. Allen et al, Bulletin of Environmental Contamination and Toxicology, 1979, 21, 463-469.

7) 'Who do you believe?', Jock Ferguson; Chemosphere, 1985, 14 791-796.

8) PCBs, PCDDs and PCDFs in Breast Milk: Assessment of Health Risks; WHO, Regional Office for Europe; EH 29 (1988).

9) W.R. Swain; Aquatic Toxicology, 1988, 11, 357-377.

10) Monitor 1988, Sweden's Marine Environment - Ecosystems Under Pressure; National Swedish Environmental Protection Board.

11) a) R.R. Bumb et al (Dow Chemical), Science, 1980, 210, 385.
   b) Nestrick et al (Dow Chemical), Chemosphere, 1983, 12, 617-626.

12) J.M. Czuczwa, R.A. Hites, Chemosphere, 1986, 15, 1417-1420.

13) a) A. Schector et al, Chemosphere, 1988, 17, 627.
   b) A. Schector et al, poster at the 9th Int'l Dioxin Symposium, Toronto, 1989.

14) W.V. Ligon et al (General Electric), Environ. Sci. Technol. 1989, 23, 1286-1290.

15) Report of the Joint Health and Welfare Canada/ Environment Canada Advisory Committee on Dioxins, November 1983.

GREENPEACE

Founded in Canada, 1971
Fondé au Canada, 1971

Vancouver

1726 Commercial Drive,
Vancouver
British Columbia
Canada V5N 4A3
✆ 604 253-7701
FAX 604 253-0114

Toronto

578 Bloor Street West
Toronto, Ontario
Canada M6G 1K1
✆ 416 538-6470
Fax 416 538-6479

Montréal

2444 Notre-Dame Ouest
Montréal (Québec)
Canada H3J 1N5
✆ 514 933--0021
Fax 514 933-1017

Press Gang Printers - a feminist worker-controlled collective

OREGON
INSIDER
A BIWEEKLY DIGEST OF ENVIRONMENTAL NEWS

Inside the Dioxin Standard: Is it Defensible?

CONTENTS

■ The Environmental Quality Commission (EQC) will decide Nov. 2 whether to hold public hearings on a complex proposal to update the state's water quality standards. The proposal covers an enormous number of topics including a new "anti-degradation standard" to protect pristine waterways, a new "wetlands" definition, and new standards for dissolved oxygen, bacteria, toxic pollutants, particulate matter and bacteria (see Issue 20).

Tucked somewhere in the middle of the package, the Department of Environmental Quality (DEQ) has proposed to keep unchanged the current and seemingly incomprehensible water quality standard for dioxin: 0.013 parts per quadrillion (ppq). In addition, the agency has for the first time proposed a standard limiting the amount of dioxin that can accumulate in fish tissue. Both proposals are sure to draw the attention of the pulp and paper industry and environmentalists.

Industry representatives have long questioned the scientific underpinnings of the dioxin standard. They have even challenged the assertion that dioxin poses any threat to human health or the environment, comparing it to broccoli in one study. On the other hand, environmentalists see a standard that leaves completely unregulated hundreds of closely related toxic organo-chlorine compounds that are discharged from bleach kraft pulp mills every day. Based only on protecting human populations from cancer, they also see a standard that ignores documented impacts on fish and wildlife and fails to address non-cancerous affects on human health such as reproductive interference and immune system suppression.

Each side contends that the standard for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) – the only compound regulated by DEQ's dioxin standard – should be changed in some way. For now, DEQ has decided to keep the standard as it is.

The standard "answers" a very narrow question for DEQ and the public: How much 2,3,7,8-TCDD can exist in the water column without creating more than a 1-in-a-million cancer risk?

The standard does not regulate the amount of dioxin in river bottom sediments, where a seemingly significant percentage of these insoluble compounds settle. It does not take into account the natural loss, or "attenuation," of dioxin through breakdown and binding with particles suspended in the water column. And, since compliance with the standard is measured down river at the edge of the "mixing zone," it isn't even used to directly regulate the amount of dioxin coming out of pulp mill discharge pipes.

There are significant gaps in the scientific understanding of this toxin and in the regulatory mechanism by which it is controlled. While it is impossible to resolve the many questions surrounding dioxin, it is not particularly difficult to understand the guts of the standard and how the federal government came up with the result of 0.013 parts per quadrillion.

An Understandable Formula

For all the rhetoric, battling experts, and discussions of "linearized multistage models," "LD_{50} values" and all the rest, the standard is surprisingly understandable. The Environmental Protection Agency developed the dioxin standard using a relatively simple formula that includes six factors:

$$\text{Dioxin Standard} = \frac{\text{RISK} \times \text{WT}}{[\text{WCR} + (\text{BCF} \times \text{FCR}) \times \text{CPF}]}$$

The Six Factors

RISK: The cancer risk society is willing to tolerate from dioxin.

WT: The weight of the average adult.

WCR: The amount of water ingested by the average person each day -- called the water consumption rate.

BCF: The extent to which fish concentrate dioxin in their tissues by swimming in contaminated water -- called the bio-concentration factor.

FCR: The amount of fish ingested by the average person each day -- called the fish consumption rate.

CPF: The chemical's cancer potency, a measure of how harmful the toxin really is -- called the cancer potency factor.

The Overall Debate

Agency officials, industry representatives and environmentalists seem to agree that the formula itself is scientifically defensible. The debate rages over what numbers go into the formula and to many broader issues surrounding dioxin regulation.

EPA/DEQ Numbers

Through laboratory tests and simple assumptions, EPA assigned values to each of these factors, plugged them into a formula, and came up with the dioxin standard. DEQ adopted all of EPA's recommended values. With estimates of potential compliance costs running in the hundreds of millions of dollars and predictions of disastrous human health and environmental impacts, there is a surprisingly high degree of "play" in the numbers used to calculate the final standard. As a result, experts on both sides have been free to tweak the

THE EPA/DEQ NUMBERS:

RISK	1-in-a-million
WT	70 kilograms*
WCR	2 liters/day
BCF	5,000
FCR	6.5 grams/day*
CPF	156,000

* 6.5 grams per day is about ¼ of an ounce of fish. 70 kgs is about 155 pounds.

OREGON INSIDER (ISSN 1043-7142) is published biweekly (twenty-four times a year) as a news service of the Oregon Environmental Foundation, 2637 SW Water Avenue, Portland, Oregon 97201 (503) 222-2252. The Foundation is a non-profit corporation dedicated to education and research. Executive Editor: Peter A. Ravella, OSB No. 86264, Staff Writers: Jeff Bernstein & Sarah McCoy. Business Manager: Greg Tozian. Advisory Board Members: Roy Hemmingway, Consultant; Margaret Kirkpatrick, Attorney, Stoel, Rives, Boley, Jones & Grey; Judy Roumpf, Publisher, Resource Recycling magazine; Connie Taylor, Associate, HartCrowser; Dan Saltzman, President, Environmental Management Solutions and Diane Dimon Snow, Assistant to Earl Blumenauer. Subscription Rates: $245 per year including first-class delivery, $135 for private, non-profit 501(c)(3) organizations. Multiple subscription rates available. Letters to the Editor and comments welcome at above address.

numbers to better fit their view of the relative risks and benefits of dioxin regulation.

Three of the six factors are generally accepted and attract little attention. These are the water consumption rate, body weight, and the acceptable risk (RISK) determination.

THE "ACCEPTED" NUMBERS

WCR - 2 liters/day

Water Consumption Rate (WCR). Because of how the formula works, this factor has virtually no affect on the final standard and consequently draws little attention. If DEQ were to eliminate drinking water as a route of dioxin exposure altogether -- and plug in a "0" for the WCF -- the final standard would not change.

WT - 70 kilograms

Body Weight Factor (WT). EPA used 70 kilograms for the body "weight" factor. At about 155 pounds, this seems to be a pretty good approximation of the average adult's weight. The dioxin standard would be stricter if the agency plugged in a smaller number for body weight. For example, had EPA used 50 kilograms -- about 110 pounds -- the final dioxin standard would be .009 PPQ instead of .013 PPQ.

All else being equal, people weighing less than 155 pounds, such as children and women would, on average, face a slightly greater risk of cancer than their heavier counterparts under the .013 PPQ standard.

RISK - 1-in-a-million

Acceptable Cancer Risk (RISK). There is no magic behind DEQ's decision to base the state's dioxin standard on a 1-in-a-million cancer risk. It is not mandated by federal or state law; it is a policy decision. According to Lydia Taylor, administrator of the Water Quality Division, all DEQ water quality standards have been based on this risk level since 1987.

1-in-10-million?

Reasonable people differ whether it would be appropriate to set environmental regulatory policy on a less demanding cancer risk limit. John Bonine, a professor of environmental law at the University of Oregon, questioned whether the general population should be subjected to any greater cancer risk for the sake of industry profits. "EPA has developed guidance for dioxin based on a 1-in-10-million cancer risk. Oregon is free to adopt it but hasn't," he said.

A standard based on a 1-in-10-million cancer risk would be ten times tougher than the current one, or .0013 PPQ.

1-in-10,000?

According to Doug Morrison, environmental counsel for the Northwest Pulp & Paper Association, using a 1-in-a-million cancer risk level can be overly protective. Morrison said it would be statistically sound to accept cancer risks as high as 1-in-100,000 or 1-in-10,000 for certain sub-populations -- such as Native Americans, Asians and recreational fisherman who eat more river fish -- because there are fewer than 1 million in the group. "You can allow a higher risk factor for these smaller groups and still not cause any additional cancers," he said.

Other States Vary

At least one other state has decided to accept greater risks. Maryland's dioxin standard is based on a 1-in-100,000 cancer risk and is 1.2 PPQ, about 100 times less stringent than Oregon's.

DEQ Uses 1-in-a-million

Because DEQ's Water Quality Division has uniformly set its standards based on a 1-in-a-million cancer risk, it seems unlikely that the state would follow Maryland's lead. The EQC has made it an agency-wide goal to apply a uniform risk level to all regulatory programs, but that level has not been defined, (see DEQ 1990 "Strategic Plan."

THE "CONTROVERSIAL" NUMBERS

The remaining three factors -- fish consumption (FCR), cancer potency (CPF), and bio-concentration (BCF) -- have attracted the most debate for a couple of reasons. Not only do these factors have the greatest impact on the final standard, but the information on them is less developed. The bio-concentration and cancer potency numbers are based on laboratory studies that remain open to interpretation in the scientific community. Definitive surveys on consumption of Columbia River fish have not been done.

FCR: Who Does the Standard Protect?

Fish Consumption Rate (FCR). The debate over this factor is not complicated. Because different people eat different amounts and kinds of fish, a simple question arises: What single number best represents the public's average fish consumption? The answer may be, "There isn't one."

EPA's Number

In adopting the dioxin standard, DEQ accepted EPA's estimate that the average person consumes 6½ grams of freshwater or estuarine fish per day. That's a little less than one-quarter of an ounce per day, or about 5 pounds of fish and shellfish per year. According to Gene Foster, DEQ's expert on the dioxin standard, EPA based its estimate on a limited nationwide market survey of consumer buying habits.

Complete Data is Unavailable

"Complete fish consumption data has not been compiled specifically for the Columbia River system -- where the pulp mills discharge their effluent -- or for the fish most commonly consumed," said Foster. With the help of the Columbia River Intertribal Fish Commission, EPA is studying the diets of Native Americans along the river. Results could be available by year's end.

Accounting for Sub-Groups

Foster said differences between identifiable sub-groups cannot be overlooked when compiling fish consumption data. Native Americans -- particularly those living along the river -- Asians, commercial and recreational fisherman, and low-income subsistence fisherman all eat more fish than the general population.

FCR Range: 6.5 to 150 g/day

According to a preliminary risk assessment done by EPA this Summer, members of some sub-groups along the Columbia consume as much as 100 to 150 grams or about 3½ to 5¼ ounces of fish per day. "These rates are not off the wall," added Foster.

Industry says 13 - 16 g/day

Even the Northwest Pulp and Paper Association (NWPPA) -- an industry trade group -- acknowledges that EPA's 6.5 g/day figure is too low. The NWPPA estimates that recreational fisherman and Native Americans eat a little more than 13 and 16 grams of fish per day, respectively.

Most Agree 6.5 g/day is Low

The table at right shows how the dioxin standard would change if higher fish consumption numbers were plugged into the formula. No one claims that the average fish consumption rate in the Northwest is less than the 6.5 g/day. While

HOW MUCH FISH DO YOU EAT?

Grams Per Day	No. of 6 oz. Meals / Wk.	New Standard*
6.5	.2	0.013
10	.4	0.089
25	1.0	0.0035
50	2.0	0.0017
75	3.0	0.0012
100	4.0	0.0009
150	6.0	0.0006

* This is how the standard would change if DEQ used a higher FCR.

individuals may consume as much as 150 g/day, the overall average for the population would be lower.

BCF: Inadequate Science

Bio-concentration Factor (BCF). Dioxin in the environment tends to concentrate in living organisms, but in different ways and in different amounts. This factor quantifies the amount of dioxin fish concentrate in their tissues by swimming in contaminated water. Surprisingly, it does not take into account dioxin entering the fish through the food chain, just absorption through the skin.

Simplistic Studies

Based on simplistic laboratory experiments, EPA concluded that some fish concentrate 5,000 times as much dioxin in their tissues as is found in the water column. As with all other factors, DEQ adopted EPA's conclusion rather than conduct its own experiments.

Food Chain Ignored

Environmentalists argue a BCF of 5,000 grossly underestimates the amount of dioxin in fish tissue and therefore, the amount ingested by humans. "This is a significant oversight in the standard," said Bonine. "Scientists have documented dioxin accumulation in fish through the food change -- called "bio-accumulation" -- and it is a more important route of exposure than absorption through the skin," he said.

BCF Could Go Higher

Agency officials, industry representatives, and environmentalists generally agree that the BCF should be higher. The debate is over how much higher. Studies conducted for the NW Pulp & Paper Association indicate the BCF for sturgeon ought to be 10,600, over twice as high as the number EPA plugged into the formula.

BCF for Non-Resident Fish at Issue

"We acknowledge that our effluent is responsible for elevated dioxin levels in local, resident fish populations near our discharge pipes, said Llewellyn Matthews, executive director of the NWPPA. "We are not convinced that pulp mill effluent contributes to dioxin levels found in non-resident fish such as salmon. There are other sources of dioxin," she said.

HOW MUCH DIOXIN DO FISH ACCUMULATE?

BCF Values	New Standard*
10,000	0.0069
25,000	0.0027
50,000	0.0013
75,000	0.0009
100,000	0.0006
150,000	0.0004

* This is how the standard would change if DEQ used a higher BCF.

BCF Range: 5,000 to 150,000

According to Bill Diamond, director of EPA's Water Quality Criteria and Standards Division, EPA studies suggest the bio-concentration factor could range as high as 159,000.

Environmentalists have even argued the BCF could be as high as 500,000 for some species, if contamination of the food chain is taken into account.

DEQ Leans to 50,000

DEQ seems to be leaning toward a moderate increase in the bio-concentration factor. "The conclusions on this factor are very crude at this point," said Foster. "My guess is it will settle in somewhere around 50,000 to 60,000." The table at right shows how the dioxin standard would change if a higher bio-concentration factors were used. According to Foster, DEQ is planning to conduct field studies to develop a more accurate BCF for Columbia River fish.

CPF: How Toxic is Dioxin?

Cancer Potency Factor. Most of the debate has focused on this factor, which indicates dioxin's human cancer-causing potential. All arguments by industry and the environmental community regarding dioxin's dangerousness are subsumed in this factor. A closer look at this factor reveals that even if the industry's lowest cancer potency number is plugged into the formula, the dioxin

standard is still less than 1 part per quadrillion.

EPA selected a CPF of 156,000 mg/kg/day. The higher the CPF, the more dangerous the chemical, and the lower the water quality standard.

The Kociba Study . . .

The federal agency based its CPF on a single, two-year rat liver study completed in 1978 by Dr. R.J. Kociba. Since then, industry representatives and some members of the scientific community have challenged the Kociba study. Critics point out that the model used to develop the CPF is too simplistic. They argue Dr. Kociba improperly counted "precancerous liver tumors," failed to incorporate a "no observable affect level" in the test, and made other errors.

Under Attack

Dr. Robert Squire, a John Hopkins researcher and participant in the original study, recently reevaluated Dr. Kociba's data and concluded that the CPF was too high, possibly by a factor of 10 or more. EPA and DEQ acknowledge that legitimate questions surround the Kociba study but they are not prepared to change the CPF yet.

Other Agencies Use Lower CPFs

Other federal agencies use cancer potency factors much lower than EPA's. The U.S. Food and Drug Administration uses a CPF of 17,500 and the federal Center for Disease Control uses 36,000. According to Lydia Taylor, the administrator of DEQ's Water Quality Division, it would not be appropriate for DEQ to regulate dioxins based strictly on these cancer potency factors. "FDA is required to take economics into account when developing their cancer potency factor and we are not," she said.

Industry Wants State Review

The NWPPA has repeatedly urged DEQ to conduct its own review of dioxin's cancer potency. "The upshot is we believe they have over estimated the cancer potency of dioxin and that the states should do their own independent analysis of this factor," said Matthews.

The Washington Department of Health — with help from University of Washington researchers — has undertaken its own study of dioxin's cancer potency. EPA also has a study underway but Oregon does not.

DEQ May Respond

"We will be looking at the cancer potency factor when the new data is available from EPA, but for now we are satisfied with the value we are using," said DEQ's Foster.

CPF Range: 6,700 to 250,000

The range of CPF values seems to be between 6,700 and 250,000. The NWPPA says 6,700 to 9,700 is justified based on the Squire re-analysis and other studies. Environmentalists have challenged the objectivity of the Squire re-analysis and argue that there is no compelling reason to lower the CPF. They also assert that the CPF could be as high as 250,000.

HOW POTENT IS DIOXIN?

CPF Values	New Standard*
6,700	0.321
9,700	0.222
17,500	0.123
36,000	0.059
250,000	0.008

* This is how the standard would change if DEQ used a lower CPF.

DEQ Leans to 15,000

According to Foster, some studies suggest that the CPF could be as low as 15,000. If such a CPF were used, the dioxin standard would be about 0.12 PPQ, or about 10 times less strict than the current standard.

The table at right shows how the dioxin standard would change if lower CPF values were plugged into the formula. None of the new standards exceeds a single part per quadrillion.

PULLING IT TOGETHER

How Does the Standard Change?

The large table on page 8 shows how the dioxin standard changes as the various parameters are "tweaked" one at a time. It also shows what happens if the controversial factors were all changed at the same time, rather than independently of each other. With the help of industry, the environmental community and DEQ, four new dioxin standards were developed – two "NWPPA Numbers," the "Bonine Numbers" and the "DEQ Lean To."

Industry's Scenario

NWPPA Numbers. These numbers were provided by Doug Morrison, an attorney for the NW Pulp and Paper Association. If DEQ were to assume a fish consumption rate of 13.4 grams per day, a bio-concentration factor of 10,600 and a cancer potency factor of 6,700, the final dioxin standard would be .073 PPQ, about 5 times less strict than the current standard but still less than 1 PPQ. If the CPF were 9,700 – the NWPPA's upper end estimate – the final standard would be .050 PPQ.

Environmentalists' Scenario

Bonine Numbers. As an "exercise in number crunching," John Bonine agreed to provided his estimates for the factors: a fish consumption rate of 100 grams per day to protect Native Americans; a body weight of 50 kilograms – about 110 pounds – to better protect women and children; a risk factor of 1-in-10-million; and a bio-concentration factor of 50,000. Based on these assumptions, the dioxin standard would be 0.0000021 PPQ or 0.0021 parts per quintillion.

Bonine is actively engaged in the dioxin debate, representing the Northwest Coalition for Alternatives to Pesticides (NCAP) in litigation over DEQ's dioxin regulations.

FOUR POSSIBLE STANDARDS

Source of Values	New Standard*
NWPPA Numbers	.050
NWPPA Numbers	.073
Bonine Numbers	.0000021
DEQ 'Lean To'	.0037

* This is how the standard would change if EPA used the unofficial values provided by industry, environmentalists and DEQ.

DEQ's 'Lean To' Scenario

DEQ 'Lean To'. This scenario was developed with DEQ's help but does not reflect the agency's position on the dioxin standard. These numbers used are values the agency may "lean to" if the standard is eventually reviewed. The values are a fish consumption rate of 25 grams per day (about 1 fish meal per week), a bio-concentration factor of 50,000, and a cancer potency factor of 15,000 (over 10 times smaller than EPA's current CPF of 156,000, and smaller than any CPF employed by other federal agencies). Based on these assumptions, the final dioxin standard would be .0037 PPQ, or about 3½ times more strict than the current standard.

CONCLUSION

No Silver Bullets

All parties to the controversy acknowledge that the .013 PPQ dioxin standard is based on rough guesses and uncertain science.

Whether DEQ's dioxin standard is too strict, or not strict enough, depends on each individual's personal sense of comfort with levels of acceptable risk, and the economics of reaching the standard. As Dr. Donald Barnes, Director of the

TWEEKING THE NUMBERS: A LOOK AT HOW THE STANDARD CHANGES

	Fish Consumpt (FCR)	Water Consumpt (WCR)	Body Weight (WT)	Accepted Risk (RISK)*	Bioconcen-tration (BCF)	Cancer Potency (CPF)*	Final Standard
DEQ's Standard	6.5	2	70	1.00E-06	5,000	156,000	.013 PPQ
	(g/day)	(l/day)	(kg)			(mg/kg/day)	
	10	2	70	1.00E-06	5,000	156,000	.0089 PPQ
Tweeking	25	2	70	1.00E-06	5,000	156,000	.0035 PPQ
the	50	2	70	1.00E-06	5,000	156,000	.0017 PPQ
FCR	75	2	70	1.00E-06	5,000	156,000	.0012 PPQ
	100	2	70	1.00E-06	5,000	156,000	.0009 PPQ
	150	2	70	1.00E-06	5,000	156,000	.0006 PPQ
	6.5	2	70	1.00E-06	10,000	156,000	.0069 PPQ
Tweeking	6.5	2	70	1.00E-06	25,000	156,000	.0034 PPQ
the	6.5	2	70	1.00E-06	50,000	156,000	.0013 PPQ
BCF	6.5	2	70	1.00E-06	75,000	156,000	.0009 PPQ
	6.5	2	70	1.00E-06	100,000	156,000	.0006 PPQ
	6.5	2	70	1.00E-06	150,000	156,000	.0004 PPQ
	6.5	2	70	1.00E-06	5,000	6,700	.321 PPQ
Tweeking	6.5	2	70	1.00E-06	5,000	9,700	.222 PPQ
the	6.5	2	70	1.00E-06	5,000	17,500	.123 PPQ
CPF	6.5	2	70	1.00E-06	5,000	36,000	.059 PPQ
	6.5	2	70	1.00E-06	5,000	250,000	.008 PPQ
NWPPA Numbers	13.4	2	70	1.00E-06	10,600	9,700	.050 PPQ
	13.4	2	70	1.00E-06	10,600	6,700	.073 PPQ
Bonine Numbers	100	2	50	1.00E-07	150,000	156,000	.0000021
DEQ's 'Lean To'	25	2	70	1.00E-06	50,000	15,000	.0037 PPQ

*NOTE: The RISK FACTOR is expressed in Lotus 1-2-3 scientific notation. A 1.00E-06 notation means a 1-in-a-million risk and 1.00E-07 means 1-in-10-million.

EPA's Science Advisory Board, told the EQC this summer, "When it comes to dioxin, there are a lot of uncertainties; there are no silver bullet answers."

Standard Unlikely to Exceed 1 PPQ

Whatever else is decided, a few conclusions can be drawn. First, no single factor will be changed in isolation. Both DEQ and EPA are committed to a full review all the factors, not just the just the cancer potency, bio-concentration, or fish consumption numbers. Second, even if adjustments are made, it appears the final standard will remain below a single part per quadrillion, far below the detectable limits of today's instruments. Third, under all the scenarios presented, it appears the Columbia River will remain "water quality limited," forcing the mills to make expensive improvements to control dioxin.

Status & References

If approved by the EQC Nov. 1, eight public hearings on DEQ's entire water quality regulatory package, including the dioxin standard, will be held between Jan. 14 and Jan. 22 (watch *OI Calendar* for details). For more information, contact Eugene Foster (DEQ) at 229-6982. References: ORS 468.735, OAR 340-41 Table 20 (proposed water quality standards for toxic substances).

AIR QUALITY

Advisory Committee to Recommend Few Changes to Protect Wilderness Area Visibility

■ After some 18 months of work, it appears a Department of Environmental Quality (DEQ) advisory committee will recommended few if any significant changes in the way the agency protects visibility and other "air quality related values" in wilderness areas. Even though the group will recommend adding some new wilderness areas to the program, it will be years before that occurs.

Low Priority

"This is a slow moving process — it's not on the front burner," said John Core, visibility program coordinator and liaison to the advisory committee.

The recommendations are being developed as part of a federally-mandated review of the state "Visibility Protection Program." The VPP is supposed to protect air quality related values such as scenic vistas, air chemistry, aquatic biology and even sensitive plants in certain designated wilderness areas.

Triennial Review Underway

First completed in 1986, the VPP was approved by the Environmental Protection Agency in 1987. The program is unique because it requires air pollution control measures even where air quality is generally very high. The idea is to "preserve, protect, and enhance" the pristine air quality often found in wilderness areas, national parks, national seashores and similar areas.

DEQ appointed a 15-member Visibility Protection Advisory Committee last April to help review the program. The group includes representatives of the public, federal land management agencies, timber and agricultural industries, environmentalists and the tourism industry.

Field & Slash Burning at Issue

The primary threat to air quality in these areas is smoke from grass seed industry field burning, forest industry slash burning, and natural forest fires. The VPP restricts field and slash burning during certain months so smoke does not interfere with recreational uses.

Twelve Areas Protected Now

Some of Oregon's most noteworthy attractions are among the 12 wilderness areas currently protected under the program. These include Crater Lake National Park, Mt. Hood Wilderness Area, and popular wilderness areas near Bend. Designated "Class I," these areas receive the greatest air quality protection under the Clean Air Act and DEQ regulations.

Two Questions

There are two general questions before the committee. First, should DEQ expand the VPP to include areas set aside as wilderness since 1977? Second, should DEQ change the way visibility and other related values are protected?

[illegible]

IF YOU THINK WHITER IS BETTER...

GREENPEACE

...THINK AGAIN.

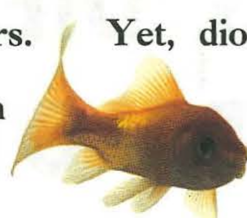
This paper is white. It was bleached with oxygen.

This paper is whiter. It was bleached with chlorine.

A SMALL DIFFERENCE TO YOU...

...MAKES A BIG DIFFERENCE TO OTHERS.

Chlorine-bleached pulp is bad for the environment. There can be no doubt about that. Studies have shown again and again that effluents from kraft or sulphite mills using chlorine technology lead to reduced reproductivity in fish, suppressed immune systems, impaired metabolism, and a multitude of other long-term effects. Chlorine-bleached paper is also bad for you. Many of the chlorinated poisons discharged by the mills will also be found in paper - like the page you are now holding in your hand. Even dioxin, one of the most toxic chemicals ever produced, is likely to be present in this chlorine-bleached paper. Dioxin has been proven to leach from bleached paper products, such as milk cartons and coffee filters. Yet, dioxin is only the tip of the iceberg when it comes to organochlorine pollution from pulp and paper mills. Up to 1,000 different chemicals can be found in the effluent of mills employing chlorine-bleaching. Many of these cause cancer or genetic damage



and are persistent and accumulate in the environment. On average, pulp mills discharge around 35 tons of toxic organochlorines every single day. Even those mills that already have upgraded their process to reduce formation of the most notorius organochlorine, dioxin, will still discharge between 10 and 20 tons of other chlorinated poisons every single day. These discharges must stop now. The page you are now reading was printed on sulphite pulp bleached with oxygen-based agents. Such chlorine-free bleaching technology is readily available and must be employed immediately by mills using the sulphite process. Chlorine-free bleaching technology available for kraft mills will yield a cream-colored pulp. That brightness is entirely sufficient for most purposes, particulary since kraft pulp is mainly used in paper products that need to be strong, not white, such as packaging, stationery or envelopes.

THINK TWICE BEFORE YOU BUY WHITE, AND SUPPORT GREENPEACE IN ITS DEMANDS FOR

- Complete elimination of all chlorine-based bleaching chemicals.
- Use of the right fiber for the right product, i.e. the use of off-white kraft and off-white sulphite pulp, or completely unbleached pulp whenever possible.

CHLORINE-FREE BY 1993!

For more information about different pulp and paper making technologies and their impact on the environment, please ask us for the Greenpeace Guide to Paper.

B.R.O., Stockholm. Werzäta, Göteborg.

GREENPEACE

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 10 1991
OFFICE OF THE DIRECTOR

7 June, 1991

Oregon Environmental Quality Commission
c/o Oregon DEQ Director's Office
811 S.W. 6th Avenue
Portland, OR 97204

Director
Oregon Department of Environmental Quality
811 S.W. 6th Avenue
Portland, OR 97204

Dear Commissioners and Director:

We understand that James River, Inc. and Boise Cascade Corp., along with several co-petitioners have asked the Commission and the DEQ to amend the state's ambient water quality standard for 2,3,7,8-TCDD from a current level 0.013 ppq to 2.3ppq.

We wish to offer comments regarding the wisdom of honoring such a petition that we hope you will make part of the public record in this decision.

INADEQUATE PUBLIC NOTICE

First we must question the lack of public notification involved in this pending decision. We have, on more than one occasion, asked to be placed on the DEQ notification list for any water quality actions the Department has pending, particularly with respect to pulp mills.

Our requests have to date been ignored, and we find that the only way to obtain a copy of a notice or a draft permit is to hear of its existence from a third party and then to call the DEQ to request a copy be sent us. Nor have we received word of final decisions regarding permits or any response to permit comments we have offered. To say that this archaic and haphazard method of public notice is deficient is an understatement. It is certainly not consistent with the mandate for public participation inherent in EPA's having delegated the water quality program to the state of Oregon.

That the petitioners themselves have the temerity to suggest they have identified all interested parties as the few listed in item 2 of the Commission Chair's notice, is absurd. A gutting of the state's water quality standard for the most potent chemical known to mankind is not something to be decided privately after consultation with just a few individuals.

Even the more narrow decision the Commission intends to make about whether or not to initiate a rulemaking that could potentially weaken the standard should have received broader notice, e.g. tribal governments, fishing interests, the state health department and those state and federal agencies charged with protecting wildlife (e.g. the U.S. Fish and Wildlife Service).

THRESHOLD MODEL CITED BY PETITIONERS AS FAVORING THE WEAKENING OF A STANDARD HAS NOT BEEN PEER REVIEWED

We remind the Commission that the much touted theory regarding a supposed threshold mechanism for 2,3,7,8-TCDD has not yet been peer reviewed. The forum in which it was first advanced, at a Banbury conference last fall, has itself become known for the controversy it created among attendees (see attachment 1). No version of the theory has yet been published in the scientific literature, and the theory has been challenged by other dioxin scientists (see attachments 2, 3).

EPA's own review of it's dioxin standard is still underway and far from finalization, and any attempt by the state of Oregon to presuppose EPA's conclusions would be ill-advised. EPA Administer William Reilly himself warned against second guessing the Agency's dioxin review, advising that in the interim state governments should go on with business as usual.

There is also new evidence coming from other quarters that tends to refute the threshold theory cited so enthusiastically by the petitioners. Abstracts for two papers to be presented at this fall's dioxin symposium are attached which argue against reliance on such a theory (see attachment 4).

Moreover, a paper by Sargent, et al published in a recent issue of Carcinogenesis (see attachment 5) suggests alarmingly that even non-planar PCB's can act by a mechanism identical to that of coplanar compounds such as 2,3,7,8-TCDD, and that exposure to mixtures resulted in superadditive effects. The authors further state that humans already are exposed to levels at which adverse effects would certainly be occurring. This in turn suggests why the epidemiology concerning exposure to 2,3,7,8-TCDD is at best equivocal, except in very exaggerated doses, as was indeed the case for a recently published NIOSH study (see attachment 6).

EVIDENCE CITED BY PETITIONERS REGARDING BIOCONCENTRATION IN FISH AND FISH CONSUMPTION RATES DIFFERS DRAMATICALLY FROM THAT OFFERED BY MORE CREDIBLE SOURCES

Petitioners suggest that the prevailing way of estimating bioconcentration (BCF) factors in fish used to calculate the current standard should be scrapped, and that a different (less conservative) method for estimating BCF's should be substituted. The method they suggest yields a number in the same ballpark as

the existing one. Yet there is much evidence from EPA's lab in Duluth to suggest that fish are far better at taking up and storing dioxin than the 5000 factor now in use supposes (see attachments 7, 8), and the Agency has requested funds in its 1992 budget to re-evaluate its BCF assumptions.

In fact it has been shown that even Columbia River salmon, species thought to be more protected from uptake because of their mobility and feeding patterns, are harboring levels of dioxin in their edible tissues (see attachment 9).

Patterns of human fish consumption in the Pacific Northwest also argue for a much stronger standard. EPA has long acknowledged that the average fish consumption rate of 6.5 grams per day per person assumed in the setting of its current standard seriously underestimates actual eating patterns, and this has been confirmed by surveys in several states. Moreover, work by EPA's Cleverly and McCormack indicates that Columbia River sports and subsistence fishers, Native Americans, and Asian Americans eat far more fish than the levels suggested by petitioners (see attachment 10). One wonders how petitioners could have arrived at the impossibly low figures they suggest.

Petitioners also make the illogical claim that only fish consumption from the Columbia River need be considered, irrespective of the rest of one's fish diet, as if to suppose that all other sources of fish (or food) are free from contamination.

THE STATE HAS A DUTY TO PROTECT US FROM OTHER HARM THAN JUST CANCER, AND FROM OTHER POLLUTANTS THAN JUST 2,3,7,8-TCDD

Petitioners make mention of Keenan, et al's re-evaluation of the Kociba rat study from which EPA's current acceptable daily intake is derived. They suggest that we should take heart from the fact that slightly more than half a team of 9 scientists funded by the industry should find that many of the liver lesions identified by Kociba as cancerous might only be pre-cancerous after all. A critique of this study is enclosed.

In any case, it is hardly reassuring to expect that one's liver be riddled with dioxin-induced lumps and bumps of any kind. We similarly find no comfort in the fact that women thoughout the industrialized world are passing dioxins and other organo-chlorines on to future generations through the placenta and via breast-feeding.

Studies on primates have shown that dioxins can cause profound behavioral and reproductive effects at very low doses. The petitioners ignore all non-cancerous effects in arguing for a weaker standard.

It must also be noted that 2,3,7,8-TCDD never occurs in

isolation. Discharges from the pulp and paper industry include other dioxins and furans and numerous other compounds which exhibit similar mechanisms of toxicity. The Sargent study mentioned above gives added weight to the likelihood that these compounds can act synergistically.

THE STATE HAS A DUTY TO PROTECT THE ENVIRONMENT AS WELL AS HUMAN HEALTH

Petitioners have offered no evidence to suggest that a weakened ambient water quality standard will be sufficiently protective of aquatic life or fish-eating birds and mammals.

Nor have petitioners demonstrated that a weakening of the current dioxin standard will not adversely effect bald eagle populations on the lower Columbia River, as required under the Endangered Species Act. Much evidence already exists to suggest that dioxins and other organochlorines are negatively impacting these birds. The pending listing of various wild salmon species will further increase the burden of proof necessary to justify any continued discharge of dioxin and other organochlorines.

A RELAXING OF THE DIOXIN STANDARD AS PROPOSED BY INDUSTRY WILL NOT RELIEVE THE INDUSTRY OF ANY FINANCIAL BURDEN FOR POLLUTION CONTROL

The same technologies that must be implemented by petitioners to meet the state's current dioxin standard will in any case be required in order to meet the technology-based standards already in their NPDES permits. Indeed, the longer the industry waits to install new bleaching technology, the greater will be their ultimate financial burden.

Capital costs for equipment will only be more expensive, and the money invested in stopgap measures such as chlorine-dioxide generators will only be money wasted. The U.S. industry can also be expected to lose market share in Europe as a result of its recalcitrance, as is already proving the case in Canada. Fletcher Challenge's failure to produce chlorine-free pulp for its foreign market has already cost them an estimated $ 5 million dollars in loss of sales.

THE ONLY ACCEPTABLE STANDARD FOR DIOXIN IS ZERO, AND THE STATE OF OREGON SHOULD TAKE IMMEDIATE STEPS TO ELIMINATE ALL KNOWN SOURCES

Dioxin is the most intensively studied compound in history, and will doubtless remain the darling of the scientific community for years to come. Even so we still do not know its precise toxicity to humans, and given the degree to which we are all already contaminated with dioxin and dioxin-like compounds, we probably never will. There is simply no such thing as a control group to serve as a baseline.

But what we do know is serious enough to make moot any further quibbling about precisely how much is too much dioxin. What we know is more than enough to justify elimination of all known sources.

We urge the Department and the Commission to deny the petition to set a weaker dioxin standard, and instead use your limited resources to moving the pulp and paper industry into chlorine-free technology. The technologies exist, and only await implementation.

Sincerely,

Shelley Stewart

Shelley Stewart
U.S. Pulp/Paper Project

***

Please note that these comments are printed on chlorine-free paper imported from Europe. No North American manufacturer has yet been willing to produce chlorine-free bleached office or printing paper.

Attachment 1

UNIVERSITY OF MARYLAND AT BALTIMORE

The University Program In Toxicology
660 West Redwood Street
Howard Hall, Room 544
Baltimore, Maryland 21201-1596
(301) 328-8196

January 29, 1991

Dr. Jan Witkowski
Director
Banbury Center
Cold Spring Harbor Laboratory
P O Box 534
Cold Spring Harbor, NY 11724

Dear Dr. Witkowski:

I was a participant in the recent Banbury Conference on "Biological Basis for Risk Assessment of Dioxins and Related Compounds" held at the Banbury Center in October 1990. I am writing you becuase I have just been informed of a very disturbing result of that conference, a press release sent out by a public relations firm along with statements by Drs Scheuplein, van der Heiden, and Gallo purporting to represent the "consensus" views of the participants at that conference with espect to regulatory conclusions related to risk assessment of dioxins. I only learned of this press release from a reporter who called me last week (Marguerite Holloway of Scientific American).

This press release, copy enclosed, was never shown to me or to most of the participants in the conference, as far as I know. Thus, in terms of process alone, it should not be represented as a "consensus" document. Morover, its contents do not accurately reflect the views of all participants, or even a consensus of those views, as best I can determine. I resent the circulation of this press release as reflecting the views of a meeting in which I was a participant, and I feel that my name attached to it somehow implies my agreement with it.

I am in fact rather astounded by such a product from a Banbury Conference. While it was rather obvious to some of us that the organizers, and some of the sponsors, of this confernece had some trans-scientific objectives in mind related to regulations concerning dioxin, I had expected that the Banbury Center would be able to keep these motives under control. The press releases and statements imply that a major focus of the conference was a discussion of the regulatory risk assessments that have been applied to the dioxins; this was not the focus of this meeting. I agreed to participate based upon my previously held high regard for Banbury and Cold Spring Harbor. I did not expect to be manipulated by industry and government spokespeople

(who are not dioxin researchers, incidentally) to be made into a supporter of their political views on dioxins and risk assessment. This is particularly annoying to me because I was invited to present the main conference paper on the topic of the scientific basis for dioxin risk assessment. In this paper, I have attempted to present the complexity of integrating the basic molecular biology of dioxins into a receptor-based model. I do not feel that the state of knowledge on this complex topic can be reduced to a simplistic press release.

The preparation and release of these documents by Drs Scheuplein, van der Heijden, Carlo, and Gallo, with the assistance of a public relations firm, discredits all of us. It challenges the precious institution of free scientific discussion, epitomized by such places as Banbury, Dahlem, and the Gordon conferences. I hope you believe that I would be just as angry if this action had been taken by an environmental group. I trust you will take aciton to dissociate Banbury from this attempt to manipulate science and scientists. Because these people have acted without consulting the rest of us, and because I have heard about this only through the press, I am with great regret also sending this letter to the persons shown under my signature, as well as to my colleagues at the conference, an action not taken by these people.

Yours sincerely,

Ellen K Silbergeld

Ellen Silbergeld, PhD
Visiting Professor of Toxicology and
Adjunct Professor of Pharmacology
and Experimental Therapeutics

cc: Leslie Roberts, Science
Marguerite Holloway, Scientific American
Cristine Russell, Washington Post
Chris Joyce, New Scientist
Judy Randall, The Economist
Betty Mushak, NIEHS
William Farland, EPA

attendees, Banbury Conference on Dioxins

History Lessons

Warfare analysts offer some disturbing—and hopeful—news

Political leaders always claim to be steering us by the lights of history toward a peaceful future. But what does a comprehensive analysis of our past actually reveal about our present course? A pessimist could conclude that our leaders are completely misreading—or misrepresenting—history. An optimist could find hope that warfare might become obsolete anyway—if the tentative spread of democracy worldwide continues.

These conclusions are both supported by the Correlates of War project, a computerized storehouse of information on 118 wars (defined as conflicts leading to at least 1,000 deaths) and more than 1,000 lesser disputes from the early 1800s to the present. Researchers at the University of Michigan created the data base in the 1970s to find statistical associations between warfare and various economic, political and social factors.

The data offer no support for the bromide "peace through strength," according to J. David Singer, a political scientist at Ann Arbor who oversees the Correlates project. A buildup of military armaments, far from deterring war, is one of the most frequent precursors of it. At the very least, Singer says, such a finding suggests that the U.S. policy of supplying arms to nations in an unstable region—such as the Middle East—is seriously flawed.

There is also no evidence that alliances help to keep the peace. In fact, a nation's participation in one or more alliances increases its risk of warfare, Singer says, particularly against its allies. History even casts doubt on the argument—used by the U.S. to justify both its current war against Iraq and its past one against Vietnam—that allowing aggression to proceed unchecked always leads to more aggression. Although Hitler's Europe certainly provides an important counterexample, Correlates of War data yielded little statistical correlation between warfare in a given region and prior unchecked aggression, Singer says.

A somewhat more hopeful finding

A Press Release on Dioxin Sets the Record Wrong

When the Chlorine Institute shopped around for a place to hold a scientific conference, they did not want just any host. "We were looking for an organization that was squeaky clean, that would not in any way, shape or form be questioned about the conference," says Robert G. Smerko, president of the Washington, D.C.-based Institute, which is supported by some 170 chemical, paper and other manufacturers.

Smerko seemed to have met his requirements when he finally landed Cold Spring Harbor Laboratory. Last October the laboratory's respected Banbury Center held a conference—jointly sponsored by the Chlorine Institute and the Environmental Protection Agency—on the toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, or TCDD. That chlorinated compound achieved notoriety during the Vietnam War, when it was identified as a contaminant of the defoliant Agent Orange. It remains controversial because it is found in some commercial herbicides and is produced in other chemical processes, such as paper bleaching.

Cold Spring Harbor Laboratory may have been squeaky clean, but the conference apparently was not. And the outcome of that meeting—attended by 38 of the world's dioxin experts, few of whom say they knew it was industry sponsored—is every bit as controversial as the substance that was the topic of discussion.

The issue is a press release sent out at the conclusion of the meeting by the Chlorine Institute's public relations firm, Daniel J. Edelman, Inc. It announced that the experts had agreed on a model for the toxicity of dioxin that "allows for the presence of a substance in the environment, with no risk experienced below a certain level of exposure." The release said that the scientists had rejected a linear exposure model, in which any level of exposure would have a biological effect, in favor of a receptor-based model that implies a threshold level. (This part of the release was approved by Cold Spring Harbor Laboratory, says the Banbury Center's director, Jan A. Witkowski—although he now says Edelman made several changes after he saw it.)

Such a consensus, of course, would have implications for setting permissible levels of the substance in the environment. But those at the conference insist that no such agreement was reached. "There was no consensus in terms of risk assessment," says George W. Lucier of the National Institute of Environmental Health Sciences. In addition, none of the scientists saw the press release, although their names accompanied it. "We were being used, clearly, and that's unfortunate," declares Arnold J. Schecter, professor of preventive medicine at the State University of New York at Binghamton. "Political layering is not particularly good, especially when it is unbeknownst," Lucier adds.

Few of the participants seem to dispute that the receptor-based mechanism of dioxin is relevant to human exposure. Nor did they before the conference, observes Alan P. Poland of the University of Wisconsin at Madison, who discovered the receptor in 1976. "The basic tenets were all known since 1981 or 1982," Poland says. But Lucier notes that now "we are at the point where we can reevaluate the linear model."

Indeed, the EPA intends to explore the question of whether there is a threshold response. The agency will investigate the receptor-based model with Michael A. Gallo, one of the conference organizers and a professor of toxicology at the University of Medicine and Dentistry of New Jersey–Robert Wood Johnson Medical School. But Gallo and others agree that discussion of thresholds in a regulatory context may be premature. At the conference, "some regulators got real excited by back-of-the-envelope calculations" and thought dioxin standards could be eased, says Linda S. Birnbaum, director of the EPA's environmental toxicology division. "Clearly, we don't know that."

Although many of the Banbury attendees were the last to know about the consensus they reportedly reached, news about the conference traveled quickly in political circles. At a recent hearing on dioxin standards in Alabama, expert witness for the pulp and paper industry Russell E. Keenan invoked the Banbury results in his testimony. "There was general agreement among the attending scientists that dioxin is much less toxic to humans than originally believed," Keenan claimed. Obviously, "it is not useless to tout Banbury results if you have a political ax to grind," comments Cate Jenkins, a chemist in the EPA's hazardous waste division. —*Marguerite Holloway*

Attachment 2

To: Dioxin Nerds, et al.
From: Tom Webster, CBNS Queens College, Flushing NY 11367
Date: 3/14/91
RE: Banbury Dioxin Model, Part 1 A Critique

A recent two article series in Science(1) covered the infamous Banbury conference on dioxin toxicity. The second article addresses the scandal aspect of the story, particularly the involvement of the Chlorine Institute. The first article (attached) addresses some of the scientific aspects, but does so in what I consider a rather opaque fashion.

In particular, the article shows an S-shaped graph which appears to show why dioxin has a threshold. Science indicates, using the graph, that "responses to dioxin increase slowly at first but then shoot up after passing a critical concentration."

However, all is not as simple as it seems at first. Since there has been some confusion regarding this business, I will address the graph in this memo.

(1) Background: The Ah receptor

First, a bit of background. 2,3,7,8-TCDD and other dioxin-like compounds (PCDFs, co-planar PCBs, chlorinated naphthalenes, etc.) are generally thought to cause toxicity through a receptor mediated mechanism. This receptor also binds aromatic hydrocarbons such as 3-methylcholanthrene and other non-halogenated aromatic hydrocarbons; hence it is termed the Ah receptor.

The Ah receptor is a protein which is normally found in the fluid (cytosol) of the cell (There is some controversy here; some people think it is found solely in the nucleus). Only certain molecules ("ligands") with certain properties (size ,shape, etc.) fit it, like a key into a lock. 2,3,7,8-TCDD has the best fit of any known compound. When this occurs, the receptor-ligand complex changes shape and moves into the nucleus. The change in shape helps it to recognize and bind to certain sequences in the DNA. This in turn causes the transcription and translation of adjacent DNA into protein. (This is quite similar to the mechanism of steroid hormones.)

The most well understood effect is the production an enzyme called P450IA1 which makes aromatic hydrocarbons more water soluble--and therefore easier to excrete--by adding hydoxyl (-OH) groups. One measure of this enzyme activity is called aryl hydrocarbon hydroxylase (AHH).

Many of the types of toxicity associated with dioxin-like compounds correlate with binding to the Ah receptor or AHH activity (also with EROD, a related enzyme activity). This provides good evidence that dioxin toxicity is mediated by the Ah receptor, i.e., binding to Ah is the first (but not only) step. It also provides both a theoretical justification and a measurement technique for 2,3,7,8-TCDD equivalents. If all dioxin-like compounds act through the receptor, then the potency of a given compound can be rated against 2,3,7,8-TCDD by their relative ability to bind Ah and induce AHH or EROD activity.

Nevertheless, other experiments show that many toxic effects are probably not directly caused by enzyme induction. Hence, other genes are probably being turned on by the Ah receptor as

well. The nature of these other genes and the biochemical mechanism of many toxic responses is not so well understood. I'll discuss some of this in a future memo.

(2) Receptor Kinetics

If the toxicity of dioxin-like compounds is mediated by the Ah receptor, clearly we need to understand this first step. Receptor-ligand relationships are mathematically described by the Michaelis-Menten equation, a standard tool for describing enzymes. This is schematically described as:

$$L + R \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} LR \qquad (1)$$

where "R" is the unbound receptor, "L" is the ligand (molecule binding to the receptor) and "LR" is the receptor-ligand complex. k_1 and k_{-1} are, respectively, the association and dissociation rate constants. At equilibrium, we find

$$K_D = [L][R]/[LR] \qquad (2)$$

$$K_D = k_{-1}/k_1$$

where the items in the brackets "[ ]" are concentrations and K_D is the dissociation equilibrium constant. The constant K_D tells us, in an inverse way, about the strength of the binding between the ligand and the receptor. A small K_D means the binding is strong, and thus the receptor-ligand complex is less likely to dissociate. Conversely, a large K_D means that the receptor-ligand binding is weak.

Equation (2) can be solved in terms of the amount of occupied (bound) receptor:

$$[LR] = [L]*R0/(K_D + [L]) \qquad (3)$$

where R0 is the total amount of receptor, bound and unbound.

Equation (3) gives the relationship between the amount of 2,3,7,8-TCDD (or other ligand) and the amount of bound receptor (LR). Remember that the toxic activity of 2,3,7,8-TCDD (and other dioxin-like compounds) is thought to be associated with the concentration of dioxin-receptor complexes. We could infer a dose-response curve with two additional pieces of information: i) the relationship between external dose (e.g., amount of exposure per day) and [L] and ii) the relationship between [LR] and toxicity.

Note that when the concentration of 2,3,7,8-TCDD is significantly less than K_D, the relationship is linear:

$$[LR] = [L]*R0/K_D \qquad \text{for } [L] << K_D \qquad (4)$$

Indeed, this equation indicates that even one molecule of 2,3,7,8-TCDD could bind to the receptor, indicating that there may be no theoretical threshold for activity. The slope of the curve is governed by the number of Ah receptors (R0) and the dissociation constant (K_D). Since 2,3,7,8-TCDD has a very small K_D compared to

other dioxin-like compounds, it binds tightly, and has a large slope.

For a high concentration of 2,3,7,8-TCDD, the curve saturates. One can't produce more receptor-dioxin complexes than there are receptors:

$$[LR] = R0 \qquad \text{for } [L] >> K_D \qquad (5)$$

(We'll ignore for now so-called "supermaximal" induction as well as circumstances which alter the number of receptors).

Finally, note that when the concentration of a compound equals its K_D, the number of bound receptors is equal to one-half the total number of receptors.

$$[LR] = R0/2 \qquad \text{for } [L] = K_D \qquad (6)$$

(3) Analysis of the Science graph

When equation (3) is plotted on normal graph paper it looks like my Figure 1, linear at low levels of 2,3,7,8-TCDD--the concentration of receptor-ligand complexes directly proportional to the concentration of ligand--and plateauing--at 100% bound receptor--at high levels of 2,3,7,8-TCDD.

When the same equation is replotted using the logarithm of the concentration of 2,3,7,8-TCDD, the graph looks like Figure 2, the same S-shaped curve seen in Science. Note that the horizontal axis in the Science graph gives concentration of 2,3,7,8-TCDD increasing by a factor of ten at each step; this is equivalent to using logarithms.

Finally, 50% of the receptors are shown as occupied in the Science graph when the concentration of 2,3,7,8-TCDD equals about 10^{-9} (Although not given, the units are undoubtably the standard moles per liter). This is the old K_D value for 2,3,7,8-TCDD. Actually, recent experiments indicate that the K_D is probably even smaller, on the order of 10^{-12} to 10^{-11} moles per liter. This means that 2,3,7,8-TCDD binds Ah more tightly than previously thought.

(4) Discussion

As a result, it should be clear that the graph in Science does not by itself indicate a threshold. The S-shape of the curve is an artifact of the graphing technique. Plotted on linear axes, the equation for ligand-receptor interaction indicates that the number of occupied receptors rises linearly from zero. In other words, this response should theoretically be linear at low doses with no threshold.

What then is really going on? Clearly, there must be more to the story. I'll be writing another memo on this, but let me give a few hints.

i) There may be other compounds inside the cell which bind to Ah, albeit with less affinity, complicating the picture.

ii) Binding to the receptor is just the first step. The other steps, binding to DNA, generation of protein, action of protein, etc., might not be linear. Hence, even though the first step might be linear, the final toxic response might not be.

ii) Binding to the receptor is reversible. However, the long half-life of dioxin-like compounds and the background exposure to them diminishes the strength of this argument.

iv) The Birnbaum[2] memo makes the following assumptions: 1) all toxicity is mediated by the Ah receptor binding; 2) induction of P450IA1 (AHH activity) is the most sensitive response of this system; 3) no effect occurs until one can measure an increase in enzyme activity. This defines a "practical" threshold that one can use to determine no-effect levels, etc.

In response to this last argument (briefly), enzyme induction may be the most sensitive response, but we don't really know. Also, lack of measurable activity doesn't necessarily mean no activity. Ability to measure a response is determined by many things including the sensitivity of the assay, the statistical power of the experiment, etc. In addition, 2,3,7,8-TCDD has a very long lifetime in the human body. Finally, the already existing body-burden of dioxin-like compounds in humans and other animals needs to be taken into consideration when examining such threshold models.

References

(1) Roberts, L. (1991a). Dioxin Risks Revisited. Science 251: 624-626. February 8.

Roberts, L. (1991b). Flap Erupts Over Dioxin Meeting. Science 251: 866-867. February 22.

(2) Birnbaum, L. (1990). Memo to E. Bretthauer (EPA-ORD) regarding Consensus at Banbury Dioxin Conference. October 31.

Figure 1 : Linear Plot

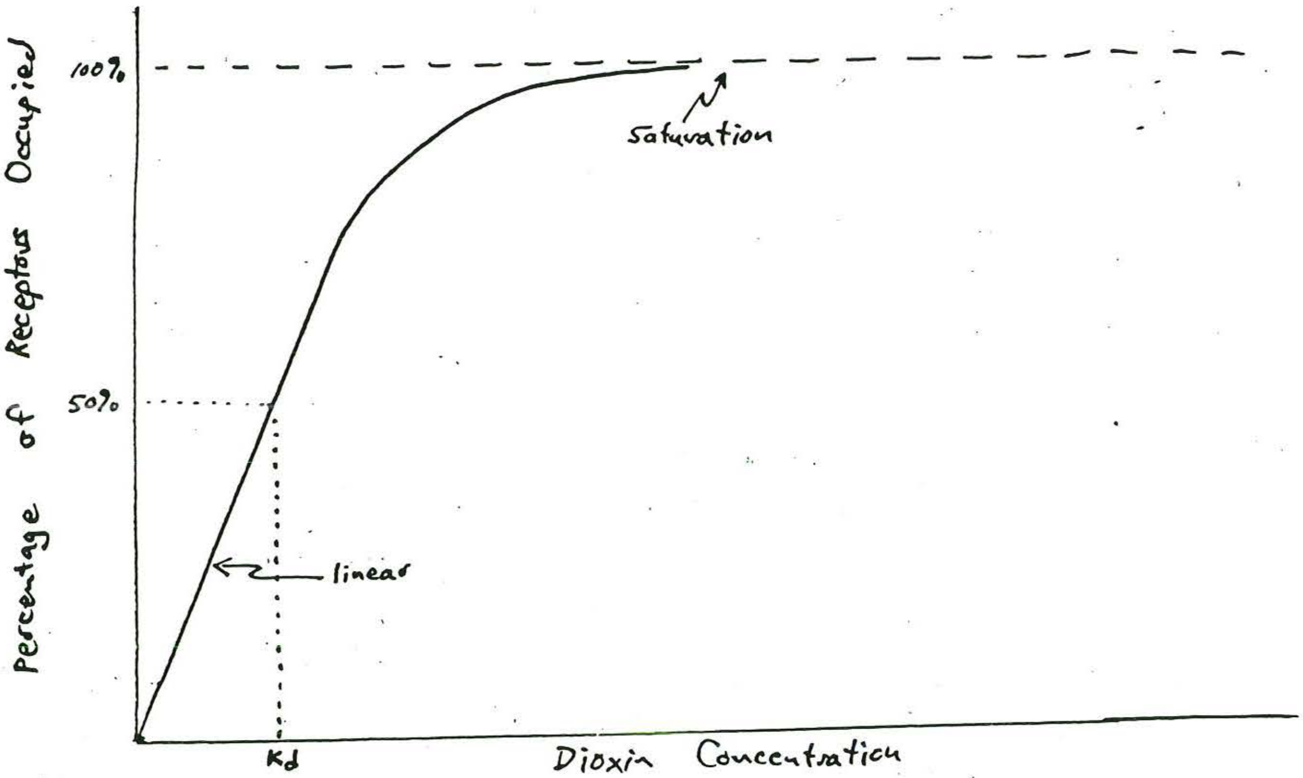
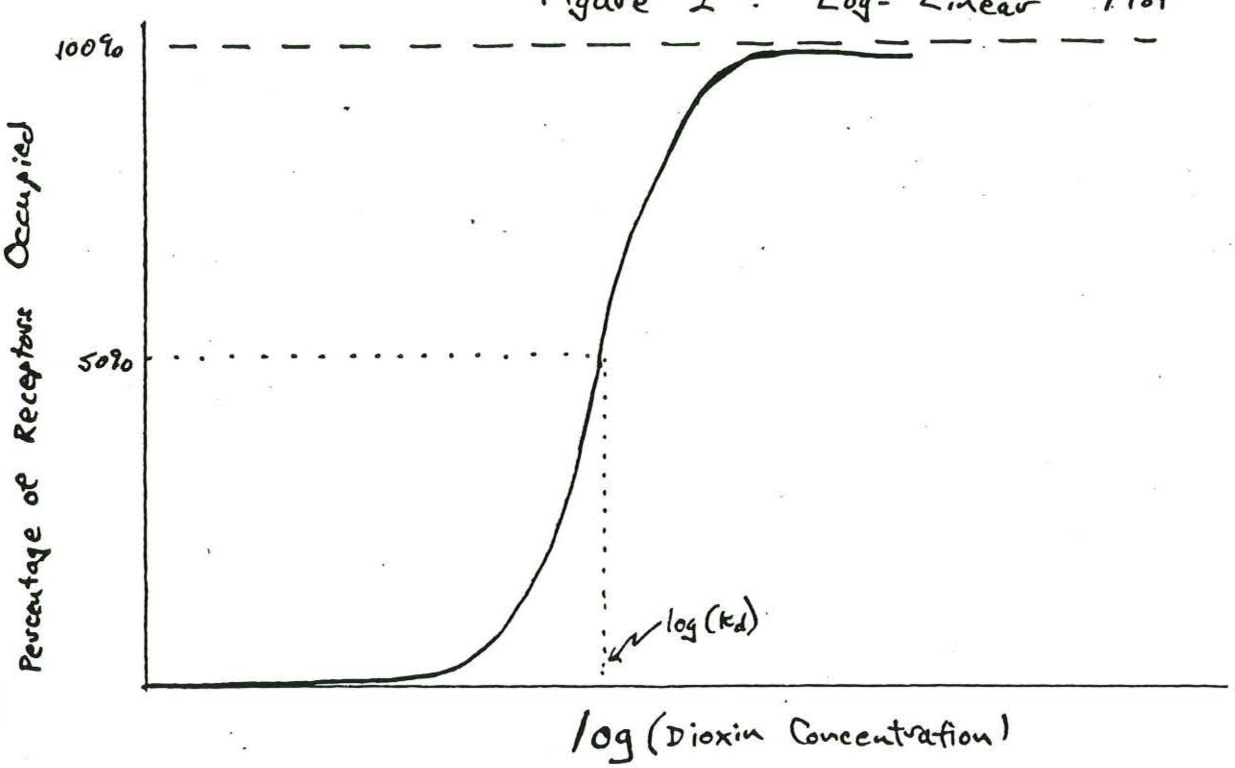


Figure 2 : Log-Linear Plot



Attachment 3

Downgrading Dioxin's Cancer Risk: Where's the Science?

By Tom Webster

Some of the concerns about the toxicity of the wood preservative pentachlorophenol have resulted because of its contamination with dioxins and furans. During manufacturing, pentachlorophenol is contaminated with several members of this family of compounds, with hexadioxins being most abundant.[1] 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD, commonly called dioxin), the most toxic dioxin, has been found in commercial pentachlorophenol formulations[1] and is often found in the soil and waste products from wood treatment plants.[2,3] This article discusses recent attempts to weaken regulatory standards for 2,3,7,8-TCDD.

-Ed.

The pulp and paper industry and certain consultants are once again attempting to relax the regulatory standards for dioxin. The consulting company ChemRisk has proposed an increase in the so-called "acceptable" dose of 2,3,7,8-TCDD by a factor as large as one thousand.[4,5] Many states are currently setting water quality standards for dioxin,[6] a regulation that depends on the "acceptable" dose.[7]

Despite assertions that the proposed change is based on new scientific evidence showing that dioxin "may be far less dangerous than previously imagined,"[8] the new information is actually a reinterpretation of the 1978 rat experiment that forms the basis for the U.S. Environmental Protection Agency's (EPA's) current estimate of dioxin's ability to cause cancer. In this reanalysis, a group of pathologists voted, according to a new set of guidelines, on the classification of tumors found in the test animals.[9]

However, if all other assumptions are left unchanged, recounting the tumors according to the revised rules [10] would result in an "acceptable" daily dioxin dose that is only two to three times larger than the current estimate. This is an insignificant change given the uncertainty in risk assessment. 2,3,7,8-TCDD is currently rated as millions of times more carcinogenic than many other compounds.

"Indeed, new scientific evidence on the amount of fish people consume, the degree to which dioxin is concentrated in fish, and the toxic equivalencies of other dioxins and furans supports stronger, not weaker, dioxin standards."

The much larger change proposed by ChemRisk was derived by altering a number of other assumptions without proper justification. Indeed, new scientific evidence on the amount of fish people consume, the degree to which dioxin is concentrated in fish, and the toxic equivalencies of other dioxins and furans (JPR 10(2):23-27) supports stronger, not weaker, dioxin standards.[7]

Human Health Effects Controversy

This episode is neither the first nor last attempt to downgrade or dismiss the toxicity of dioxin. Perhaps the best known and continuing controversy surrounds Agent Orange. 2,3,7,8-TCDD was a contaminant in the herbicide 2,4,5-T, a component of Agent Orange, which was sprayed in parts of the United States as well as in Vietnam.

Despite the claim by some that the only long-term effect of dioxin on humans is chloracne, a serious skin disorder, the compound has been hypothesized to cause a number of other health effects in humans. Several recent epidemiological studies support this position. The Agent Orange Scientific Task Force[11] linked phenoxyacetic acid herbicides (such as Agent Orange) and their dioxin contaminants to a number of diseases including certain cancers. Dioxin's close chemical relatives PCBs and dibenzofurans may cause birth defects and learning/behavioral changes in the children of exposed women.[12,13] Certain key earlier studies that found no increase in cancer in chemical workers exposed to dioxin are faulty or possibly even fraudulent,[14,15] a charge now under investigation by EPA. Recent studies of German and American chemical workers exposed to dioxin found statistically significant increases in cancer rates.[16,17]

EPA rates cancer-causing compounds qualitatively (how good is the evidence for cancer causation in humans?) and quantitatively (how much cancer is caused by a given dose?). As a result of the recent epidemiology, it is likely that EPA will upgrade the qualitative standing of 2,3,7,8-TCDD to a Class B1 probable human carcinogen (limited human data and sufficient animal data),[18] an action with important regulatory ramifications.[19]

Constructing an "Acceptable" Daily Intake of Dioxin

EPA typically assumes that cancer-causing agents have no threshold, meaning that any amount of exposure can cause damage. Some people argue that there is no acceptable exposure for dioxin, an unintentional chemical by-product with no use or benefit, and that the goal should be zero exposure to this compound. EPA, however, has stated that some level of risk is "acceptable," a decision that is a matter of policy, not science. In setting ambi-

Tom Webster is a researcher with the Center for the Biology of Natural Systems (CBNS) of Queens College. He is currently working on a project for Greenpeace concerning chlorinated compounds.

CBNS; Queens College; City University of New York; Flushing, NY 11367; (718) 670-4180.

ent water quality standards, EPA often uses an acceptable lifetime risk of cancer of one case in a million (10^{-6}).

Based on this policy, the acceptable daily dose of a chemical is established by dividing the acceptable risk level by the "potency" of the compound. EPA calls such values risk specific doses (RsD). The potency is the quantitative estimate of the strength of the carcinogen. The more potent a chemical is, the smaller the dose that is required to pose a certain level of risk.

For dioxin, as with the overwhelming majority of toxic chemicals, there are insufficient human data to establish a potency. (The new study cancer among chemical workers[17] may, however, prove sufficient.) Consequently, dioxin's potency is based on laboratory experiments with animals. The current estimate for 2,3,7,8-TCDD[1] was based on a 1978 experiment on female rats, the most sensitive sex and species tested.[20]

EPA projected from the number of tumors found in animals at experimental doses to effects at the lower doses that people might encounter using a standard mathematical technique, the linear multistage model. This model assumes that the carcinogen has no threshold and that effects at low doses are linear, i.e., directly proportional to dose.

Finally, the potency in humans is estimated by multiplying the animal value by a "scaling factor." This adjusts for differences between the experimental animal and humans. For dioxin, EPA employed the default "surface area" scaling factor, since many differences between animals and humans (e.g., metabolism) depend on relative surface area.[1,21]

The 1988 Attempt to Downgrade Dioxin

In 1988, a proposal was made by EPA's Dioxin Workgroup to decrease the carcinogenic potency of 2,3,7,8-TCDD by a factor of sixteen. The Workgroup argued that dioxin might cause cancer through several mechanisms rather than being simply a complete carcinogen (the basis of the 1985 estimate). It might, therefore, be a less potent cancer-causing agent than previously thought. The Workgroup concluded that there was "no definitive scientific basis" for determining how much less potent dioxin might be.[22]

They noted that other agencies (the Center for Disease Control, the Food and Drug Administration) as well as other countries have less stringent "acceptable" levels of dioxin. They argued that "for strictly policy purposes, there is great benefit in federal agencies adopting consistent positions in the absence of compelling scientific information" and that an order of magnitude (factor of ten) estimate conveys the uncertainty involved. Based on this somewhat arbitrary logic, the Working Group recommended increasing the "acceptable" level (RsD) from 0.006 picograms (one picogram is one trillionth of a gram) per kilogram per day (pg/kg/day) to 0.1 pg/kg/day.

In their review of this proposal, EPA's Science Advisory Panel acknowledged some criticisms of the application of the linear multistage model to dioxin. However, they rejected the Workgroup's proposal, stating that "there is no reason to necessarily believe that a new mechanism model would lead to a relaxation of the risk specific dose for 2,3,7,8-TCDD induced cancer...The Panel therefore finds no scientific basis at this time for the proposed change."[23]

Acceptable Doses of Dioxin: ChemRisk versus EPA

At about the same time that the Science Advisory Panel was rejecting the 1988 case for increasing the "acceptable" risk of dioxin by a factor of sixteen, ChemRisk's new proposal supported an increase by as much as a factor of one thousand.[4,5] Three main factors are used by ChemRisk and EPA in their respective dioxin computations (see Table 1):

> *"ChemRisk selects an "acceptable" risk of 10^{-5}. Since the level of acceptable risk is a question of policy, not science, ChemRisk's choice of this factor is arbitrary."*

• **"Acceptable" Lifetime Cancer Risk:** For water quality standards, EPA recommends an "acceptable" lifetime cancer risk ranging from one in ten million (10^{-7}) to one in one hundred thousand (10^{-5}). However, one in one million (10^{-6}) is both the default and most commonly used value.[6,24] ChemRisk selects an "acceptable" risk of 10^{-5}. Since the level of acceptable risk is a question of policy, not science, ChemRisk's choice of this factor is arbitrary.

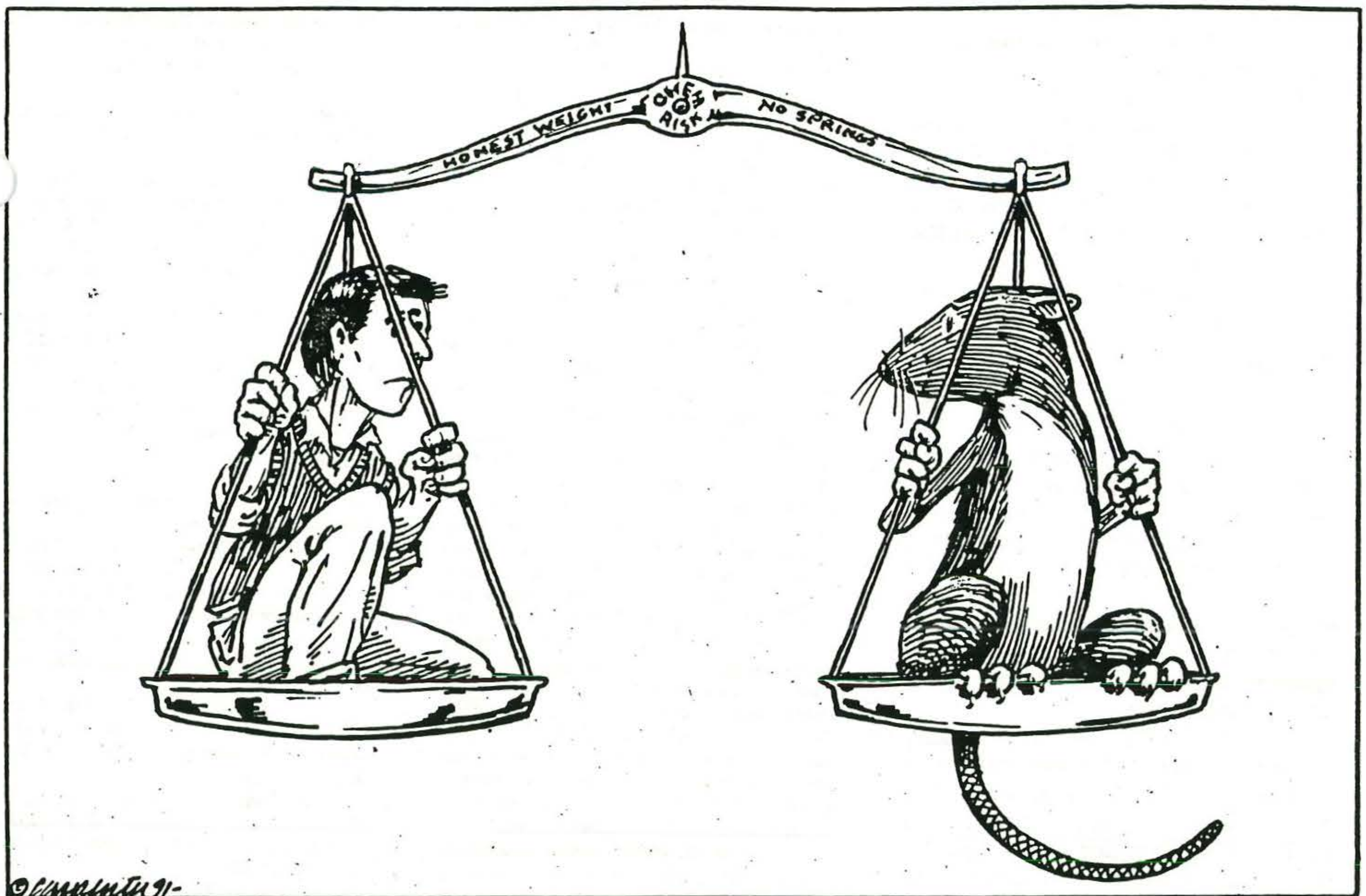
• **Interspecies Scaling Factor:** ChemRisk uses a body weight scaling factor to extrapolate from rats to humans. Since dose is commonly expressed as an amount per kilogram of body weight, ChemRisk's approach assumes that humans and rats are equally sensitive. EPA's surface area scaling factor assumes that humans will be more sensitive than rats per unit body weight by a

Table 1
Constructing an "Acceptable" Dose of Dioxin

	USEPA[1]	ChemRisk[4,5]	Factor[a]
1. Cancer potency in rats $(mg/kg/day)^{-1}$ (95% upper-bound estimate with linear multi-stage model)	29000	1500	19.3[b]
2. Scaling factor, rat to human (surface area)	5.38	1 (body weight)	5.38
3. "Acceptable" Lifetime Cancer Risk	10^{-6}[c]	10^{-5}	10
4. Risk-Specific Dose of 2,3,7,8-TCDD (pg/kg/day)	0.006[d]	6.74	1040

a. Factor by which ChemRisk is less stringent.
b. This factor would be 2-3 if the only change was the reclassification of tumors.
c. One in a million is a default and common value for water quality standards.[6,25]
d. An earlier draft by ChemRisk proposed an acceptable dose of 2.5 pg/kg/day.[4]

Note: RsD = (acceptable risk)/(rat potency * scaling factor)



Jim Carpenter

factor of about five.

ChemRisk argues that the use of the dose per body weight scaling factor is "more biologically relevant" because 2,3,7,8-TCDD is itself the active compound rather than any metabolite as is common with many carcinogens. EPA has disagreed with this line of reasoning in general,[25] but the case against body weight scaling is even stronger for 2,3,7,8-TCDD.

Since EPA's 1985 dioxin potency estimate, 2,3,7,8-TCDD half-life in humans has been determined to be 5-10 years, much longer than previously thought. In rats, the half-life of 2,3,7,8-TCDD is only about one month. Taking into account differences in tissue distribution, a scientist with EPA's Carcinogen Assessment Group estimated a scaling factor for the liver of as high as 37, much higher than ChemRisk's body weight scaling factor of one as well as EPA's surface area scaling factor of 5.38.[25] ChemRisk's reliance on the body weight scaling factor is not supportable.

• **Cancer Potency in Rats:** EPA's 1985 computation of dioxin potency was based on the occurrence in the 1978 rat study of carcinomas (cancerous tumors) and neoplastic nodules (lesions which may develop into cancerous tumors) in the liver, as well as tumors in other organs where the increase over control animals was statistically significant. In 1986, researchers proposed dividing neoplastic nodules into two groups: hepatocellular hyperplasia (a noncancerous proliferation of liver cells caused by toxicity) and hepatocellular adenomas (benign liver tumors).[10] This change has been questioned by some toxicologists.[26]

ChemRisk used the new classification system to argue in 1989 that the EPA's 1985 analysis was incorrect.[4]

At about the same time, Dr. Squire, a consulting pathologist involved in the original analysis of the female rat cancer data, was asked to re-examine the in conjunction with the setting of a water quality standard for Maine.[27] (Squire was involved earlier in a controversy over dioxin contaminants of pentachlorophenol: see article beginning on p. 4). After an initial review of the rat data, Dr. Squire helped convene a group of pathologists to re-examine the liver tissue slides from the experiment using the new classification system.

During this re-evaluation, in which "consensus" was defined as agreement by four out of seven pathologists (not all votes were unanimous), the group identified fewer carcinomas as well as fewer total tumors (carcinomas plus adenomas) than EPA's earlier analyses. The group concluded that because "the tumors were predominantly benign and usually associated with lesions of hepatic [liver] toxicity" the rat study demonstrated "a weak oncogenic [cancer-causing] effect of TCDD."[9] The implication of this controversial conclusion is that liver toxicity somehow caused or magnified the carcinogenic response.

ChemRisk used these results to calculate a new potency factor for 2,3,7,8-TCDD in rats, but counted only carcinomas in the liver (the primary target organ in this animal). They ignored carcinomas in other tissues as well as all adenomas, benign tumors that may progress into carcinomas. Both omissions are contrary to EPA guidelines for carcinogen risk assessment.[21]

ChemRisk also failed to adjust for early mortality of some test animals, another correction used by EPA.[1]

If the revised tumor pathology criteria are applied, eliminating liver hyperplasias, but all other standard EPA assumptions are employed, the calculated rat potency is reduced by only a factor of two to three from the current value. Again, ChemRisk's calculation of a new dioxin carcinogenic potency factor is indefensible.

Conclusion

A proposed acceptable daily dose for 2,3,7,8-TCDD is claimed to be based on new science regarding the classification of tumors. However, if this change alone is made, the "acceptable" dose of dioxin would only be altered by a factor of two to three. ChemRisk's proposed reduction by a factor of as much as a thousand is fundamentally based on scientifically indefensible changes in a number of other unrelated assumptions.

This series of events shows many of the problems with quantitative risk assessment. There is uncertainty about even the most basic questions such as the classification of tumors in laboratory animals. A large number of assumptions are required, each of which must be independently justified. Because of the uncertainty and the number of assumptions, it may be possible, in the absence of checks and balances, to construct nearly any result. ■

References and Notes

1. U.S. Environmental Protection Agency. 1985. *Health assessment document for polychlorinated dibenzo-p-dioxins.* EPA/600/8-84/014F. Washington, D.C.: Office of Health and Environmental Assessment.
2. U.S. Environmental Protection Agency. 1987. National dioxin study. EPA/530-SW-87-025. Washington, D.C.: Office of Solid Waste and Emergency Response.
3. State Water Resources Control Board. 1988. Chlorinated dibenzo-p-dioxin and dibenzofuran contamination in California from chlorophenol wood preservative use. Report 88-5WQ. Sacramento, CA: Division of Water Quality.
4. Keenan, R., R. Wenning, A. Parsons. 1989. Sensitivity analysis for dioxin risk assessment and implications for determining acceptable daily exposure: Executive summary. Portland, ME.: ChemRisk, October 20.
5. Keenan, R. Letter to Dr. R. Loehr, Chair, Executive Committee, Science Advisory Board, U.S. Environmental Protection Agency. March 20, 1990.
6. U.S. Environmental Protection Agency. 1990. *Tracking report: State water quality criteria for dioxin (2,3,7,8-TCDD).* Washington, D.C.: Office of Water Regulations and Standards. May.
7. Where people can consume both fish and water, the water quality standard is computed as:

   C = (RsD*BW)/((FC*BCF)+WC)

   RsD = risk specific dose ("acceptable" dose at a given risk level)

   BW = human body weight

   FC = fish consumption

   BCF = bioconcentration factor, the ratio between the concentration of the compound found in the fish and the concentration in water.

   WC = water consumption rate by humans (negligible when BCF is large).

   The current EPA water quality standard for 2,3,7,8-TCDD assumes a fish consumption rate of 6.5 grams per day (0.23 oz.) and a bioconcentration factor of 5000.[6,24] Both of these factors are low. New data indicate that sport fishermen can consume 30 grams per day of fish while subsistence fishermen may consume 140 grams per day.[24,28] These values are about five and twenty two times higher than the current EPA value. Recent studies of the bioconcentration of 2,3,7,8-TCDD have found values from 39,000 to 140,000.[29,30] Thus, even if the RsD for 2,3,7,8-TCDD was raised by a factor of two to three to account for changes in tumor classification, a water quality standard tens to hundreds of time lower could be constructed.

   Furthermore, water quality standards are set compound by compound, ignoring the fact that compounds closely related to 2,3,7,8-TCDD—such as 2,3,7,8-tetrachlorodibenzofuran, also emitted by pulp and paper mills that bleach with chlorine—are added together in other regulatory contexts, after adjusting for relative potency using the 2,3,7,8-TCDD equivalence methodology.
8. Gladwell, M. 1990. Scientists temper views on cancer-causing potential of dioxin. *Washington Post,* May 31, p. A3.
9. Sauer, R. and PATHCO, Inc. 1990. Pathology Working Group 2,3,7,8-tetrachlorodibenzo-p-dioxin in Sprague-Dawley Rats. 10075 Tyler Place #16, Ijamsville, MD 21754. March 13.
10. Maronpot, R., C. Montgomery, G. Boorman, and E. McConnell 1986. National Toxicology Program nomenclature for hepatoproliferative lesions of rats. *Toxicologic Pathology* 14(2): 263-273.
11. Agent Orange Scientific Task Force. 1990. *Human health effects associated with exposure to herbicides and/or their associated contaminants - chlorinated dioxins.* Washington, D.C.: National Veterans Legal Services Project.
12. Rogan, W., B. Gladen, C. Hsu, Y. Chen, and H. Ko. 1990. Yucheng: Studies in children. Presented at Dioxin '90, The Tenth International Meeting. Bayreuth, Germany.
13. Jacobson, J., S. Jacobson, and H. Humphrey. 1990. Effects of in utero exposure to polychlorinated biphenyls and related contaminants on cognitive functioning in young children. *J. Pediatrics* 116: 38-45.
14. Rohleder, F. 1989. Dioxins and cancer mortality: Reanalysis of the BASF cohort. Ninth International Symposium on Chlorinated Dioxins and Related Compounds, Toronto, Ontario, Sept. 17-22.
15. Van Strum, C. and P. Merrell. 1990. Dioxin human health damage studies: Damaged data? *Journal of Pesticide Reform* 10(1): 8-12.
16. Zober, A., P. Messerer, and P. Huber. 1 Thirty-four-year mortality follow-up of B... employees exposed to 2,3,7,8-TCDD after the 1953 accident. *International Archives of Occupational and Environmental Health.* 62: 139-157.
17. Fingerhut, M., et al. (1991). Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324(4): 212-218.
18. "EPA likely to upgrade dioxin cancer classification to reflect new data." *Inside EPA.* February 1, 1991. p.4.
19. Jenkins, C. 1991. U.S. Environmental Protection Agency Memorandum. January 24.
20. Kociba, R., D. Keyes, J. Beyer, R. Carreon, C. Wade, D. Dittenber, R. Kalnins, L. Frauson, C. Park, S. Barnard, R. Hummel, and and C. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicology and Applied Pharmacology* 46: 279-303.
21. U.S. Environmental Protection Agency. 1986. Guidelines for carcinogen risk assessment. *Federal Register* 51(185): 33991. September 24.
22. U.S. Environmental Protection Agency. 1988. *A cancer risk-specific dose estimate for 2,3,7,8-TCDD: Draft.* EPA/600/6-88/007Aa. June. pp. 49-50.
23. Goldstein, B., N. Kim. 1989. Letter from the Chair and Co-Chair of the Ad Hoc Dioxin Panel to Dr. R. Loehr, Chair, Science Advisory Board Executive Committee, U.S. Environmental Protection Agency. Novem... 28.
24. U.S. Environmental Protection Agency. 1990. EPA's position on Georgia's adoption of a dioxin water quality standard. Region IV. March.
25. Bayard, S. 1988. Quantitative implications of the use of different extrapolation procedures for low-dose cancer risk estimates from exposure to 2,3,7,8-TCDD. Appendix A of reference 22.
26. Alsen-Hinrichs, C, Department of Toxicology, University of Kiel School of Medicine, Kiel, Germany. Letter to the *Washington Post* (unpublished). June 21, 1990.
27. Squire, R. 1990. Letter to Dr. Robert Michaels acknowledging the request of November 28, 1989. January 8.
28. U.S. Environmental Protection Agency (1989). *Exposure factors handbook.* Versar, Inc. EPA 600/8-89-043. Washington, D.C.: EPA.
29. Mehrle, P., et al. 1988. Toxicity and bioconcentration of 2,3,7,8-tetrachlorodibenzo-p-dioxin and 2,3,7,8-tetrachlorodibenzofuran in rainbow trout. *Environ. Toxicol. Chem.* 7: 47-62.
30. Cook, P., A. Batterman, and B. Butterworth. 1990. *Laboratory study of TCDD bioaccumulation by lake trout from Lake Ontario sediments, food chain and water.* Duluth, MN: U.S. Environmental Protection Agency Environmental Research Laboratory.

Eleventh International Symposium on Chlorinated Dioxins and Related Compounds

MAR 20 1991

cc Steve
CR
Dr Ch
Jim N

DIOXIN '91

September 23-27, 1991

Conference Information

School of Public Health
Office of Continuing Education
The University of North Carolina at Chapel Hill
CB# 8165, Miller Hall
Chapel Hill, NC 27599-8165
Phone: 919/966-1104
Fax: 919/966-7141

Organizing Committee

Memo

To: Conference Participants Who Plan to Submit Papers

From: Sharon Johnson Wills
Program Assistant

Date: February 10, 1991

Re: Abstract Format Instructions

The Organizing Committee of Dioxin '91 invites you to submit your abstract for the 11th International Symposium on Chlorinated Dioxins and Related Compounds. The conference will be held in Research Triangle Park, North Carolina, Sept. 23-27, 1991. Enclosed please find one instruction sheet and two forms for submitting your abstract. Also enclosed is an acknowledgment card that you should send back with your completed package. Fill in the lines marked "title" and "author" and return it with your abstract package to the Office of Continuing Education. I will return the card to you to acknowledge receipt of your abstract.

Please read the instructions carefully and take note of all mailing advisories so that we may include your abstract in this year's program. Remember that all abstracts must be received no later than April 1, 1991. Abstracts received after this date will not be considered for acceptance, published or printed.

If you have any questions or concerns, please call or write.

P.S. A complete brochure describing this program will be mailed to you in April. To register for Dioxin '91 before that time, please call me at 919/966-1104.

DOSE RESPONSE RELATIONSHIPS FOR CHRONIC EXPOSURE TO 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD) IN A RAT TUMOR PROMOTION MODEL: 2. QUANTIFICATION AND IMMUNOLOCALIZATION OF CYTOCHROMES P450c(1A1) AND P450d(1A2) IN THE LIVER. A Tritscher, G Clark, Z McCoy, C Portier, W Greenlee, J Goldstein, and G Lucier. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

TCDD and its structural analogs produce a broad spectrum of biochemical and toxic effects in animals and humans. The mechanisms responsible for these effects involve interactions with the Ah receptor but many of the steps necessary for biological response remain unknown. One of the troublesome knowledge gaps that causes uncertainty in risk assessments for TCDD is the lack of adequate dose-response relationships following chronic exposure to TCDD. One of the most sensitive responses to TCDD and its structural analogs is the induction of specific isozymes of cytochrome P450 (CYP1A1 and CYP1A2). CYP1A1 is induced in many tissues whereas CYP1A2 is induced only in liver. We have employed a two-stage model for hepatocarcinogenesis in female Sprague-Dawley rats to evaluate dose-response relationships for CYP1A1 and CYP1A2. A single dose of diethylnitrosamine was used as the initiating agent followed by biweekly gavage of TCDD at doses equivalent to 3.5, 10, 35 and 125 ng/kg/day for 30 weeks. CYP1A1 and CYP1A2 were quantified in liver microsomes from control and treated rats by immunoassay. Data revealed a maximum induction of CYP1A2 of 10-fold and induction was nearly 3-fold at the 3.5 ng/kg/day dose. The no detectable effect for 1A2 induction was estimated to be 0.1 to 0.3 TCDD ng/kg/day. A chronic dosing experiment is in progress to determine if this is an accurate estimate of the no detectable effect. Interestingly, TCDD-mediated induction of 1A2 appeared to occur at lower doses in DEN-initiated rats compared to non-initiated rats. Also, CYP1A2 induction appeared to be a slightly more sensitive marker of TCDD exposure than CYP1A1 in our rat liver tumor promotion model. We also analyzed liver TCDD concentrations by GC-MS. These data revealed a linear relationship between administered dose and TCDD liver concentrations throughout the entire dose range of our study. Therefore, induction of 1A2 does not enhance TCDD retention in liver, a hypothesis that had been proposed because 1A2 is a binding protein for TCDD. We also used immunocytochemical techniques to analyze the pattern of CYP1A1 and CYP1A2 distribution in livers of control and TCDD-treated rats. 1A2 was localized primarily in the centrolobular region with small amounts in the midzonal and periportal regions. Induction by TCDD increases the number of cells containing detectable amounts of 1A2 but not the intensity of staining of cells constitutively expressing this cytochrome. Localization patterns, in induced rats, were similar for 1A1 and 1A2. Taken together, these studies are characterizing dose response relationships for CYP1A1 and CYP1A2 that represent characteristic Ah receptor dependent responses to TCDD exposure. (Funding for TCDD analyses provided by the American Paper Institute.

DOSE RESPONSE RELATIONSHIPS FOR CHRONIC EXPOSURE TO 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD) IN A RAT LIVER TUMOR PROMOTION MODEL: 1. RELATIONSHIPS OF TCDD TISSUE CONCENTRATIONS TO SERUM CLINICAL CHEMISTRY, CELL PROLIFERATION, AND PRENEOPLASTIC FOCI. G Clark, A Tritscher, Z McCoy, C Portier, M Thompson, R Wilson, J Foley, R Maronpot, [1]T Goldsworthy, W Greenlee, and G Lucier. National Institute of Environmental Health Sciences, Research Triangle Park, NC and [1]Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

One of the important issues in a risk assessment for exposure to dioxins is the pharmacokinetic distribution of TCDD in a long term chronic exposure regimen and the biological responses associated with a potential carcinogenic outcome. A specific cytoplasmic binding protein, the Ah receptor, is generally thought to mediate most of the biological responses to TCDD including its action as a tumor promoter. We have used a rat liver tumor promotion model to investigate biochemical responses that may be associated with promotion of carcinogenesis. In previous studies we have found that alterations of hepatic cell proliferation and the appearance of enzyme altered foci (γ-glutamyl transpeptidase and glutathione S-transferase-positive foci) correlate with liver tumor formation but that the ovaries are necessary for the expression of these effects. In the current study we are investigating dose response relationships in female Sprague-Dawley rats with an initiating dose of 175 mg/kg DEN and biweekly exposure to TCDD for 30 weeks to give doses equivalent to 3.5, 10.7, 35.7, and 125 ng/kg/day TCDD. A linear distribution of TCDD in livers of exposed animals was found. The mean liver concentration of TCDD was 19.9 ppb at 125 ng/kg/day and the mean liver concentration was 0.5 ppb at 3.5 ng/kg/day. In serum samples from the rats exposed to 125 ng/kg/day the TCDD concentration was 23.9 ppt while the concentration at the lowest dose was 8 ppt. Several serum clinical chemistry parameters were measured including alkaline phosphatase, glucose, alanine transaminase, total cholesterol, triglycerides, sorbitol dehydrogenase, 5' nucleotidase, and total bile acids. A significant dose effect for TCDD exposure was determined for serum alkaline phosphatase, 5' nucleotidase activities and on the levels of serum cholesterol. We are in the process of analyzing cell proliferation in livers from these animals by incorporation of bromodeoxyuridine into newly-formed cells and immunohistochemical analysis. We are also quantifying γ-glutamyl transpeptidase and placental glutathione S-transferase-positive foci as indicators of preneoplastic lesions. These parameters will be correlated with the applied dose, the tissue specific dose, and the levels of occupied Ah receptors. We hope to determine a) what is the most sensitive biochemical response to TCDD exposure and b) which parameter correlates with carcinogenicity. These data will be useful in the development of mechanistic models for dioxin risk assessment. (Funding for TCDD analyses provided by the American Paper Institute).

Carcinogenesis vol.12 no.5 pp.793–800, 1991

Attachment 5

Study of the separate and combined effects of the non-planar 2,5,2',5'- and the planar 3,4,3',4'-tetrachlorobiphenyl in liver and lymphocytes *in vivo*

Linda Sargent[1], Yvonne P.Dragan, Chris Erickson, Chris J.Laufer and Henry C.Pitot[2]

McArdle Laboratory for Cancer Research, Department of Oncology and the Center for Environmental Toxicology, The Medical School, University of Wisconsin, Madison, WI 53706, USA

[1]Present address: Chemical Industry Institute of Toxicology, 6 Davis Drive, Research Triangle Park, NC 27709, USA
[2]To whom reprint requests should be sent

Polychlorinated biphenyls (PCBs) are a group of industrial chemicals that are widely distributed in the environment. Because these compounds occur as mixtures, studies of their possible interactive effects are essential for an understanding of the mechanism of the toxicity of these mixtures. For the determination of a possible interaction of the effects *in vivo* of 2,5,2',5'-tetrachlorobiphenyl (TCB) and 3,4,3',4'-TCB, rats were exposed to a single dose of diethylnitrosamine (DEN) and subsequently to 0.1 p.p.m. 3,4,3',4'-TCB and/or 10 p.p.m. 2,5,2',5'-TCB in the feed for 1 year. The two major targets of PCB toxicity, the liver and the peripheral blood, were examined after these treatments. TCB treatment after DEN exposure caused a predominance of increased placental glutathione S-transferase (PGST) and deficiencies of ATPase as preneoplastic markers in focal hepatic lesions. When 0.05% phenobarbital (PB) was administered after DEN exposure, the distribution of markers in altered hepatic foci (AHF) was essentially equal for increased PGST and γ-glutamyltranspeptidase (GGT) and for ATPase deficiency. Many of these AHF also exhibited increased P450 b/e expression. Our results demonstrated that the two PCB congeners interacted *in vivo* to produce an increase in AHF that were PGST positive and ATPase negative. PGST-positive and ATPase-negative AHF correlated best with focal areas of P450 b/e expression. The combination of the two PCBs caused a greater than additive decrease in the total number of lymphocytes and antibody-producing B-cells. Also the thymocyte-dependent T-helper cells isolated from the animals receiving the combination of TCBs demonstrated a morphologically abnormal subpopulation. The results indicate that the interaction of 2,5,2',5'-TCB and 3,4,3',4'-TCB *in vivo* induced much greater toxicity and mutagenicity in peripheral lympyhocytes and hepatocytes than treatment with either congener alone.

Introduction

Polychlorinated biphenyls (PCBs*) are a group of industrial chemicals that, in the past, had diverse uses owing to their chemical stability and their miscibility in organic solvents. These properties resulted in the use of PCBs as hydraulic fluids, plasticizers, adhesives, heat transfer fluids, wax extenders, dedusting agents, organic diluents, lubricants, flame retardants and as dielectric fluids in capacitors and transformers (1). The advantages that made PCBs such a versatile industrial chemical proved to be the source of their problem in the environment. Traces of PCBs have been found in environmental samples world-wide (2,3). Analyses of human breast milk, blood and adipose tissue have demonstrated that most individuals have been exposed to PCBs (2,3). The primary route of human exposure is through oral ingestion of contaminated products.

Technical mixtures of PCBs contain a combination of planar and non-planar congeners. The planar congeners bind to the Ah receptor, induce cytochrome P450 c and P450 d (4–7), and cause a cascade of events primarily in the liver and immune cells, including weight loss, thymic atrophy, decreased spleen weights (8), reduction of circulating lymphocytes of both the bursae and thymic cell populations (9–11), hepatomegaly, and subcapsular and midzonal hepatic necrosis. They are also potent promoters of the growth of preneoplastic hepatic foci (12). The non-planar congeners are less toxic, have a low affinity for the Ah receptor, and induce P450 b/e. The non-planar congeners cause hepatic enlargement and are relatively weak promoting agents in hepatocarcinogenesis (12,13). They do not cause thymic atrophy or reduction in immune function (5,6,14).

Planar and non-planar congeners occur as mixtures, yet there are few studies which have examined the potency of specific combinations of PCB congeners. The planar 3,4,3',4'-tetrachlorobiphenyl (TCB) and the non-planar 2,5,2',5'-TCB are found in the Aroclor mixtures 1254, 1248 and 1242. The ratio of the concentration of these two congeners in the major Aroclors was used to determine the concentration ratio for this study. In addition, we chose to use low-level, environmentally relevant doses of these TCBs in order to assess the potency of the combination for the determination of doses in this experiment. The sample of Aroclor that was used as a standard contained 0.002 μg of 3,4,3',4'-TCB/ml and 0.2 μg of 2,5,2',5'-TCB/ml. Hepatocytes and lymphocytes were chosen as target cells to study a possible superadditive toxicity and promotion potency of the combination of the planar and the non-planar TCBs, since these two target cell types are among the most sensitive to PCB toxicity.

Materials and methods

Chemicals

The Pariza purified diet was purchased from Teklad (Madison, WI). Diethylnitrosamine (DEN) was obtained from the Eastman Kodak Co. (Rochester, NY). 3,4,3',4'-TCB was purchased from Ultra Scientific (Hope, RI) and 2,5,2',5'-TCB was a gift from Dr James Miller (McArdle Laboratory, Madison, WI). All of the antibodies used for immunohistochemistry were obtained from Bioproducts for Science Inc. (Indianapolis, IN).

Animals and treatment protocol

Female Sprague–Dawley rats (Harlan Sprague Dawley, Madison, WI) weighing an average of 90 g were housed in wire mesh cages and fed the Pariza diet (30% casein, 5% corn oil, 10% partially hydrogenated corn oil, 40% sucrose, 15% cornstarch) and water *ad libitum*. A 70% partial hepatectomy was performed under ether anesthesia and 24 h later 50% of the animals were intubated with

*Abbreviations: PCBs, polychlorinated biphenyls; TCB, tetrachlorobiphenyl; DEN, diethylnitrosamine; PB, phenobarbital; AHF, altered hepatic foci; GGT, γ-glutamyl transpeptidase; PGST, placental form of glutathione S-transferase; ATP, canalicular ATPase; G6P, glucose-6-phosphatase; HCC, hepatocellular carcinoma; TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin; HCB, hexachlorobiphenyl.

10 mg DEN in trioctanoin/kg. After 1 week, the animals were randomly assigned to the treatment groups outlined in Figure 1. TCBs were dissolved in methylene chloride, added to the powdered chow, and mixed thoroughly in plastic bags. The solvent was evaporated in the hood for 24 h. Randomly selected rats were then placed on a control diet or control diet with one of the following additions: 0.1 p.p.m. 3,4,3',4'-TCB only, 10 p.p.m. 2,5,2',5'-TCB only, 0.1 p.p.m. 3,4,3',4'-TCB and 10 p.p.m. 2,5,2',5'-TCB, or 100 p.p.m. 2,5,2',5'-TCB. Another group was fed phenobarbital (PB) at a level of 0.05% in the diet as a positive control (15,16).

Analysis of lymphocytes

Rats were treated with 100 mg cyclophosphamide/kg and anesthetized with ether; blood was drawn by cardiac puncture 48 h later. The red blood cells were lysed with 2 ml hypotonic buffer (1000 ml of deionized water, 8.29 g NH_4Cl, 1.0 g KH_2CO_3, 0.372 g disodium EDTA, pH 7.4) and washed with phosphate-buffered saline. Washed lymphocytes were then mixed with fluorescein-conjugated antibodies generated against the CD-4 protein, the CD-8 protein, the 1.1 Thy protein and a general B-cell protein (17). The stained cells were then analyzed on the flow cytometer by standard methods (18). Lymphocytes of abnormal morphology were examined by scanning electron microscopy according to standard methods. Sections of the spleen were frozen on solid CO_2 and fixed in 10% buffered formalin.

Analysis of preneoplastic foci (altered hepatic foci, AHF)

The liver was removed, weighed, and sections from each liver lobe were immediately frozen on solid CO_2. Five 10-μ-thick serial sections were stained for γ-glutamyl transpeptidase (GGT), the placental form of glutathione S-transferase (PGST), canalicular ATPase (ATP), cytochrome P450 b/e, P450 c/d and glucose-6-phosphatase (G6P), according to the methods for staining outlined by Xu *et al.* (19). AHF were then quantitated by the procedure of Campbell *et al.* (20). Additional slices of tissue were stored in 10% formalin for histopathological analysis.

Statistics

Non-parametric Wilcoxon statistics were used to compare groups. For the determination of additivity, Steel and Torrie's χ-square test for additivity (21) was used.

Results

Lymphocyte analysis

The total number of circulating antibody-producing cells (B-cells) was reduced in the peripheral blood prepared from animals treated with 3,4,3',4'-TCB, but not from those treated with 2,5,2',5'-TCB (groups 3 and 5, Figure 2) when compared with untreated controls. The number of circulating B-cells isolated from animals treated with both TCBs was reduced by a greater than additive level ($P < 0.001$, group 7) when analyzed by flow cytometry. When DEN was included in the treatment protocol (Figure 3), the level of circulating B-cells was reduced in the 2,5,2',5'-TCB group as well as the 3,4,3',4'-TCB group ($P < 0.05$, groups 4 and 6). The level of B-cells in the group with DEN plus both TCBs (group 8) was reduced to 1%. A reduction to this level was greater than would be expected by an additive model when analyzed by the χ-square test for additivity.

There was no statistical reduction in the number of CD-4, CD-8 or Thy 1.1 cells. Although the total number of cells was the same, a population of light-staining CD-4 cells was observed by flow cytometry (Figure 4). Of the CD-4 cells, 50 ± 8% from group 7 (both TCBs) and 95 ± 5% of the samples from group 8 (DEN + both TCBs) had an abnormal population of light-staining CD-4 cells. The forward scatter of these cells was the same as that of the normal CD-4 cells, but the side scatter was different (Figure 4). A difference in the side scatter would indicate a difference in size or morphology. When these light-staining CD-4 cells were separated and examined by scanning electron microscopy, the surface morphology of all of the cells examined was distinctly different from the normal population (Figure 5). By standard methods (17), these abnormal cells were further examined for esterase activity and were determined to be negative and therefore not monocytes.

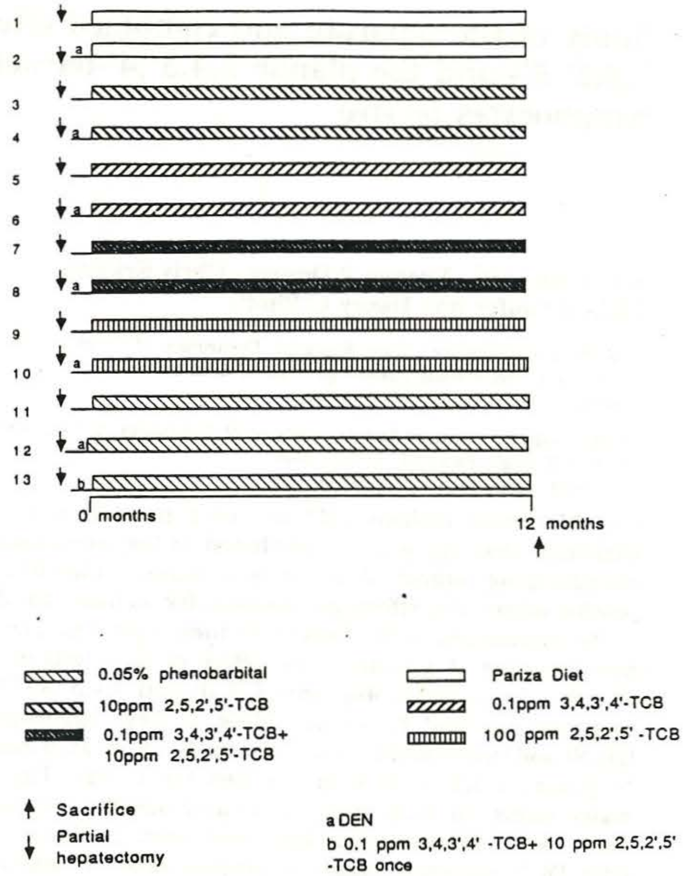


Fig. 1. Format of the protocol used for the initiation and promotion of AHF in female Sprague–Dawley rats.

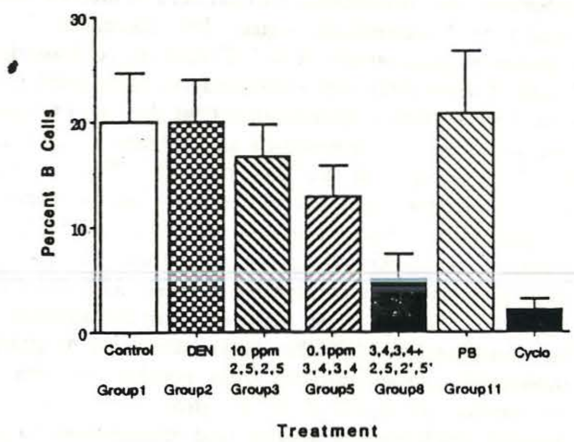


Fig. 2. Percentage of B-cells in the peripheral blood after chronic exposure to DEN alone or followed by 0.05% PB, 3,4,3',4'-TCB, 2,5,2',5'-TCB, or a combination of 3,4,3',4'-TCB + 2,5,2',5'-TCB or to cyclophosphamide. See text for details. Steel and Torrie's χ-square test for additivity (21) was used to examine an additive or greater than additive result. The conclusions of this test are given in the text. The bars above the columns indicate the standard error of the mean for analysis (1/rat in duplicate). The numbers of rats/group may be obtained from Table I.

Liver analysis

Number of preneoplastic foci. There was no statistical increase in the ratio of residual liver wt to body wt with any of the TCB treatments, but there was a significant increase in the PB and DEN + PB groups (Figure 6). A single dose of 0.1 p.p.m. 3,4,3',4'-TCB and 10 p.p.m. 2,5,2',5'-TCB did not increase the

Table I. Histopathologic changes in livers of rats on protocols depicted in Figure 1[a]

Group no.	Treatment	Portal damage[b]	Bile duct proliferation	Neoplastic nodules/rat	Cellular atypia/ neoplastic nodule/rat[c]	HCC/rat
1	Control	–	2/8	–	–	1/8
2	DEN	0/8	2/8	1/8	1/8	1/8
3	2,5,2',5'-TCB (10 p.p.m.)	0/14	2/14	2/14	0/14	0/14
4	DEN + 10 p.p.m. 2,5,2',5'-TCB	2/12	1/12	4/12	1/12	1/12
5	3,4,3',4'-TCB (0.1 p.p.m.)	0/14	5/14	3/14	0/14	0/14
6	DEN + 0.1 p.p.m. 3,4,3',4'-TCB	0/12	4/12	4/12	0/12	0/12
7	3,4,3',4'-TCB + 2,5,2',5'-TCB	9/12	9/12	1/12	1/12	0/12
8	DEN + 3,4,3',4'-TCB + 2,5,2',5'-TCB	9/11	11/11	11/11	9/11	2/11
10	DEN + 100 p.p.m. 2,5,2',5'-TCB	3/5	2/5			
12	DEN + PB	2/11	11/11	11/11	11/11	9/11

[a]Data are presented as the number of rats exhibiting the pathologic process/total number of rats examined.
[b]Includes fibrosis, chronic inflammation and/or hydopic change of periportal hepatocytes. Control animals receiving control diets showed only occasional minimal portal damage and bile duct proliferation. The histopathology of livers of rats in groups 9, 11 and 13 (Figure 1) was no different from that seen in groups 1, 3 and 5.
[c]Cellular atypia is defined as morphological and cytological changes, usually focal, seen in neoplastic nodules, such changes being histologically compatible with one or more patterns of well-differentiated hepatocellular carcinomas (43–45).

total number of AHF or the volume fraction of the regenerated liver occupied by AHF.

Treatment with TCBs caused a predominance of AHF that were scored by the presence of PGST (PGST$^+$) and ATP deficiency as preneoplastic markers (Figure 7), whereas PGST$^+$, ATP deficiency and GGT$^+$ markers were equally distributed in AHF after DEN + PB (Figure 8). TCB treatment alone did not elevate the number of AHF when compared with the control livers; however, treatment with both TCBs increased the number of AHF to a level that was greater than that of the untreated control and statistically the same as the DEN control (groups 2, 3 and 5 in Figure 1; see also Figure 9). The numbers of preneoplastic foci per liver in the DEN + 10 p.p.m. 2,5,2',5'-TCB group (group 4) or the DEN + 0.1 p.p.m. 3,4,3',4'-TCB group (group 6 in Figure 1) were not significantly different from the DEN group (group 2, Figure 1). When rats were treated with DEN followed by both TCBs, the number of AHF was dramatically greater than additive (Figure 9) ($P < 0.001$). Treatment with DEN + 100 p.p.m. 2,5,2',5'-TCB (group 10) did not cause a significant increase in the number of AHF when compared with DEN (Figure 9). Rats treated with the standard DEN + PB protocol had a significant increase in the number of AHF ($P < 0.001$, Figure 9).

Volume fraction of preneoplastic foci. When the volume fraction of AHF was analyzed, rats inititated with DEN and fed 10 p.p.m. 2,5,2',5'-TCB (group 4) exhibited statistically the same volume percentage AHF as the DEN group (group 2 in Figure 10); however, the volume of AHF in the DEN + 3,4,3',4'-TCB group (group 6) was slightly increased over that in the regenerated livers of animals receiving DEN only (group 2, Figure 10). The combination of DEN + both TCBs (group 8 in Figure 1) greatly increased the volume of the residual liver occupied by preneoplastic foci to a level that was much greater than would be expected by an additive model ($P < 0.001$; Figure 10). The group given a 10-fold greater level of 2,5,2',5'-TCB (group 10) exhibited a significant increase in the volume of the regenerated liver occupied by AHF to 7% of the liver (Figure 10). This level was statistically greater than that of rats given DEN alone but not as great as the DEN plus both TCBs group. When the livers of rats given DEN followed by 0.05% PB in the diet were examined, there was a significant increase in the volume fraction of preneoplastic foci to 20% of the total regenerated liver (group 12 in Figure 1; see Figure 10).

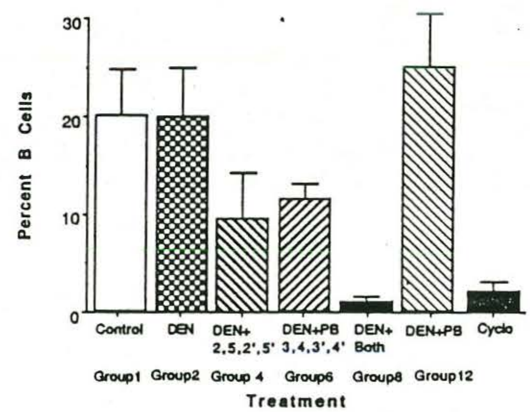


Fig. 3. Percentage of B-cells in the peripheral blood after 10 mg DEN/kg and 1 year of exposure to 0.1 p.p.m. 3,4,3',4'-TCB, 10 p.p.m. 2,5,2',5'-TCB, or a combination of 3,4,3',4'-TCB + 2,5,2',5'-TCB or to cyclophosphamide. See text and legend to Figure 2 for details and statistical conclusions. Steel and Torrie's χ-square test for additivity was used to assess significance. $P < 0.05$.

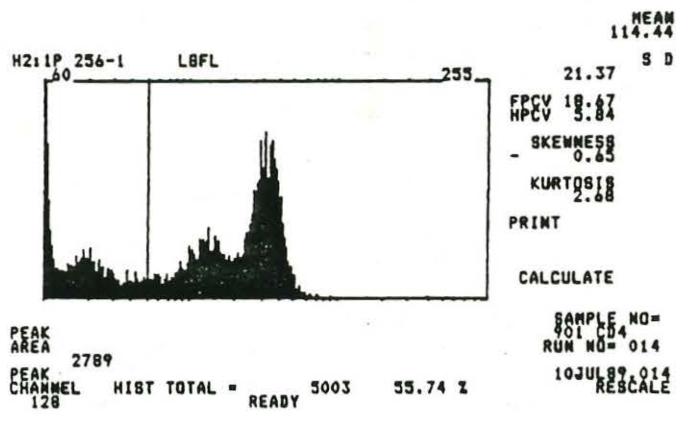


Fig. 4. Histogram of the fluorescence of T-helper cells following 1 year of exposure to 0.1 p.p.m. 3,4,3',4'-TCB + 10 p.p.m. 2,5,2',5'-TCB. Antibodies conjugated with fluorescence and generated to the CD-4 protein were used to identify the T-helper cells. See text for experimental details.

Cytochrome P450 b/e was found in 10 ± 7% of the preneoplastic foci marked by PGST or ATP of the DEN + 10 p.p.m. 2,5,2',5'-TCB, but 68 ± 10% of the AHF expressed the

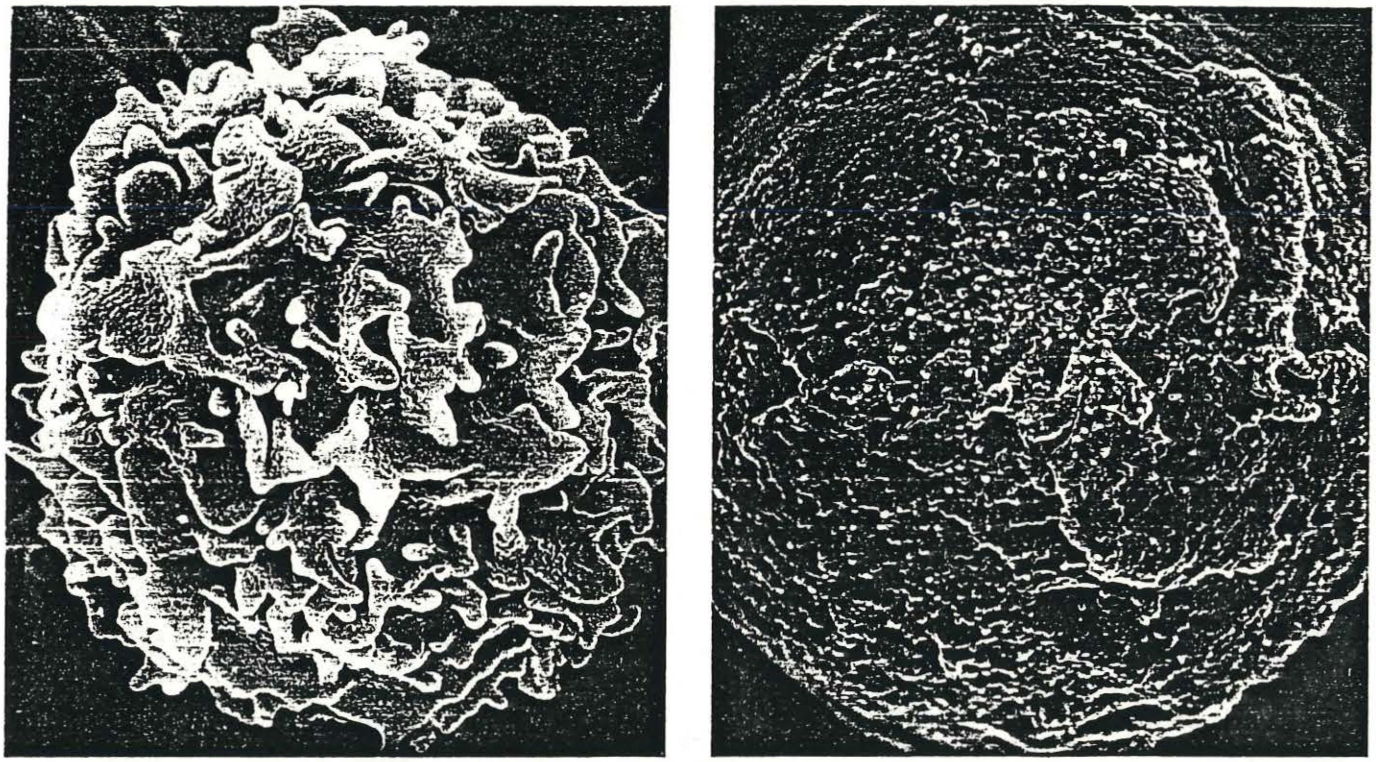


Fig. 5. Scanning electron micrograph of a normal T-helper cell (**left**) and an abnormal T-helper cell (**right**) isolated from the peripheral blood of an animal fed 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB for 1 year (×5000). See text for details.

cytochrome P450 marker in the DEN + 100 p.p.m. 2,5,2′.5′-TCB group. A larger number of positive foci was found in the group treated with DEN + both TCBs (60 ± 5%) than would be expected on the basis of the result seen with 10 p.p.m. 2,5,2′,5′-TCB alone. The number of P450 b/e positive foci found in the DEN + PB group was as large as that of the group given DEN + both TCBs (65 ± 5%) (Table II).

The expression of P450 c/d was localized to the centrolobular and midzonal region of the regenerated liver in the DEN + 3,4,3′,4′-TCB group, the DEN + both TCBs group, and the TCBs group (groups 6, 8 and 9). Centrilobular to midzonal staining was also seen with P450 b/e in the DEN + 10 p.p.m. 2,5,2′,5′-TCB, the DEN + 100 p.p.m. 2,5,2′,5′-TCB, the DEN + both TCBs and the DEN + PB groups. This degree of staining indicates that P450 c/d was induced by these regimens. In addition, P450 b/e was examined; in the DEN + PB group (group 12 in Figure 1), 76% of the PGST and 32% of the ATP-deficient foci were positive for this enzyme. In the DEN + 100 p.p.m. 2,5,2′,5′-TCB group, 22% of the PGST-positive AHF and 41% of the ATP-negative AHF were positive for P450 b/e. When both TCBs were administered, 40% of the PGST and 40% of the ATP-deficient foci were positive for P450 b/e.

The combination of both TCBs also caused a superadditive increase in the number of animals with neoplastic nodules exhibiting cellular atypia ($P < 0.05$, Table I); however, only two of the animals treated with DEN + both TCBs developed hepatocellular carcinoma (HCC). Treatment with DEN + PB for 1 year caused 80% of the animals to develop HCC.

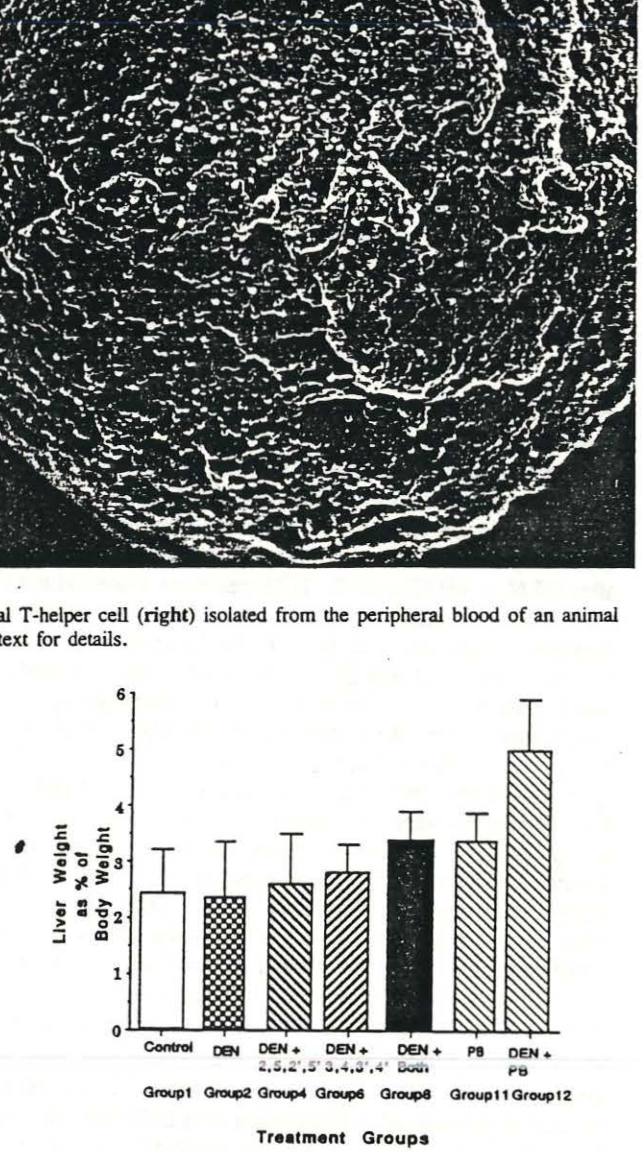


Fig. 6. Histogram of the ratio of the regenerated liver to body wt following 10 mg DEN/kg and 1 year of exposure to TCBs or to PB. The group numbers below each bar refer to the groups listed in Figure 1. The group designated PB is group 11 of Figure 1. Groups seen in Figure 1 not shown in this figure exhibited no significant change from the group 1 control.

Discussion

The planar congener, 3,4,3′,4′-TCB, and its non-planar isomer, 2,5,2′,5′-TCB, which are found in the major Aroclor mixtures 1254, 1242 and 1248, induced a greater than additive toxicity in the two major target cell types of PCB toxicity, hepatocytes and lymphocytes, in the studies described here. Our results demonstrated that low doses of the planar 3,4,3′,4′-TCB were more toxic to lymphocytes than a 100-fold higher dose of the non-planar 2,5,2′,5′-TCB congener. The 3,4,3′,4′-TCB congener caused a reduction in the number of B-cells. A similar reduction of B-cells has been noted after acute exposure to 3,4,3′,4′-TCB (10). The combination of the two TCBs caused a greater than additive decrease in the number of circulating B-cells as well as the appearance of an abnormal subpopulation of T-helper cells. The esterase test verified that this abnormal population of

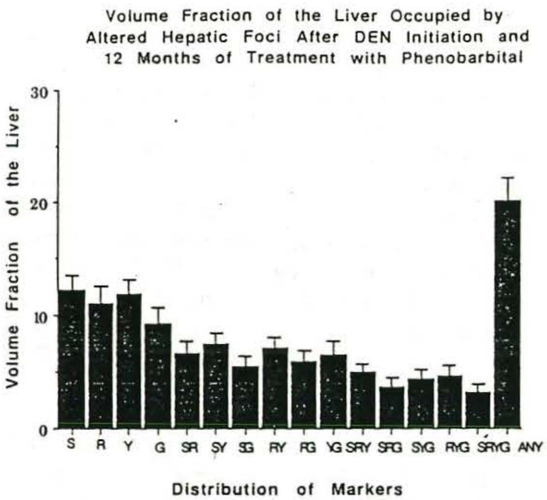


Fig. 7. Distribution of the volume fraction of AHF scored by multiple markers for AHF following initiation with 10 mg DEN/kg and 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB and 10 p.p.m. 2,5,2′,5′-TCB (group 8, Figure 1). Abbreviations: S, glutathione S-transferase-positive volume fraction; R, GGT-positive volume. Y, ATPase-negative volume; G, G6Pase-negative volume; SR, S and R combined; SY, S and Y combined. SG, S and G combined; RY, R and Y combined; RG, R and G combined; YG, Y and G combined; SYG, S and Y and G combined; SRY, S and R and Y combined. See ref. 19 for further details.

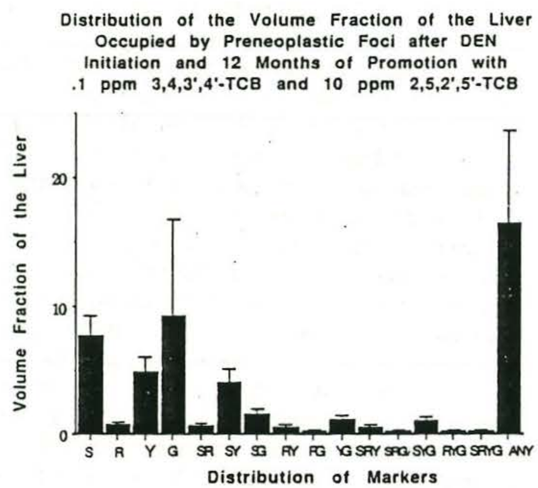


Fig. 8. Histogram of the distribution of the volume fraction of AHF scored by multiple markers for AHF following initiation with 10 mg DEN/kg and 1 year of exposure to 0.05% PB (group 12, Figure 1). See legend to Figure 7 for marker designation.

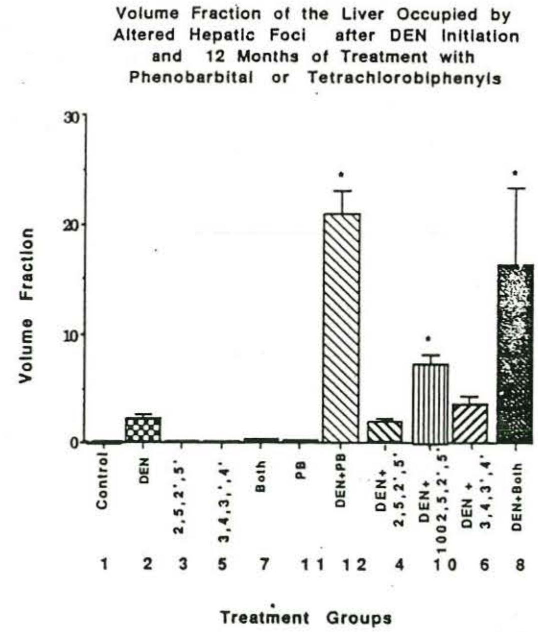


Fig. 9. Number of AHF per liver after initiation with 10 mg DEN/kg and/or 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB (groups 6 and 5), 10 p.p.m. 2,5,2′,5′-TCB (groups 4 and 3), 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB (groups 8 and 7) or to 0.05% PB in the diet for 1 year (groups 12 and 11). Eleven animals per group were killed after each treatment. The bars above the columns indicate the standard error of the mean from 11 animals. See Figure 1 for details of each group designated by number under the columns. $^*P < 0.001$ by Student's t-test.

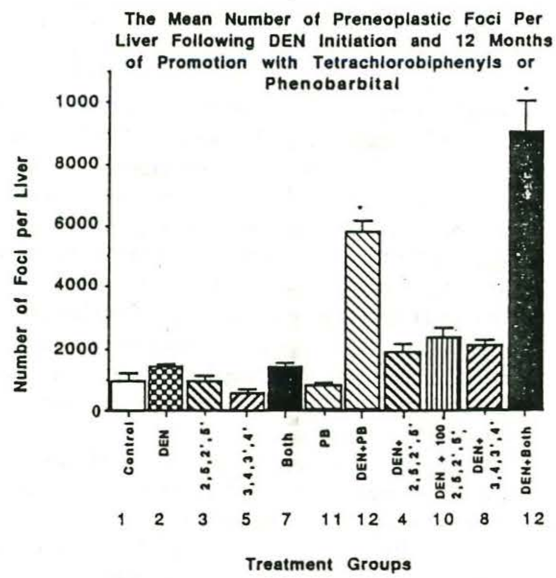


Fig. 10. Volume fraction (%) of AHF following initiation with 10 mg DEN/kg and/or 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB (groups 6 and 5), 10 p.p.m. 2,5,2′,5′-TCB (groups 4 and 3), 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB (groups 8 and 7) or to 0.05% PB (groups 12 and 11) in the diet for 1 year. Each group had 11 animals. See legend to Figure 9 for further details.

light-staining CD-4 cells was not a monocyte population, but was a new population of CD-4 cells exhibiting an abnormal surface membrane configuration.

The results from this research also demonstrated that the planar congener had more potent effects in liver cells than the non-planar TCB. The low dose of 3,4,3′,4′-TCB chosen for this study produced a moderate increase in the volume of preneoplastic foci as well as an increase in chromosome damage (L.Sargent and H.C.Pitot, unpublished observations). The relative potency of promoting agents has been expressed by the following relationship:

$$\text{promotion index} = V_f/V_c \times 1/\text{mmol per week}$$

where V_f is the total volume fraction (%) occupied by AHF in the livers of rats treated with the promoting agent, V_c is the total volume of AHF in control animals that have only been initiated and not treated with the promoting agent, and mmol is the number of millimoles of the promoting agent.

The promotion index (22) is based on the total number of altered cells within all AHF, thus giving a measure of tumor promotion. Table III shows the relative promotion indices of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB as well as their combination

Table II. AHF-positive P450 b/e expression after 1 year of treatment (%)

Groups	Foci positive for P450 b/e (%)
4	10 ± 7
10	68 ± 10
8	60 ± 5
12	65 ± 5
11	–[a]
3	–[a]
5	–[a]
9	40 ± 6

[a]Too few AHF to report significant data.

Table III. Promoting agents and promotion index

Promoting agents	Promotion index[a]
PB	100
3,4,3',4'-TCB (0.1 p.p.m.)	1.5×10^4
2,5,2',5'-TCB (10 p.p.m.)	200
2,5,2',5'-TCB (100 p.p.m.)	250
2,5,2',5'-TCB (10 p.p.m.) and 3,4,3',4'-TCB (0.1 p.p.m.)	8×10^5
2,3,7,8-TCDD[b]	2.8×10^7

[a]See text for details of calculations. Promotion indices were determined in animals that had been initiated with DEN (10 mg/kg) following a 70% partial hepatectomy (see text for details).
[b]Ref. 22.

in comparison with PB from this experiment and 2,3,7,8-tetra-chlorodibenzo-*p*-dioxin (TCDD) from an earlier study (22). By contrast, a 10-fold higher dose of 2,5,2',5'-TCB did not cause a significant increase in either the promotion index or the number of hepatic preneoplastic foci (Figure 9). The promotion index of 2,5,2',5'-TCB was also considerably less than that of 3,4,3',4'-TCB. The combination of the two congeners caused a dramatic increase in the number (Figure 9) and volume fraction (Figure 10) of preneoplastic foci. Indeed, the promotion index of the TCB combination is almost within one order of magnitude of that of TCDD, which has the highest known promotion potency of any compound (Table III). The number of animals treated with both TCBs that had numerous large neoplastic nodules exhibiting cellular atypia was also greater than that seen in either group treated with a single TCB.

The two TCB congeners differ in toxicity and binding affinity for the Ah receptor (8,23,24); however, the systemic clearance and volume of distribution of 3,4,3',4'-TCB and 2,5,2',5'-TCB are essentially the same (15). When single PCB congeners were examined by others, the promotion potency could be correlated with the affinity for the Ah receptor (23). Our results also demonstrated that the strong Ah receptor ligand, 3,4,3',4'-TCB, was a strong promoter of AHF, but the non-planar congener was a weak promoter relative to 3,4,3',4'-TCB and TCDD. Furthermore, previous results have shown that TCDD, which has a 500-fold greater affinity for the Ah receptor than TCBs, was a stronger promoter than 3,4,3',4'-TCB (24). The non-planar congeners, 2,4,5,2',4',5'-TCB (23), 2,4,2',4'-TCB and 2,5,2',5'-TCB, have been reported to exhibit promoting activity for hepatic preneoplastic foci (14). The presence of chlorine substitution in the *para* position correlated with an enhancement of promoting potency, but all the non-planar congeners were less potent than the planar 3,4,3',4'-TCB.

An enhancement of the amount of P450 b/e enzymes was seen in preneoplastic hepatic foci (AHF) of rats receiving 10 p.p.m. 2,5,2',5'-TCB or 100 p.p.m. 2,5,2',5'-TCB and to an even greater extent in the DEN + both TCBs group. This same enhancement of the P450 b/e enzymes was observed in AHF of the DEN + PB treatment group. Many of the changes in gene expression seen in AHF may occur as a result of the selection of a population of altered cells that are resistant to the specific treatment utilized (25) or are selectively stimulated to grow by the particular promoting agent (26). Enhancement of the expression of this detoxification enzyme in cells of AHF is also exemplified by an increase of P450 b/e following promotion with PB as well as hexachlorocyclohexane (27,28).

The greater than additive toxicity of 3,4,3',4'-TCB and 2,5,2',5'-TCB that was seen *in vivo* in hepatocytes and lymphocytes may have been owing to the metabolic activation of the 2,5,2',5'-TCB congener to an epoxide intermediate (14, 29,30). This epoxide intermediate is more toxic and more chromosome damaging than the parent compound (31) and has been shown to bind to DNA (29,32). PCB congeners that have both the *meta* and *para* sites available for oxidation can be metabolized through an epoxide intermediate. These intermediates can bind to DNA and have been found to be mutagenic (25,31). Examination of the dose–response curves of previous *in vitro* studies of chromosome damage in human lymphocytes (33) caused by 3,4,3',4'-TCB and a combination of 3,4,3',4'-TCB + 2,5,2',5'-TCB demonstrated that the two dose–response curves are parallel. This would suggest that the two events occurred by a common mechanism. Lymphocytes express the Ah receptor and have been shown to respond to the Ah receptor ligands by an increase in P450 c/d. Metabolic changes resulting from the combined induction of P450 c/d and P450 b/e can result in the metabolic activation of 4-chlorobiphenyl (34). Inhibition of P450 c/d metabolism of 2,5,2',5'-TCB results in greater formation of the 3,4-diol and the 4-OH form, indicating that more 3,4-oxide occurs following P450 c/d induction. The induction of P450 b/e enzymes results in detoxification of the 2,5,2',5'-TCB congener by direct *meta*-hydroxylation (32). The absence of the detoxification pathway (P450 b/e) and the presence of the activation pathway (c/d induction) may explain the greater sensitivity of the lymphocytes to 2,5,2',5'-TCB observed in the *in vivo* studies (35). The enhancement of the P450 b/e expression in preneoplastic foci resulting from treatment with both TCBs and with DEN + 2,5,2',5'-TCB as well as with DEN + PB may result in a selective reduced toxicity to 2,5,2',5'-TCB conferred to these cells by this gene expression.

Although centrilobular to midzonal staining for P450 b/e was observed by Buchman *et al.* (36) after DEN initiation and promotion with 3,4,5,3',4',5'-hexachlorobiphenyl (HCB) or with 2,4,5,2',4',5'-HCB, no increased staining for the P450 b/e isozyme occurred in AHF with this protocol. The 2,4,5,2',4',5'-HCB congener is an inducer of the P450 b/e isozyme; however, this congener is not known to be metabolized by this form or any other form of P450. Increased expression of a detoxification enzyme in cells of AHF has been observed as an increase of P450 b/e after promotion with PB as well as with hexachlorocyclohexane (36). Cells of AHF resulting from *N*-hydroxy ethylnitrosamine treatment exhibit reduced levels of P450 b/e and P450 c/d forms and an increase in glutathione S-transferase and expoxide hydrolase (23). Chronic treatment of rats with 2-acetyl-aminofluorene, which is metabolized by multiple forms of P450 (36), causes the proliferation of focal areas of preneoplastic hepatocytes; this may significantly lower the expression of many P450 genes as well as increase the conjugating enzymes that

detoxify the reactive intermediate (37). When PB administration followed AAF treatment, however, the level of P450 b/e was induced in AHF that had previously been negative for the enzyme (38). Thus, as a result of the alteration of drug-metabolizing enzymes, cells of AHF may have a selective advantage in a toxic environment. Since the growth of normal cells is suppressed by the cytotoxic effects of these treatments, the preneoplastic cells have an additional proliferative advantage.

The centrilobular to midzonal staining for P450 b/e that was evident in the livers of rats treated with DEN + PB or DEN + both TCBs indicates that enzyme induction occurred in response to these compounds in hepatocytes in these zones. Centrilobular staining with P450 c/d after treatment with DEN + 3,4,3′,4′-TCB or DEN + both TCBs indicates that induction of this isozyme also occurred. The dose of 3,4,3′,4′-TCB was 0.3% of the 6-day chronic dose used for maximal induction by Clevenger (14), and 0.003% of the acute dose used by Parkinson (6). The dose of 2,5,2′,5′-TCB utilized in our studies was 33% of the maximal chronic dose and 3% of the maximal acute dose used in other studies (13,23,24).

The greater than additive effect of the mixture of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB reported in this study may be the result of one or more of three possible mechanisms: (i) Ah receptor gene expression (1,4,5); (ii) the PB-type of cytochrome P450 response (24,39); (iii) the metabolic activation of PCBs to epoxides (29,30). Glutathione conjugation is the major phase II detoxification pathway for the 3,4-oxide of 2,5,2′-TCB. Several different mechanisms can contribute to the toxic effects of 2,5,2′,5′-TCB. Although the mechanism of glutathione depletion may be different in hepatocytes and lymphocytes, continuous exposure to the TCB combination may have resulted in depletion of the glutathione levels in both cell types. Depletion of glutathione would prevent a major part of the detoxification of the 3,4-oxide of 2,5,2′,5′-TCB (32).

Our results demonstrate an interaction of low doses of two PCBs *in vivo* in the two major target organs of PCB toxicity, the liver and the immune system, at doses that are relevant to human exposure levels (40). The observation of immune depression and promotion of AHF with very low PCB concentrations suggests that the biological effects of a complex Aroclor mixture in two different target cell populations of PCB toxicity may not be owing simply to the summed effects of each of the constituent chemicals or to the individual concentrations of the most toxic congeners, but rather largely to the effects of only a few constituents interacting at low concentrations.

This study also represents the first report of the appearance of an abnormal population of CD-4 lymphocytes in the peripheral blood after PCB exposure. This may be an important finding not only for rodent exposure, but also for human exposure, because this same PCB combination was very genotoxic to cultured human lymphocytes. The abnormal population of CD-4 cells in the peripheral blood may be the result of a genetic change that occurred in these cells. The aneuploidy of many hepatocytes (L.M.Sargent, G.Sattler, C.A.Sattler, B.Roloff, Y.Xu and H.C.Pitot, in preparation) and numerous large neoplastic nodules exhibiting cellular atypia in the liver are indications that the combination of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB induces the stage of progression of hepatocarcinogenesis (41,42). Confirmation of this hypothesis will require further testing because the percentage of animals with hepatocellular carcinoma was not elevated after 1 year of treatment in this experiment. The numerous large neoplastic nodules with cellular atypia probably represent rapidly growing populations of abnormal cells. If this protocol had been allowed to continue further, it is possible that there would have been an increase in the frequency of hepatocellular carcinoma in the livers of rats receiving the combination compared with those administered each TCB alone.

Acknowledgements

We would like to thank Dr Colin Jefcoate for supplying the P450 antibodies. We would like to extend our gratitude to Dr James A.Miller for the gift of 2,5,2′,5′-TCB. We also thank Dr David Auerbach and the State Laboratory of Hygiene for their help in performing the flow cytometry. The expert histotechnology of Ms Jane Weeks and Mrs Jennifer Potter is also gratefully acknowledged, as well as the expert technical typing of Mrs Mary Jo Markham. The authors are grateful to Dr Ilse Riegel for technical editing and comments on the manuscript. The experiments described in this document were funded in part by grants from the National Cancer Institute (CA-07175, CA-2284 and CA-45700) and by a training grant from the National Institute of Environmental Health Sciences (ES-07015).

References

1. Safe,S. (1989) Polychlorinated biphenyls (PCBs): mutagenicity and carcinogenicity. *Mutat. Res.*, **220**, 31−47.
2. Passivirta,J. and Linko,R. (1980) Environmental toxins in Finnish wildlife. A study of trends of residue contents in fish during 1973−1978. *Chemosphere*, **9**, 643.
3. Jacobs,L.W., Chou,S.F. and Tiedje,J.M. (1978) Field concentrations and persistence of polybrominated biphenyls in soils and solubility of polybrominated biphenyls in natural waters. *Environ. Health Perspect.*, **23**, 1.
4. Safe,S., Bandiera,S., Sawyer,T., Robertson,L.W., Safe,L., Parkinson,A., Thomas,P.E., Ryan,D.E., Reik,L.M., Levin,W., Denomme,M.A. and Fujita,T. (1985) PCBs: structure−function relationships and mechanisms of action. *Environ. Health Perspect.*, **60**, 47−56.
5. Poland,A. and Knutson,J.C. (1982) 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin and related halogenated aromatic hydrocarbons: examination of the mechanism of toxicity. *Annu. Rev. Pharmacol. Toxicol.*, **22**, 517−554.
6. Parkinson,A., Robertson,L., Safe,L. and Safe,S. (1981) Polychlorinated biphenyls as inducers of hepatic microsomal enzymes: structure−activity rules. *Chem.-Biol. Interactions*, **35**, 1−2.
7. McKinney,J.D. and Singh,P. (1981) Structure−activity relationships in halogenated biphenyls: unifying hypothesis for structural specificity. *Chem.-Biol. Interactions*, **333**, 271−283.
8. Yoshimura,H., Yoshihara,S., Ozawa,N. and Miki,M. (1979) Possible correlation between induction modes of hepatic enzymes by PCBs and their toxicity in rats. *Ann. NY Acad. Sci.*, **320**, 179−192.
9. Silkworth,J.B. and Grabstein,E.M. (1982) Polychlorinated biphenyl immunotoxicity: dependence on isomer planarity and the *Ah* gene complex. *Toxicol. Appl. Pharmacol.*, **65**, 109−119.
10. Greenlee,W.F. and Irons,R.E. (1981) Modulation of benzene-induced lymphocytopenia in the rat by 2,4,5,2′,4′,5′-hexachlorobiphenyl and 3,4,4′,5′-tetrachlorobiphenyl. *Chem.-Biol. Interactions*, **33**, 345−360.
11. Wölfle,D., Münzel,P., Fischer,G. and Bock,K.-W. (1988) Altered growth control of rat hepatocytes after treatment with 3,4,3′,4′-tetrachlorobiphenyl *in vivo* and *in vitro*. *Carcinogenesis*, **9**, 919−924.
12. Osterele,D. and Deml,E. (1981) Promotion effect of various PCBs and DDT on enzyme altered islands in rat liver. *Nauyn-Schmiedberg's Arch. Pharmacol. Suppl. R*, **16**, 316.
13. Preston,B.D., Miller,E.C. and Miller,J.A. (1985) The activities of 2,2′,5,5′-tetrachlorobiphenyl, its 3,4-oxide metabolite and 2,2′,5,5′-tetrachlorobiphenyl in tumor induction and promotion assays. *Carcinogenesis*, **6**, 451−453.
14. Clevenger,M.A., Roberts,S.M., Sattin,D.L., Harbison,R.D. and James,R.C. (1989) The pharmacokinetics of 2,2′,5,5′-tetrachlorobiphenyl and 3,3′,4,4′-tetrachlorobiphenyl and its relationship to toxicity. *Toxicol. Appl. Pharmacol.*, **100**, 315−327.
15. Pitot,H.C., Campbell,H.A., Maronpot,R., Nimrat,B., Rizvi,T.A., Xu,Y.-H., Sargent,L.M., Dragan,Y. and Pyron,M. (1989) Critical parameters in the quantitation of the stages of initiation, promotion, and progression in one model of hepatocarcinogenesis in the rat. *Toxicol. Pathol.*, **17**, 594−612.
16. Pitot,H.C., Barsness,L., Goldsworthy,T. and Kitagawa,T. (1978) Biochemical characterization of stages of hepatocarcinogenesis after a single dose of diethylnitrosamine. *Nature*, **271**, 456−458.
17. Yam,L.T., Li,C. and CrosbyW.H. (1971) Cytochemical identification of monocytes and granulocytes. *Am. J. Clin. Pathol.*, **55**, 283−290.
18. Braylan,R.C. (1983) Attributes and applications of flow cytometry. *Ann. Clin. Lab. Sci.*, **13**, 379−384.

19. Xu,Y.-H., Campbell,H.A., Sattler,G.L., Hendrich,S., Maronpot,R., Sato,K. and Pitot,H.C. (1990) Quantitative stereological analysis of the effects of age and sex on multistage hepatocarcinogenesis in the rat by use of four cytochemical markers. *Cancer Res.*, **50**, 472–479.
20. Campbell,H.A., Xu,Y.-H., Hanigan,M.H. and Pitot,H.C. (1986) Application of quantitative stereology to the evaluation of phenotypically heterogeneous enzyme-altered foci in the rat liver. *J. Natl. Cancer Inst.*, **76**, 751–767.
21. Steel,R.G.D. and Torrie,J.H. (1980) Enumeration data II: contingency tables, some uses of χ-square. In *Principles and Procedures of Statistics, a Biometrical Approach.* McGraw-Hill Book Company, New York, pp. 469–520.
22. Pitot,H.C., Goldsworthy,T.L., Moran,S., Kennan,W., Glauert,H.P., Maronpot,R.R. and Campbell,H.A. (1987) A method to quantitate the relative initiating and promoting potencies of hepatocarcinogenic agents in their dose–response relationships to altered hepatic foci. *Carcinogenesis*, **8**, 1491–1499.
23. Safe,S. (1983) Polychlorinated biphenyls (PCBs) and polybrominated biphenyls: biochemistry, toxicology and mechanisms. *CRC Rev. Toxicol.*, **13**, 319–325.
24. Silberhorn,E.M., Glauert,H.P. and Robertson,L.W. (1990) Carcinogenicity of polyhalogenated biphenyls: PCBs and PBBs. *Crit. Rev. Toxicol.*, **20**, 439–496.
25. Eriksson,L., Ahluwalia,M., Spiewak,J., Lee,G., Sarma,D.S.R., Roomi,M.J. and Farber,E. (1983) Distinctive biochemical pattern associated with resistance to hepatocytes in hepatocyte nodules during liver carcinogenesis. *Environ. Health Perspect.*, **49**, 171–174.
26. Dragan,Y.P., Xu,Y.-H., Hully,J.R., Bawa,N., Rizvi,T., Campbell,H.A., Maronpot,R.R. and Pitot,H.C. (19??) An initiation-promotion asay in rat liver as a potential complement to the two-year carcinogenesis bioassay. *Fund. Appl. Toxicol.*, in press.
27. Schulte-Hermann,R., Roome,N., Timmermann-Trosiener,I. and Schuppler,J. (1984) Immunocytochemical demonstration of a phenobarbital-induced cytochrome P450 in putative preneoplastic foci of rat liver. *Carcinogenesis*, **5**, 149–153.
28. Schwarz,M., Peres,G., Buchmann,A., Friedberg,T., Waxman,D.J. and Kunz,W. (1987) Phenobarbital induction of cytochrome P450 in normal and preneoplastic rat liver: comparison of enzyme and mRNA expression as detected by immunohistochemistry and *in situ* hybridization. *Carcinogenesis*, **8**, 1355–1357.
29. Forgue,S.T., Preston,B.D., Hargraves,W.A., Reich,I.L. and Allen,J.R. (1979) Direct evidence that an aerene oxide is a metabolic intermediate of 2,5,2',5'-tetrachlorobiphenyl. *Biochem. Biophys. Res. Commun.*, **91**, 475–483.
30. Forgue,S.T. and Allen,J.R. (1982) Identification of an aerene oxide metabolite of 2,5,2',5'-tetrachlorobiphenyl by gas chromatography–mass spectroscopy. *Chem.-Biol. Interactions*, **40**, 233–245.
31. Stadnicki,S.S., Francis,S.D.L. and Allen,J.R. (1979) DNA strand breaks caused by 2,5,2',5'-tetrachlorobiphenyl and its metabolites. *Res. Commun. Chem. Pathol. Pharmacol.*, **24**, 313–325.
32. Preston,B.D., Miller,J.A. and Miller,E.C. (1984) Reactions of 2,2',5,5'-tetrachlorobiphenyl 3,4-oxide with methionine, cysteine and glutathione in relation to the formation of methylthio-metabolites of 2,2',5,5'-tetrachlorobiphenyl in the rat and mouse. *Chem.-Biol. Interactions*, **50**, 289–312.
33. Sargent,L.M., Roloff,B.D. and Meisner,L.F. (1989) *In vitro* chromosome damage due to PCB interactions. *Mutat. Res.*, **224**, 79–88.
34. Wyndhman,C., Devenish,J. and Safe.S. (1978) The *in vitro* metabolism, macromolecular binding and bacterial mutagenicity of 4-chlorobiphenyl, a model PCB substrate. *Res. Commun. Chem. Pathol. Pharmacol.*, **15**, 563–570.
35. Kawabata,T.T. and White,K.L., Jr (1989) Benzo[*a*]pyrene metabolism by murine spleen microsomes. *Cancer Res.*, **49**, 5816–5822.
36. Buchmann,A., Kunz,W., Wolf,C.R., Oesch,F. and Robertson,L.W. (1986) Polychlorinated biphenyls, classified as either phenobarbital- or 3-methylcholanthrene-type inducers of cytochrome P450, are both hepatic tumor promoters in diethylnitrosamine-initiated rats. *Cancer Lett.*, **32**, 243–253.
37. Roomi,M.W., Ho,R.K., Sarma,D.S.R. and Farber,E. (1985) A common biochemical pattern in preneoplastic hepatocyte nodules generated in four different models in the rat. *Cancer Res.*, **45**, 564–571.
38. Ghoshal,A., Gurtoo,H.L., Faletto,M.B., Koo,P., Nagi,M. and Farber,E. (1990) Molecular basis for the constitutive decrease in cytochromes P450 in putative preneoplastic hepatocytes. *Proc. Am. Assoc. Cancer Res.*, **31**, 136.
39. Goldstein,J.A., Hickman,P., Bergman,H., McKinney,J.D. and Walker, M.P.(1977) Separation of pure polychlorinated biphenyl isomers into two types of inducers on the basis of induction of P450 or P448. *Chem.-Biol. Interactions*, **17**, 69–87.
40. Cordle,F., Corneliussen,P., Jelinek,C., Hackley,B., Lehman,R., McLaughlin,J., Rhoden,R. and Shapiro,R. (1978) Human exposure to polychlorinated biphenyls and polybrominated biphenyls. *Environ. Health Perspect.*, **24**, 157–172.
41. Sherer,E., Feringa,A.W. and Emmelot,P.(1984) Initiation–promotion–initiation induction of neoplastic foci within islands of precancerous liver cells in the rat. In Börzxönyi,M., Lapi,K., Day,N. and Yamasaki,H. (eds), *Models, Mechanisms and Etiology of Tumour Promotion.* IARC Scient. Pub. 56, Lyon, pp. 57–66.
42. Pitot,H.C. (1989) Progression: the terminal stages in carcinogenesis. *Jpn. J. Cancer Res.*, **80**, 599–607.
43. Schauer,A. and Kunze,E. (1976) Tumours of the liver. In Turusov,V.S. (ed.), *Pathology of Tumours in Laboratory Animals: Vol. 1. Tumours of the Rat, Part 2.* IARC, Lyon, pp. 41–72.
44. Squire,R.A. and Levitt,M.H. (1975) Report of a workshop on classification of specific hepatocellular lesions in rats. *Cancer Res.*, **35**, 3214–3223.
45. National Research Council (1980) Histologic typing of liver tumors in the rat. *J. Natl. Cancer Inst.*, **64**, 179–206.

Received on August 20, 1990; revised on January 17, 1991; accepted on January 25, 1991

Attachment 6

CANCER MORTALITY IN WORKERS EXPOSED TO 2,3,7,8-TETRACHLORODIBENZO-*p*-DIOXIN

Marilyn A. Fingerhut, Ph.D., William E. Halperin, M.D., David A. Marlow, B.S., Laurie A. Piacitelli, M.S., Patricia A. Honchar, Ph.D., Marie H. Sweeney, Ph.D., Alice L. Greife, Ph.D., Patricia A. Dill, A.B., Kyle Steenland, Ph.D., and Anthony J. Suruda, M.D.

Abstract *Background.* In both animal and epidemiologic studies, exposure to dioxin (2,3,7,8-tetrachlorodibenzo-*p*-dioxin, or TCDD) has been associated with an increased risk of cancer.

Methods. We conducted a retrospective cohort study of mortality among the 5172 workers at 12 plants in the United States that produced chemicals contaminated with TCDD. Occupational exposure was documented by reviewing job descriptions and by measuring TCDD in serum from a sample of 253 workers. Causes of death were taken from death certificates.

Results. Mortality from several cancers previously associated with TCDD (stomach, liver, and nasal cancers, Hodgkin's disease, and non-Hodgkin's lymphoma) was not significantly elevated in this cohort. Mortality from soft-tissue sarcoma was increased, but not significantly (4 deaths; standardized mortality ratio [SMR], 338; 95 percent confidence interval, 92 to 865). In the subcohort of 1520 workers with ≥1 year of exposure and ≥20 years of latency, however, mortality was significantly increased for soft-tissue sarcoma (3 deaths; SMR, 922; 95 percent confidence interval, 190 to 2695) and for cancers of the respiratory system (SMR, 142; 95 percent confidence interval, 103 to 192). Mortality from all cancers combined was slightly but significantly elevated in the overall cohort (SMR, 115; 95 percent confidence interval, 102 to 130) and was higher in the subcohort with ≥1 year of exposure and ≥20 years of latency (SMR, 146; 95 percent confidence interval, 121 to 176).

Conclusions. This study of mortality among workers with occupational exposure to TCDD does not confirm the high relative risks reported for many cancers in previous studies. Conclusions about an increase in the risk of soft-tissue sarcoma are limited by small numbers and misclassification on death certificates. Excess mortality from all cancers combined, cancers of the respiratory tract, and soft-tissue sarcoma may result from exposure to TCDD, although we cannot exclude the possible contribution of factors such as smoking and occupational exposure to other chemicals. (N Engl J Med 1991; 324:212-8.)

SEVERAL epidemiologic and toxicologic studies have suggested an association between 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), or the chemicals it contaminates, and soft-tissue sarcoma,[1-4] Hodgkin's disease,[5] non-Hodgkin's lymphoma,[6-8] stomach cancer,[9,10] nasal cancer,[11] and cancer of the liver.[12,13] In other studies of these cancers, no significant associations with TCDD exposure were found.[14-19] The carcinogenicity of TCDD has been demonstrated in studies of rats, mice, and hamsters; histiocytic lymphomas, fibrosarcomas, and tumors of liver, skin, lung, thyroid, tongue, hard palate, and nasal turbinates have been found.[12,13,20] TCDD acts as a promoter[21,22] and may also initiate carcinogenesis.[12,13,20] To evaluate the effect of occupational exposure to TCDD, particularly with respect to the cancers listed above, we conducted a retrospective cohort study of mortality among U.S. chemical workers assigned to the production of substances contaminated with TCDD.

Methods

Identification of Companies

In 1978 the National Institute for Occupational Safety and Health began an effort that would eventually identify the exposed workers at all U.S. chemical companies that had made TCDD-contaminated products between 1942 and 1984. TCDD was generated as a contaminant in the production of 2,4,5-trichlorophenol and was carried into subsequent production processes.[23] One derivative, 2,4,5-trichlorophenoxyacetic acid, was widely used in the United States to kill brush and was a constituent of defoliants such as Agent Orange. Other derivatives included the herbicides 2-(2,4,5-trichlorophenoxy)propionic acid (Silvex) and 2-(2,4,5-trichlorophenoxy)-ethyl 2,2-dichloropropionate (Erbon), the insecticide *O,O*-dimethyl *O*-(2,4,5-trichlorophenyl)phosphorothioate (Ronnel), and the bactericide 2,2′-methylene-bis[3,4,6-trichlorophenol] (hexachlorophene).

Identification of Exposed Workers

Workers from 12 companies were included in the study cohort if a personnel or payroll record documented that they had been assigned to a production or maintenance job in a process involving TCDD contamination (n = 5000), or if they had been identified in a previously published study on the basis of exposure to TCDD (n = 172).[24] Personnel records for 202 workers did not reveal the duration of their assignment to processes involving TCDD contamination; they were therefore included in the analysis of overall mortality but excluded from analyses according to duration of exposure. Sixty-seven women are not included in this report; there were 10 deaths among them, including a single death from cancer (lung cancer).

At each plant, we made a thorough review of operating conditions, job duties, and records of TCDD levels in industrial-hygiene samples, intermediate reactants, products, and wastes. This review provided clear evidence of potential daily exposure to TCDD. The production of TCDD-contaminated substances at the various plants involved similar raw materials, processes, and job duties.[25] However, there were differences between jobs and between plants in the extent of TCDD exposures. Occupational exposure to substances contaminated with TCDD was confirmed by measuring serum TCDD levels, as adjusted for lipids, in 253 surviving members of the study cohort from two plants who were also participants in a related cross-sectional medical study.[26]

Life-Table Analysis

Vital status was determined as of December 31, 1987, from records of the Social Security Administration or Internal Revenue Service, or from the National Death Index. All death certificates

From the Industrywide Studies Branch, Division of Surveillance, Hazard Evaluations, and Field Studies, National Institute for Occupational Safety and Health, Centers for Disease Control, 4676 Columbia Pky., Cincinnati, OH 45226, where reprint requests should be addressed to Dr. Fingerhut.

Supported in part by the Agency for Toxic Substances and Disease Registry.

were independently classified by two nosologists according to the rules of the revision of the *International Classification of Diseases* (ICD) in effect at the date of death.[27]

Life-table analysis was used to evaluate mortality in the cohort.[28] At each plant, the number of person-years at risk was calculated as the interval between the first systematically documented assignment to a process involving TCDD contamination and the date of death or December 31, 1987, whichever occurred first. Those whose vital status was unknown were assumed to be alive at the end of the study. Standardized mortality ratios (SMRs) were computed by dividing the observed number of deaths by the expected number and multiplying by 100, after stratification to adjust for the confounding effects of age, race, and year of death. Two-sided 95 percent confidence intervals were computed for each cause-specific SMR, with use of the Byar approximation for eight deaths or more and Fisher's exact method for fewer than eight deaths.[29] The U.S. population was used as the reference group, because the 12 plants were located in 11 states throughout the country.

Analyses According to Duration of Exposure and Employment

Duration of exposure was defined as the number of years the worker was employed in processes involving TCDD contamination and was calculated with data from personnel records. We used duration of exposure as a surrogate for cumulative exposure to TCDD on the basis of the high correlation of the logarithm of serum TCDD levels with the logarithm of the number of years assigned to processes involving TCDD contamination in our sample of 253 workers (Pearson's product-moment coefficient $r = 0.72$) (Fig. 1), and on the assumption that the production processes were similar in the 12 plants.[25]

Because of the concentration of person-years in the short-duration categories, duration of exposure was stratified before analysis into categories of <1, 1 to <5, 5 to <15, and ≥15 years (Table 1). Mortality was also examined according to time since first exposure (latency) in periods of 0 to <10, 10 to <20, and ≥20 years since first exposure. To examine mortality in a subgroup with substantial exposure and adequate time for cancer to develop, we identified a group of workers who had 1 year or more of exposure to processes involving TCDD contamination and at least 20 years of latency. One year was chosen as a cutoff point for this high-exposure subcohort because in the sample of workers whose serum TCDD levels were measured, 100 percent of those exposed for more than one year had serum TCDD levels higher than the mean level in the unexposed reference group (7 pg per gram of lipid). For this subcohort, the number of person-years at risk was calculated from the date the person attained both 20 years of latency and 1 year of exposure.

Most of the 12 plants were large U.S. chemical manufacturing sites that produced thousands of chemicals. Complete documentation of each worker's exposures was impossible. A separate measure called "duration of employment," defined as the total time that each worker was employed at a study plant, was therefore used. Because of the long total employment at the plants, analyses according to duration of employment were stratified into periods of <5, 5 to <10, 10 to <15, 15 to <20, 20 to <25, 25 to <30, and ≥30 years (Table 1). For these analyses, latency was defined as time since first employment.

When the SMRs showed an apparent trend associated with duration of exposure or employment and when the observed numbers of deaths were sufficiently large, we conducted internal comparisons using directly standardized rate ratios and tests for trend.[30] For the standardized rate ratios, the cause-specific mortality rate in each of the categories of longer duration was compared with the rate in the category of shortest duration, after stratification of the rates for the potential confounding effects of age, race, and calendar time.

Results

The cohort of 5172 male workers from 12 plants had 116,748 person-years of observation. Table 1 describes the vital status, race, latency, and duration of exposure and employment of the workers. Overall mortality for all causes of death was similar to national rates in the United States (1052 deaths; SMR, 99; 95 percent confidence interval, 93 to 105). Mortality from heart disease was also similar to national rates

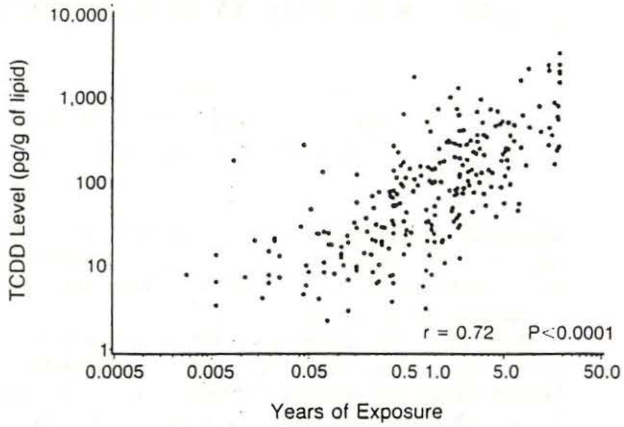


Figure 1. Serum Levels of TCDD, as Adjusted for Lipids, in 253 Workers, According to Years of Exposure.

Table 1. Vital Status and Demographic and Employment Characteristics of the Study Cohort.

Variable	Number (Percent)
Vital status*	
Alive	4043 (78)
Dead	1052 (20)
Unknown	77 (2)
Total	5172 (100)
Deaths*	
White men	985 (94)
Nonwhite men	67 (6)
Total	1052 (100)
Death certificates obtained	1037 (99)
Race	
White	4590 (89)
Nonwhite	385 (7)
Unknown	197 (4)
Total	5172 (100)
Duration of exposure (yr)†	
<1	2697 (54)
1 to <5	1427 (29)
5 to <15	639 (13)
≥15	207 (4)
Total	4970 (100)
Duration of employment (yr)†	
<5	2125 (43)
5 to <10	501 (10)
10 to <15	605 (12)
15 to <20	403 (8)
20 to <25	391 (8)
25 to <30	415 (8)
≥30	530 (11)
Total	4970 (100)
Years since first exposure (latency)†	
<10	271 (5)
10 to <20	1663 (33)
≥20	3036 (61)
Total	4970 (100)
Years since last exposure†	
<10	453 (9)
10 to <20	1789 (36)
≥20	2728 (55)
Total	4970 (100)

*As of December 31, 1987.

†Excludes 202 workers for whom duration of assignment to processes involving TCDD contamination was not available from work records.

(393 deaths; SMR, 96; 95 percent confidence interval, 87 to 106). There were significant reductions in the mortality rates for diseases of the circulatory system (67 deaths; SMR, 77; 95 percent confidence interval, 60 to 98), primarily because of fewer deaths from stroke, and for diseases of the digestive system (38 deaths; SMR, 70; 95 percent confidence interval, 49 to 96), primarily because of fewer deaths from cirrhosis. There were also significantly fewer deaths from alcoholism and personality disorders (2 deaths; SMR, 23; 95 percent confidence interval, 3 to 87). The low mortality from circulatory disease may be a reflection of the "healthy worker" effect — cohorts of workers die at lower rates than the general population, particularly of causes other than cancer.[31] The reduced number of deaths from cirrhosis and alcoholism implies that this cohort consumed less alcohol than the general population. Reduction may also have occurred simply by chance, since numerous comparisons were made between the cohort and the U.S. population. Fatal injuries were significantly more frequent in the cohort (106 deaths; SMR, 128; 95 percent confidence interval, 104 to 154), but they did not appear to be associated particularly with exposure to TCDD. Mortality from all cancers combined (265 deaths; SMR, 115; 95 percent confidence interval, 102 to 130) was significantly elevated in the cohort.

Cancers of a Priori Interest

The term "soft-tissue sarcoma" describes the group of rare malignant neoplasms arising from supporting tissue other than bone.[32] We restricted our analysis of mortality due to soft-tissue sarcoma to cases of soft-tissue sarcoma listed as the underlying cause of death

Table 2. Cancer Mortality in the Entire Cohort and in Workers with More Than 20 Years of Latency.

Site of Cancer	ICD Code*	Entire Cohort (N = 5172)†			Subcohort with ≥20 Yr of Latency (N = 3036)‡					
					<1 yr of exposure (N = 1516)§			>1 yr of exposure (N = 1520)¶		
		deaths observed	deaths expected	SMR‖	deaths observed	deaths expected	SMR‖	deaths observed	deaths expected	SMR‖
All cancers	140–208	265	229.9	115 (102–130)**	48	46.8	102 (76–136)	114	78.0	146 (121–176)**
Buccal and pharynx	140–149	5	7.0	70 (23–166)	2	1.4	145 (18–524)	2	2.2	90 (11–325)
Pharynx	146–149	3	3.4	88 (18–259)	2	0.7	298 (36–1080)	0	1.2	0 (—)
Other parts	142–145	2	1.9	105 (13–379)	0	0.4	0 (—)	2	0.6	329 (40–1190)
Digestive organs	150–159	67	59.7	112 (87–143)	13	11.8	111 (59–189)	28	20.1	140 (93–202)
Esophagus	150	9	5.9	152 (70–290)	2	1.2	165 (20–602)	4	2.0	200 (55–513)
Stomach	151	10	9.7	103 (50–190)	3	1.7	178 (37–521)	4	2.9	138 (38–353)
Small intestine and colon	152–153	25	20.4	122 (79–181)	5	4.3	117 (38–274)	13	7.3	178 (95–304)
Rectum	154	5	5.6	89 (29–209)	1	1.0	100 (3–557)	2	1.7	115 (14–415)
Liver and biliary	155, 156	6	5.2	116 (42–252)	1	1.0	100 (3–557)	1	1.7	59 (1–327)
Pancreas	157	10	11.9	84 (40–155)	1	2.4	41 (1–232)	4	4.0	100 (27–253)
Peritoneum and unspecified	158, 159	2	1.1	184 (22–666)	0	0.2	0 (—)	0	0.4	0 (—)
Respiratory system	160–165	96	84.5	113 (92–139)	19	18.4	103 (62–161)	43	30.2	142 (103–192)
Larynx	161	7	3.3	211 (84–434)	2	0.7	297 (36–1074)	3	1.1	268 (55–783)
Trachea, bronchus, and lung	162	89	80.1	111 (89–137)	17	17.5	96 (56–155)	40	28.8	139 (99–189)
Male genital organs	185–187	17	15.3	111 (65–177)	2	3.2	63 (8–229)	9	6.0	149 (68–283)
Prostate	185	17	13.9	122 (71–195)	2	3.0	67 (8–237)	9	5.9	152 (70–290)
Urinary organs	188–189	17	11.4	148 (86–238)	3	2.4	128 (26–373)	6	4.0	149 (55–324)
Kidney	189.0–189.2	8	5.7	140 (60–275)	3	1.2	253 (52–742)	2	1.9	106 (13–384)
Bladder and other	188, 189.3–189.9	9	5.7	157 (72–298)	0	1.2	0 (—)	4	2.2	186 (51–476)
Lymphatic and hematopoietic tissue	200–208	24	22.1	109 (70–162)	4	3.9	102 (28–260)	8	6.4	125 (54–247)
Hodgkin's disease	201	3	2.5	119 (25–349)	0	0.2	0 (—)	1	0.4	276 (7–1534)
Non-Hodgkin's lymphoma††	200, 202	10	7.3	137 (66–254)	2	1.5	135 (16–488)	2	2.1	93 (11–337)
Lymphosarcoma and reticulosarcoma††	200	5	3.5	142 (46–332)	0	0.6	0 (—)	1	0.9	107 (3–594)
Other lymphatic††	202	5	3.7	133 (43–313)	2	0.9	215 (26–779)	1	1.4	71 (2–385)
Multiple myeloma††	203	5	3.0	164 (53–385)	0	0.6	0 (—)	3	1.1	262 (54–766)
Leukemia and aleukemia	204–208	6	8.9	67 (24–146)	2	1.6	126 (15–457)	2	2.6	77 (9–277)
Other sites	170–173, 190–199	39	29.6	131 (94–180)	5	5.8	87 (28–202)	18	9.0	201 (118–316)**
Skin	172, 173	4	4.9	82 (22–211)	0	0.9	0 (—)	2	1.3	155 (19–559)
Brain and nervous system	191, 192	5	7.3	68 (22–160)	0	1.3	0 (—)	2	1.9	106 (13–384)
Bone	170	2	0.9	227 (27–819)	0	0.1	0 (—)	1	0.2	521 (13–2903)
Connective tissue and soft tissue	171	4	1.2	338 (92–865)	0	0.2	0 (—)	3	0.3	922 (190–2695)**
Other and unspecified	194–199	24	14.8	162 (104–241)**	5	3.1	159 (52–372)	10	5.1	196 (94–361)

*From the *International Classification of Diseases*, 9th revision.

†Mean number of years exposed, 2.7; mean number of years employed, 12.6.

‡Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records.

§Mean number of years exposed, 0.3; mean number of years employed, 10.7; 12,299 person-years at risk.

¶Mean number of years exposed, 6.8; mean number of years employed, 19.2; 15,136 person-years at risk.

‖SMR equals deaths observed divided by deaths expected and multiplied by 100. Slight differences are due to rounding. Values in parentheses are 95 percent confidence intervals.

**P<0.05.

††Person-years at risk and observed deaths are computed from 1960; no deaths occurred before that year.

on death certificates and assigned to the ICD category "malignant neoplasms of connective and other soft tissue." In the cohort, mortality from soft-tissue sarcoma was nonsignificantly higher than in the reference population (four deaths; SMR, 338; 95 percent confidence interval, 92 to 865) (Table 2). The deaths occurred at 2 of the 12 plants, with a significant increase at 1 plant (two deaths; SMR, 1512; 95 percent confidence interval, 183 to 5462). A review of tissue specimens from the four men whose deaths were attributed to soft-tissue sarcoma showed that only two were in fact soft-tissue sarcomas (Cases 1 and 4, Table 3).[33] Mortality from soft-tissue sarcomas was increased significantly in the subcohort of 1520 workers with 1 year or more of exposure and at least 20 years of latency (the high-exposure subcohort) (three deaths; SMR, 922; 95 percent confidence interval, 190 to 2695). Two other deaths in the cohort (Cases 5 and 6) were attributed to soft-tissue sarcoma according to hospital records, and one of them (Case 5) was confirmed by review of a tissue specimen. These two deaths did not contribute to mortality due to soft-tissue sarcoma in our life-table analysis, because the deaths were assigned other ICD codes. We are aware of a seventh death from soft-tissue sarcoma, which occurred in a group of 139 workers with chloracne who were excluded from the cohort because they did not meet the entry criteria.

In the cohort, the SMRs for the other cancers of a priori interest were nonsignificantly increased (Table 2). There were no deaths from nasal cancer, although approximately one was expected. In the high-exposure subcohort, the SMRs were nonsignificantly higher for Hodgkin's disease and stomach cancer and lower for non-Hodgkin's lymphoma and cancer of the liver, biliary passages, and gallbladder (Table 2).

A Posteriori Findings

A small but significant increase in mortality due to all cancers combined was observed in the entire cohort (SMR, 115; 95 percent confidence interval, 102 to 130). In the high-exposure subcohort the SMR was 146 (95 percent confidence interval, 121 to 176) (Table 2). At 9 of the 12 plants, mortality from all cancers combined was increased; at one of these plants the increase was statistically significant. Mortality was significantly higher than expected in the category of cancers of unspecified sites, which included those of rare sites not included in a category of the life-table analysis and those for which no primary site was listed on the death certificate. Hospital records, which were obtained for 96 percent of these cancers, revealed no particular clustering according to site.

The cohort had a nonsignificant increase in mortality from cancers of the trachea, bronchus, and lung (ICD code 162; SMR, 111; 95 percent confidence interval, 89 to 137). Mortality from cancers of the respiratory system (ICD codes 160 to 165) was significantly higher than expected in the high-exposure subcohort (SMR, 142; 95 percent confidence interval, 103 to 192) (Table 2). To estimate the effect of smoking on the increase in lung cancer, the expected number of lung cancers was adjusted according to the smoking prevalence found in lifetime histories obtained in 1987 by interviewing 223 workers from two plants.[25] This adjustment increased the expected number of lung cancers in the overall cohort by 5 percent and in the high-exposure subcohort by 1 percent, which reduced the SMR in the full cohort to 105 (95 percent confidence interval, 85 to 130) and in the high-exposure subcohort to 137 (95 percent confidence interval, 98 to 187).

Analyses According to Duration of Exposure and Employment

The study cohort worked a mean of 2.7 years in processes involving TCDD contamination and 12.6 years at the plants. The high-exposure subcohort worked a mean of 6.8 years in processes involving TCDD contamination and a mean of 19.2 years in total employment at the plants.

The numbers of deaths due to the rare cancers of

Table 3. Deaths from Soft-Tissue Sarcoma among Workers in the Cohort.*

Case No.	Years Employed	Type of Exposure	Year First Exposed	Years Exposed	Year of Death	Latency (yr)†	Cause of Death: Death Certificate	Cause of Death: Hospital Records	Cause of Death: Tissue Review‡
1	1946–1978	TCP and 2,4,5-T	1950	8.8	1978	28	MFH	MFH	MFH
2	1946–1972	TCP and 2,4,5-T	1948	7.1	1972	24	Liposarcoma	Liposarcoma	Carcinoma, poorly differentiated§
3	1950–1975	TCP	1963	1.2	1975	12	Fibrosarcoma	Fibrosarcoma	Renal carcinoma§
4	1951–1982	TCP	1951	14.9	1983	32	MFH	MFH	MFH
5¶	1943–1975	TCP or 2,4,5-T	Intermittent	Unknown	1980	Unknown	Carcinomatosis§	Myxoid neurogenic sarcoma	Leiomyosarcoma
6¶	1941–1964	TCP	1949	Unknown	1965	16	Metastatic osteosarcoma§	Fibrosarcoma	Not available

*Cases 1 through 5 have been previously described.[33] For other previously described cases, records of exposure to TCDD were not available, and the cases were not included in this cohort study. Some information differs slightly from that reported earlier, since additional records were reviewed. Few details about exposure were available for Cases 5 and 6. TCP denotes 2,4,5-trichlorophenol; 2,4,5-T, 2,4,5-trichlorophenoxyacetic acid; and MFH, malignant fibrous histiocytoma.

†Time from first exposure to death.

‡Conducted at the Armed Forces Institute of Pathology.

§Not a soft-tissue sarcoma.

¶Death was not attributed to soft-tissue sarcoma in the life-table analysis.

Table 4. Mortality from All Cancers and from Cancers of the Trachea, Bronchus, and Lung, According to Latency Period and Duration of Exposure to Processes Involving TCDD Contamination.*

Cause/Latency Period	Duration of Exposure (yr)										Test for Trend
	<1		1 to <5		5 to <15		≥15		Overall		
	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	
All cancers											
<10 Yr	10	68	8	71	3	71	0	0	21	70	
10 to <20 Yr	28	109	16	87	18	122	7	340†	69	113	
≥20 Yr	48	102	59	165‡	37	138	18	115	162	129‡	
Total	86	98	83	127†	58	126	25	141	252	116†	
SRR		100		127		123		129			0.3
Trachea, bronchus, and lung											
<10 Yr	3	77	3	95	1	79	0	0	7	84	
10 to <20 Yr	6	69	5	79	9	180	1	137	21	101	
≥20 Yr	17	96	17	126	14	146	9	156	57	123	
Total	26	86	25	109	24	151	10	154	85	112	
SRR		100		109		166		136			0.2

*Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records. The number of observed deaths and the SMRs therefore differ slightly from those in Table 2. SRR denotes standardized rate ratio.

†P<0.05. ‡P<0.01.

a priori interest were too small to permit meaningful analyses according to duration. For all cancers combined and for cancers of the trachea, bronchus, and lung, Table 4 shows the distribution of mortality with increasing duration of exposure to products contaminated with TCDD. The standardized rate ratios were increased in the strata of longer duration for both these categories, but significant linear trends were not found. Mortality increased with increasing latency for both these categories of cancer. Table 5 shows the distribution of mortality for the same categories with increasing duration of employment. Significant linear trends were not observed for either category with increasing length of employment, although standardized rate ratios were higher than expected in several strata of employment ≥20 years. Mortality increased with increasing latency for both categories of cancer.

Serum Levels of TCDD

The mean serum TCDD level, as adjusted for lipids, in the sample of 253 workers from two plants was 233 pg per gram of lipid (range, 2 to 3400) (Fig. 1). A mean level of 7 pg per gram was found in the comparison group of 79 unexposed persons, all of whose levels were under 20, a range found in other unexposed populations.[34] The mean for 119 workers with one year or more of exposure was 418 pg per gram. All the workers had received their last occupational exposures 15 to 37 years earlier.

Discussion

TCDD, widely known as dioxin, has acquired the reputation of a potent carcinogen. Our study, although limited in its ability to detect increased numbers of rare cancers, found little increase in mortality from the cancers associated with TCDD in previous studies in humans. The exception was an increase in soft-tissue sarcoma. The difficulties of evaluating soft-tissue sarcomas in a cohort study of mortality have been described.[33] These include variability in pathological diagnosis and misclassification on death certificates. Consequently, the interpretation of the increased mortality from soft-tissue sarcoma in our study is limited by the small number of cases and the fact that the cause of death was sometimes misclassified on the death certificates of the workers (Table 3) and in the U.S. comparison population.[35]

Several case–control studies have found significant fourfold increases in non-Hodgkin's lymphoma in persons reporting exposure to phenoxy herbicides or chlorophenols, some of which contained TCDD.[6,8] The magnitude of the increase in mortality in the cohort described here (SMR, 137; 95 percent confidence interval, 66 to 254) suggests a smaller increase in this risk, or no increase at all. Mortality was not significantly higher than expected for other cancers of a priori interest — liver and stomach cancers and Hodgkin's disease. No deaths from nasal cancer were observed. The inconsistency between the results reported here and those of earlier epidemiologic studies is accentuated by the longer and probably greater exposure of this cohort to phenoxy herbicides and chlorophenols contaminated with TCDD.

Mortality from cancers of the trachea, bronchus, and lung was nonsignificantly higher in the cohort. Among the workers with 20 years or more of latency, mortality from respiratory cancer was significantly increased in the high-exposure subcohort, which had 1 year or more of exposure (SMR, 142; 95 percent confidence interval, 103 to 192) but not in the subcohort with less than 1 year of exposure (SMR, 103; 95 percent confidence interval, 62 to 161) (Table 2). SMRs for lung cancer are known to be somewhat higher in blue-collar groups than in the general U.S. population because of more cigarette smoking in the blue-collar groups.[36] However, the increased number of lung cancers in the high-exposure subcohort was probably not due to confounding by smoking, for several reasons. First, other diseases related to smoking were not more common than expected in this subco-

Table 5. Mortality from All Cancers and from Cancers of the Trachea, Bronchus, and Lung, According to Latency Period and Duration of Employment at the Study Plants.*

CAUSE/LATENCY PERIOD	DURATION OF EMPLOYMENT (YR)																TEST FOR TREND
	<5		5 TO <10		10 TO <15		15 TO <20		20 TO <25		25 TO <30		≥30		OVERALL		
	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	
All cancers																	
<10 Yr	10	85	1	18	0	0	0	0	0	0	0	0	0	0	11	64	
10 to <20 Yr	21	114	5	126	12	103	8	80	0	0	0	0	0	0	46	105	
≥20 Yr	40	138	15	140	6	70	15	98	34	134	31	116	54	135†	195	125‡	
Total	71	120	21	104	18	89	23	91	34	134	31	116	54	135†	252	116	
SRR		100		99		61		76		128		84		115			0.9
Trachea, bronchus, and lung																	
<10 Yr	3	103	1	74	0	0	0	0	0	0	0	0	0	0	4	94	
10 to <20 Yr	5	82	0	0	5	139	4	122	0	0	0	0	0	0	14	98	
≥20 Yr	11	102	2	51	2	65	3	55	12	133	18	180†	19	126	67	117	
Total	19	96	3	46	7	105	7	81	12	133	18	180†	19	126	85	112	
SRR		100		65		91		89		171		147		98			0.6

*Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records. SRR denotes standardized rate ratio.
†P<0.05. ‡P<0.01.

hort; mortality from nonmalignant respiratory disease (ICD codes 470 to 478 and 490 to 519), which is often associated with smoking, was lower than expected (15 deaths; SMR, 96; 95 percent confidence interval, 54 to 158). Second, in the exposed population with 20 years of latency, whose members presumably shared similar smoking habits, the increase was confined to the high-exposure subcohort. Third, on the basis of empirical evidence from other studies, Siemiatycki et al.[36] have shown that between a blue-collar population and the general U.S. population, confounding by smoking is unlikely to account for an excess risk of more than 10 to 20 percent. Finally, a limited adjustment in the risk of lung cancer,[37,38] based on the smoking prevalence of surviving workers at only two plants, did not substantially change our results.[25] Although confounding by smoking is unlikely to explain the higher rate of respiratory cancer in the high-exposure subcohort, it remains possible that the increase was due to confounding by occupational exposures other than TCDD. For example, asbestos may have contributed to mortality from lung cancer in the cohort, since two deaths were due to mesotheliomas.

An unexpected finding was the small but significant increase in mortality from all cancers combined. The observed increase is consistent with a carcinogenic effect of TCDD. For all cancers combined, mortality was significantly higher than expected in the entire cohort, more pronounced in the high-exposure subcohort, and increased at 9 of 12 plants. With mortality from cancers of the trachea, bronchus, and lung excluded, mortality from all remaining cancers combined was still higher than expected in the overall cohort (SMR, 117; 95 percent confidence interval, 100 to 136) and in the high-exposure subcohort (SMR, 150; 95 percent confidence interval, 118 to 189). Consequently, the increased risk for all cancers combined is not explained by smoking or by increased mortality due to cancer of the trachea, bronchus, and lung. The generation of tumors in a number of organs in animals exposed to TCDD[12,13] and the demonstration that TCDD promoted tumors in two organs[21,22] make it biologically plausible that TCDD may produce tumors in more than one organ in humans. Moreover, a significantly increased SMR for all cancers combined is unusual in occupational studies of chemical workers. Results similar to ours were observed in a study of German workers exposed to TCDD after a 2,4,5-trichlorophenol reactor accident in 1953. A subgroup of workers with chloracne (used as a surrogate for exposure) and at least 20 years of latency had an SMR of 201 (90 percent confidence interval, 122 to 315) for all cancers combined, based on 14 deaths.[39] This is the only other industrial cohort with both substantial exposure to TCDD and a long period of latency during which mortality was examined. Workers from U.S. production cohorts described in previous studies were included in the current study if they met our entry criteria.[40-42]

Two observations argue against a carcinogenic effect of TCDD. First, there was not a significant linear trend of increasing mortality with increasing duration of exposure to products contaminated with TCDD (Table 4). However, our use of duration of exposure may have misclassified the cumulative dose of some workers. In addition, a dose–response relation is generally viewed as strong evidence for an association when it is present, but as fairly weak evidence against an association when it is absent.[43] Second, our study did not directly assess the effect of exposure to TCDD alone. The workers were exposed concurrently to the chlorophenols and phenoxy herbicides that were contaminated with TCDD. In addition, they may have been exposed to numerous other chemicals while employed at the plants.

Because the exposure of our cohort was substantially higher than that of most nonoccupational populations, the estimates of effect in this study may provide an upper level of risk to be anticipated in humans. For several types of cancer previously associated with

TCDD, we found no increases above expected levels. Soft-tissue sarcoma was an exception; a ninefold increase was found among workers who were exposed for 1 year or more and who had at least 20 years of latency. Interpretation of the increased SMR is limited, however, by the small number of cases and because this cause of death was sometimes misclassified on the death certificates of the workers and in the national comparison population. Continued surveillance of the cohort may provide a firmer estimate of risk.

Mortality from all cancers combined was 15 percent higher than expected in the overall cohort. The subcohort with 1 year or more of exposure and 20 years or more of latency had a 46 percent increase in all cancers combined and a 42 percent increase in cancers of the respiratory tract. Although the study could not completely exclude the possible contribution of other occupational carcinogens or smoking, the increased mortality, especially in the subcohort with one year or more of exposure, is consistent with the status of TCDD as a carcinogen.

We are indebted to the National Institute for Occupational Safety and Health statistical clerks, Steve Green, Joyce Godfrey, and others, for their technical contributions; to representatives of the companies and unions for assistance in gathering the data for the study; to our colleagues at the Center for Environmental Health and Injury Control, Centers for Disease Control, for analysis of the serum samples; and to Lawrence Fine, David Brown, and the members of our blue-ribbon review panel for their helpful advice.

References

1. Hardell L, Sandstrom A. Case-control study: soft-tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. Br J Cancer 1979; 39:711-7.
2. Eriksson M, Hardell L, Adami HO. Exposure to dioxins as a risk factor for soft tissue sarcoma: a population-based case-control study. J Natl Cancer Inst 1990; 82:486-90.
3. Eriksson M, Hardell L, Berg N, Moller T, Axelson O. Soft-tissue sarcomas and exposure to chemical substances: a case-referent study. Br J Ind Med 1981; 38:27-33.
4. Hardell L, Eriksson M. The association between soft tissue sarcomas and exposure to phenoxyacetic acids: a new case-referent study. Cancer 1988; 62:652-6.
5. Hardell L, Bengtsson NO. Epidemiologic study of socioeconomic factors and clinical findings in Hodgkin's disease, and reanalysis of previous data regarding chemical exposure. Br J Cancer 1983; 48:217-25.
6. Hardell L, Eriksson M, Lenner P, Lundgren E. Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols and phenoxy acids: a case-control study. Br J Cancer 1981; 43:169-76.
7. Woods JS, Polissar L, Severson RK, Heuser LS, Kulander BG. Soft tissue sarcoma and non-Hodgkin's lymphoma in relation to phenoxyherbicide and chlorinated phenol exposure in western Washington. J Natl Cancer Inst 1987; 78:899-910.
8. Persson B, Dahlander A, Fredriksson M, Brage HN, Ohlson CG, Axelson O. Malignant lymphomas and occupational exposures. Br J Ind Med 1989; 46:516-20.
9. Axelson O, Sundell L, Andersson K, Edling C, Hogstedt C, Kling H. Herbicide exposure and tumor mortality: an updated epidemiologic investigation on Swedish railroad car workers. Scand J Work Environ Health 1980; 6:73-9.
10. Thiess AM, Frentzel-Beyme R, Link R. Mortality study of persons exposed to dioxin in a trichlorophenol-process accident that occurred in the BASF AG on November 17, 1953. Am J Ind Med 1982; 3:179-89.
11. Hardell L, Johansson B, Axelson O. Epidemiological study of nasal and nasopharyngeal cancer and their relation to phenoxy acid or chlorophenol exposure. Am J Ind Med 1982; 3:247-57.
12. Kociba R, Keyes D, Beyer J, et al. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. Toxicol Appl Pharmacol 1978; 46:279-303.
13. National Toxicology Program (NTP). Carcinogenesis bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin (CAS No. 1746-01-6) in Osborne-Mendel rats and B6C3F1 mice (gavage study) 1982. Washington, D.C.: Government Printing Office, 1982. (DHHS publication no. (NIH) 82-1765.)
14. Smith AH, Pearce NE, Fisher DO, Giles HJ, Teague CA, Howard JK. Soft tissue sarcoma and exposure to phenoxyherbicides and chlorophenols in New Zealand. J Natl Cancer Inst 1984; 73:1111-7.
15. Wiklund K, Holm L. Soft tissue sarcoma risk in Swedish agricultural and forestry workers. J Natl Cancer Inst 1986; 76:229-34.
16. Pearce NE, Sheppard RA, Smith AH, Teague CA. Non-Hodgkin's lymphoma and farming: an expanded case-control study. Int J Cancer 1987; 39:155-61.
17. Wiklund K, Dich J, Holm LE. Risk of malignant lymphoma in Swedish pesticide appliers. Br J Cancer 1987; 56:505-8.
18. Olsen JH, Jensen OM. Nasal cancer and chlorophenols. Lancet 1984; 2:47-8.
19. Hardell L, Bengtsson N, Jonsson V, Ericksson S, Larsson L. Aetiological aspects on primary liver cancer with special regard to alcohol, organic solvents and acute intermittent porphyria — an epidemiological investigation. Br J Cancer 1984; 50:389-97.
20. Rao MS, Subbarao V, Prasad JD, Scarpelli DG. Carcinogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the Syrian golden hamster. Carcinogenesis 1988; 9:1677-9.
21. Poland A, Palen D, Glover E. Tumour promotion by TCDD in skin of HRS/J hairless mice. Nature 1982; 300:271-3.
22. Pitot HC, Goldsworthy T, Campbell HA, Poland A. Quantitative evaluation of the promotion by 2,3,7,8-tetrachlorodibenzo-p-dioxin of hepatocarcinogenesis from diethylnitrosamine. Cancer Res 1980; 40:3616-20.
23. Esposito M, Tiernan T, Dryden F. Dioxins. 1980. Cincinnati: Industrial Environmental Research Laboratory, 1980. (EPA publication 600/2-80-197.)
24. Suskind RR, Hertzberg VS. Human health effects of 2,4,5-T and its toxic contaminants. JAMA 1984; 251:2372-80.
25. Fingerhut M, Halperin W, Marlow D, et al. Mortality among U.S. workers employed in the production of chemicals contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). NIOSH Final Report PB91125971. Springfield, Va.: National Technical Information Service, 1990.
26. Sweeney MH, Fingerhut MA, Connally LB, et al. Progress of the NIOSH cross-sectional medical study of workers occupationally exposed to chemicals contaminated with 2,3,7,8-TCDD. Chemosphere 1989; 19:973-7.
27. World Health Organization. International classification of diseases: manual of the international statistical classification of diseases, injuries, and causes of death. Geneva: World Health Organization, 1977.
28. Steenland K, Beaumont J, Spaeth S, et al. New developments in the NIOSH lifetable analysis system. J Occup Med 1990; 32:1091-8.
29. Rothman K, Boice J. Epidemiologic analysis with a programmable calculator. Washington, D.C.: Government Printing Office, 1979:30-1. (DHEW publication no. (NIH) 79-1649.)
30. Rothman KJ. Modern epidemiology. Boston: Little, Brown, 1986:229, 338-9.
31. Fox AJ, Collier PF. Low mortality rates in industrial cohort studies due to selection for work and survival in the industry. Br J Prev Soc Med 1976; 30:225-30.
32. Suit HD. Sarcoma of soft tissue. CA 1978; 28:284-95.
33. Fingerhut MA, Halperin WE, Honchar PA, Smith AB, Groth DH, Russell WO. An evaluation of reports of dioxin exposure and soft tissue sarcoma pathology among chemical workers in the United States. Scand J Work Environ Health 1984; 10:299-303.
34. Patterson DG Jr, Fingerhut MA, Roberts DR, et al. Levels of polychlorinated dibenzo-p-dioxins and dibenzofurans in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Am J Ind Med 1989; 16:135-46.
35. Percy C, Stanek E III, Gloekler L. Accuracy of cancer death certificates and its effect on cancer mortality statistics. Am J Public Health 1981; 71:242-50.
36. Siemiatycki J, Wacholder S, Dewar R, Cardis E, Greenwood C, Richardson L. Degree of confounding bias related to smoking, ethnic group, and socioeconomic status in estimates of the association between occupation and cancer. J Occup Med 1988; 30:617-25.
37. Axelson O. Aspects on confounding in occupational health epidemiology. Scand J Work Environ Health 1978; 4:98-102.
38. Steenland K, Beaumont J, Halperin W. Methods of control for smoking in occupational cohort mortality studies. Scand J Work Environ Health 1984; 10:143-9.
39. Zober A, Messerer P, Huber P. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. Int Arch Occup Environ Health 1990; 62:139-57.
40. Zack JA, Suskind R. The mortality experience of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident. J Occup Med 1980; 22:11-4.
41. Zack JA, Gaffey WR. A mortality study of workers employed at the Monsanto Company plant in Nitro, West Virginia. Environ Sci Res 1983; 26:575-91.
42. Ott MG, Olson RA, Cook RR, Bond GG. Cohort mortality study of chemical workers with potential exposure to the higher chlorinated dioxins. J Occup Med 1987; 29:422-9.
43. Monson RA. Occupational epidemiology. Boca Raton, Fla.: CRC Press, 1990:100.

750 · 30# 1012082 ATTACHMENT 7 02/10 09:22

7

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE 4 February 1987

SUBJECT 2,3,7,8-TCDD in Aquatic Environments

FROM Philip M. Cook, Ph.D. PMC
Chief, Hazardous Waste Research Branch, ERL-Duluth

TO Jim Cummings
Office of the Assistant Administrator
for Solid Waste and Emergency Response

This memorandum is provided in response to your request for an update on the state of knowledge concerning 2,3,7,8-TCDD in aquatic environments. A considerable amount of new information is being generated and much will be reported during 1987. Most of the information I can provide results from our own research. I believe you have already received reprints for research results already published.

I reported bioconcentration factor (BCF) determinations for 2,3,7,8-TCDD, 1,2,3,4-TCDD, 1,3,6,8-TCDD and 1,3,7,9-TCDD at the Society for Environmental Toxicology and Chemistry meeting last November. A journal publication is in preparation. The EPA Water Quality Criteria Document presently uses a value of 5000 for the 2,3,7,8-TCDD BCF. We determined a value of 66,000 for carp and 97,000 and 159,000 for fathead minnows at two different exposure concentrations. Our BCF data for the four TCDD isomers is summarized in the attached table. We concluded from this study that ---

1. BCFs for different TCDD isomers vary greatly as expected from field monitoring data.

2. TCDD isomers other than 2,3,7,8-TCDD have lower BCFs than predicted on the basis of structure or log Kow due to more rapid rates of elimination.

3. Differences in rates of metabolism probably explain differences in TCDD rates of elimination and thus BCFs.

4. The gill uptake efficiencies for the four TCDD isomers studied appear to be similar despite structural differences and different uptake rate measurements attributed to large differences in elimination rates.

5. Approximately 90% of the TCDD in the fish exposure water was associated with particulate and dissolved organic matter. Thus, BCFs calculated on the basis of organic carbon free TCDD in the water would be ten times greater.

EPA Form 1320-6 (Rev. 3-76)

6. The Water Quality Criteria Document BCF value for 2,3,7,8-TCDD is very low because previously reported BCF determinations were made on the basis of very short exposure periods, inadequate depuration data, static exposure conditions, overestimates of water exposure concentrations, and other factors which lower the estimate of equilibrium fish concentrations with respect to actual water concentrations.

7. 2,3,7,8-TCDD is so toxic to fish that BCF determinations have not yet been made over long exposure periods without toxic effects and mortality occurring. No-effect levels are likely to be less than 10 ppq total 2,3,7,8-TCDD in water and possibly less than 1 ppq if only "dissolved" 2,3,7,8-TCDD is considered in the bioaccumulatable and toxic component.

8. 2,3,7,8-TCDD was lethal to carp at an accumulated dose of 2 ug/Kg. Rainbow trout appear to be a little more sensitive. This toxicity is comparable to the 1 ug/Kg LD50 found for the guinea pig, the most sensitive mammalian species known. Fathead minnows appear to be at least five times less sensitive than carp or rainbow trout.

It is likely that fish bioaccumulation of PCDDs and PCDFs is greatly influenced by food chain links to contaminated sediments and contact time of fish with sediment. Field monitoring data generally supports this premise. For example, fish collected from field surveys when analyzed for all TCDD isomers generally only have detectable amounts of 2,3,7,8-TCDD despite the presence of greater amounts of other TCDD isomers in contaminated sediments. Many of the TCDD isomers have relatively low bioaccumulation potential as seen from our BCF measurements for 1,2,3,4-TCDD and 1,3,7,9-TCDD and thus are not likely to be detected. 1,3,6,8-TCDD, however, would be expected in the fish in detectable levels if uptake from water was the major route for bioaccumulation. The lack of 1,3,6,8-TCDD in the fish is consistent with a kinetic effect involving decreasing amounts of 1,3,6,8-TCDD with respect to 2,3,7,8-TCDD in each step along the food chain to a fish and the absence of significant uptake from water.

For higher chlorinated PCDD and PCDF congeners, differences in elimination rates from fish and their food chain organisms create similar preferential bioaccumulation of 2,3,7,8-substituted planar molecules which are likely to be metabolized at a slower rate. In addition, as molecular weight and size increase with increasing degree of chlorination, it is apparent that the rate uptake from water across the gills decreases. Absorption efficiency from ingested material is also probably less for higher chlorinated congeners.

The net result of the above considerations is that many PCDDs and PCDFs found in sediments are not detectable in fish. The attached table on "Congener Dependent Bioavailability of PCDDs and PCDFs"

demonstrates how this same effect occurs for laboratory exposure of fish to municipal incinerator fly ash. The effect is more extreme when the "food chain chromatography" effect is present and longer exposure times are involved (much longer time required to reach steady state) as with the fish exposed to sediment in a reservoir. The compounds included in the table are all members of the "biosignificant fraction of PCDDs and PCDFs in that they do appear to bioaccumulate, are all 2,3,7,8-substituted and thus all have significant toxic potential. We developed a simple expression called the "bioavailability index" (BI) for comparing relative bioaccumulation tendencies for different chemicals associated with different solid wastes on sediments. The BI is simply the ratio of chemicals accumulated per gram of fish lipid to the amount present per gram of organic carbon in the solid material the fish are exposed to. The BI can be normalized to a value of 1.0 for 2,3,7,8-TCDD in order to make comparison of the other PCDD and PCDF congener's BIs easier. Although the magnitudes of the fly ash and sediment BIs cannot be directly compared due to great differences in the fish exposures, the normalized BIs for both fly ash and sediment show the same trends. For both PCDDs and PCDFs the normalized BIs decrease as the degree of chlorination increases. There also appears to be a tendency for 2,3,7,8-TCDF to be less bioaccumulable than 2,3,7,8-TCDD. The penta-CDD and -CDF results for the sediment seem divergent and will be rechecked before this data is published in this form. We will soon have much more of this kind of data when results are obtained for Lake Ontario sediments and paper mill sludges.

EPA is frequently faced with the question of what fish TCDD contamination levels will result from known or projected environmental contamination levels. The use of a BCF value, no matter how accurate, for predicting fish residues has a major limitation in that environmental TCDD water concentrations can never be detected even with the most sensitive techniques. Even if water measurements could be made, it would be difficult to determine what fraction of TCDD in water is not associated with dissolved or particulate organic carbon so that a laboratory derived BCF could be applied. An alternative approach is to use expected equilibrium partitioning relationships for sediment and fish to predict maximum levels of fish contamination and rely on site-specific sediment to fish TCDD ratios to determine more realistic "approach to steady-state" relationships likely to exist between sediments and fish. This should be done on the basis of partitioning between organic carbon in sediment and lipid in fish. In theory there should be a simple 1:1 equilibrium relationship between sediment organic carbon and lipid concentrations for very hydrophobic organic compounds such as 2,3,7,8-TCDD which are very slowly metabolized and eliminated from the organism. There are data for compounds such as PCBs which indicate approximately a four-fold preference of these compounds for lipids over organic carbon in sediment. Our 2,3,7,8-TCDD BI value of .27 for sediment is 4X less than the theoretical partitioning value of 1.0 and ~~8X~~ 16X less than the lipid preference value of 4.0 at least in part because steady-state conditions were not reached when the fish were exposed to the sediment.

In many environmental situations expected steady-state relationships between fish bioaccumulation levels and sediment contamination levels will

4

not be reached. Kinetic models and appropriate rate constants are needed to accurately predict fish bioaccumulation levels. When an aquatic ecosystem has a constant input of TCDD so that surface sediment concentrations are relatively constant, fish concentrations will approach a steady-state level dependent on rates of uptake from water, food and contact with sediment. For Lake Ontario we are investigating sediment to fish TCDD ratios under present conditions so that remedial actions for Superfund sites and other sources of TCDD can be evaluated with respect to changes in fish residues which will result in the future. That is, if sediment TCDD levels are decreased or increased in the future through man's activities, we should be able to predict eventual changes in fish contamination levels when a new "approach to steady-state" system results. In Lake Ontario our preliminary data indicates that fish lipids have only about 5% of the TCDD concentration found in the organic carbon fraction of the surface sediments. An extensive survey of sediment and fish TCDD levels throughout Lake Ontario is scheduled for this summer.

CONGENER DEPENDENT BIOAVAILABILITY OF PCDDs AND PCDFs IN FLY ASH AND SEDIMENT

Compound	Fly Ash pg/g Carbon	Fish pg/g Lipid	BI	Normalized BI	Sediment pg/g Carbon	Fish pg/g Lipid	BI	Normalized BI
2,3,7,8-TCDD	1.3×10^5	93	7.4×10^{-4}	1.00	5450	1500	.27	1.00
2,3,4,8-TCDF	1.7×10^5	95	5.7×10^{-4}	.77	5870	300	.06	.22
1,2,3,7,8-PeCDD	1.2×10^6	540	4.3×10^{-4}	.58	1000	60	.06	.22
2,3,4,7,8-PeCDF	7.3×10^5	180	2.5×10^{-4}	.34	190	55	.28	1.04
1,2,3,6,7,8-; 1,2,3,4,7,8-H_xCDD	5.0×10^6	1300	2.6×10^{-4}	.35	5800	200	.04	.15
1,2,3,6,7,8-H_xCDF	8.2×10^5	290	3.5×10^{-4}	.47	360	~~200~~ 12	.04	.14
1,2,3,4,6,7,8-H_pCDD	1.6×10^7	1300	7.8×10^{-5}	.11	71000	540	.005	.018
1,2,3,4,6,7,8-H_pCDF	3.7×10^6	340	9.2×10^{-5}	.12	9400	31	.003	.012

Attachment 8

Environmental Toxicology and Chemistry, Vol. 7, pp. 47–62, 1988
Printed in the USA. Pergamon Journals Ltd.

555

TOXICITY AND BIOCONCENTRATION OF 2,3,7,8-TETRACHLORODIBENZODIOXIN AND 2,3,7,8-TETRACHLORODIBENZOFURAN IN RAINBOW TROUT

PAUL M. MEHRLE,* DENNY R. BUCKLER, EDWARD E. LITTLE,
LARRY M. SMITH, JIM D. PETTY, PAUL H. PETERMAN
and DAVID L. STALLING
National Fisheries Contaminant Research Center, U.S. Fish and Wildlife Service,
Columbia, Missouri 65201

G. M. DE GRAEVE and JAMES J. COYLE
Battelle Laboratories—Columbus, Columbus, Ohio 43201

WILLIAM J. ADAMS
Monsanto, St. Louis, Missouri 63167

(*Received* 25 *March* 1987; *Accepted* 14 *July* 1987)

Abstract—Among the most toxic isomers of polychlorinated dibenzodioxins and polychlorinated dibenzofurans, two groups of toxic aromatic compounds, are 2,3,7,8-tetrachlorodibenzodioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF). We examined the chronic toxicity of these compounds to rainbow trout (*Salmo gairdneri*). The fish (0.38 ± 0.09 g) were continuously exposed in an intermittent-flow proportional diluter for 28 d to 0, 38, 79, 176, 382, and 789 pg TCDD/L (parts per quadrillion) or to 0, 0.41, 0.90, 1.79, 3.93, and 8.78 ng TCDF/L (parts per trillion); exposures to each chemical were followed by a 28-d depuration phase. TCDD had significant effects on survival, growth, and behavior during the exposure and depuration phases. The no observed effect concentration was lower than the lowest exposure concentration of 38 pg/L. The average measured BCF at 28 days was 26,707. The estimated bioconcentration factor at steady-state equilibrium was 39,000 in the lowest exposure concentration where fish were least affected. TCDF, like TCDD, induced similar effects on survival, growth and behavior. The no observed effect concentration, based on survival, was 1.79 ng/L; that based on growth was 0.41 ng/L. The measured bioconcentration factor was 6,049 in fish exposed to 0.41 ng/L, and 2,455 in fish exposed to 3.93 ng/L for 28 d.

Keywords—Dioxin Furan 2,3,7,8-tetrachlorodibenzodioxin (TCDD) Rainbow trout 2,3,7,8-tetrachlorodibenzofuran (TCDF)

INTRODUCTION

Polychlorinated dibenzofurans (PCDFs) and polychlorinated dibenzo-*p*-dioxins (PCDDs) are two groups of toxic compounds composed of 135 and 75 individual isomers, respectively. Certain of these isomers are extremely toxic, particularly those with chlorine substituents in the 2,3,7,8-positions of the aromatic rings. PCDFs occur as trace contaminants in polychlorinated biphenyls (PCBs) and are sometimes formed in significant quantities from pyrolysis or incomplete combustion of PCBs [1]. Isomer specific PCDFs and PCDDs also occur as contaminants in the manufacture and pyrolysis of certain chlorinated phenols [2]. During combustion of these formulations, PCDDs are formed primarily from thermal dimerization and conversion of chlorinated phenoxyphenols, whereas PCDFs are formed from chlorinated diphenyl ethers. PCDDs and PCDFs have also been found in fly ash of municipal waste incinerators [3].

The isomers 2,3,7,8-tetrachlorodibenzodioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF) have been reported as contaminants in fish and sediment. Both have been detected in fish from the Great Lakes [4–6], and residues have been found in resident and migratory fish, crustaceans and sediment in the Chesapeake Bay area [7] and in industrialized and heavily populated areas of the northeastern United States [8]. The concentrations of these compounds in fish vary widely from low pg/g to ng/g quantities, and those of

*To whom correspondence may be addressed.

TCDF are usually higher than those of TCDD. In certain areas of the Great Lakes and the northeastern United States (Newark Bay, Passaic River), TCDD residues in fish and crustaceans exceed the U.S. Food and Drug Administration (FDA) "levels of concern" of 25 pg/g and 50 pg/g, respectively [8,9].

The chronic toxicity and bioconcentration of TCDD and TCDF in aquatic species have not been elucidated. Helder [10,11] reported that exposing fertilized eggs of rainbow trout (*Salmo gairdneri*) for 96 h to TCDD concentrations of 0.1 ng/L significantly decreased the growth of the resulting fry, and that exposing rainbow trout fry for 96 h to 10 and 100 ng/L TCDD retarded growth, caused histological changes in tissues and delayed mortality. Miller et al. [12] reported the toxicity and pathologic changes induced by short-term exposures of guppies (*Poecilia reticulata*) and coho salmon (*Oncorhyncus kisutch*) to TCDD. Coho salmon exposed to 56 pg/L and 1,000 ng/L for 24 h exhibited delayed mortality. Cooper et al. [13] observed delayed development and decreased survival in Japanese medaka (*Oryzias latipes*) exposed to TCDD concentrations of 6 to 500 ng/L. The oral toxicity and metabolism of TCDD in rainbow trout and yellow perch (*Perca flavescens*) were recently reported by Kleeman et al. [14,15]. In rainbow trout exposed for 6 h to 107 ng/L TCDD, followed by a 139-d depuration period, Branson et al. [16] estimated the bioconcentration factor (BCF) to be 9,270 and the elimination half-life to be 58 d. Significant delayed effects were similar to those reported by Miller et al. [12]. No similar studies have been conducted to characterize the toxicity and bioconcentration of TCDF in aquatic species.

Because of the lack of chronic toxicity data involving continuous low-level exposures of fish to TCDD and TCDF, we attempted to measure the chronic toxicity of these two compounds to rainbow trout. Their effects on survival, growth, and behavior were evaluated during a 28-d continuous exposure followed by a 28-d depuration phase. Uptake and depuration kinetics and BCFs for TCDD and TCDF were also evaluated.

METHODS

Test organisms

Eyed eggs of rainbow trout obtained from the Erwin (Tennessee) National Fish Hatchery came from two-year-old spawners of the "Fish Lake" strain; they were transferred to the National Fisheries Contaminant Research Center (NFCRC), Columbia, Missouri, where they hatched on 11 April 1985. About 2,000 swim-up fry produced from the eggs were shipped by air to Battelle Laboratories, Columbus, Ohio, on 2 May 1985. Mortality associated with shipping was less than 5%.

The fish were maintained in reconstituted water in 1,200-liter fiberglass tanks until the study was begun. The fish were held at a temperature of 11°C (±1°C), and were fed Tetramin floating flake food ad libitum. Analysis of the food showed no detectable quantities of TCDD (detection limit, less than 0.06 ng/g), TCDF (detection limit, less than 0.04 ng/g) or other organochlorine compounds.

Experimental approach

A flow-through diluter was used to continuously expose rainbow trout for 28 d to five duplicated concentrations each of [^{3}H]TCDD and TCDF plus duplicated controls. After the exposure period, toxicant input to the exposure chambers was terminated and the fish were held in laboratory water under flow-through conditions in the same test chambers during the 28-d depuration period. The fish were fed Tetramin floating flake food ad libitum throughout the study.

Fifty fish (0.38 ± 0.09 g each) were stocked in each aquarium. Samples of fish for residue analyses were taken on days 7, 14, 21, and 28 of the exposure phase and on day 28 of the depuration phase. To determine initial background concentrations of TCDD and TCDF, 30 fry with no previous TCDD and TCDF exposure history were weighed, measured, frozen, and analyzed for TCDD and TCDF. Fish collected for residue analyses were frozen until the time of analysis.

Daily survival records were maintained throughout the study. In addition, we recorded daily observations of swimming behavior, feeding behavior, location and position in the exposure tank, external lesions, and deformities.

Diluter and toxicant exposure system

The diluter system used in the study was constructed at NFCRC and installed in the West Jefferson Environmental Research Laboratory, Battelle Laboratories, Columbus, Ohio. The system consisted of two separate proportional flow-through diluters in a temperature-controlled waterbath. Both the diluter and waterbath were enclosed in a vented Plexiglas structure to reduce environmental exposures resulting from volatilization of the compounds. Each diluter delivered five concentrations (50% dilutions) of each compound (plus water for controls) into duplicate tanks containing

15 liters of water. Over the course of the study the diluter cycle rate varied between 2.4 and 3.0 cycles per hour; the replacement volume was 500 ml per replicate tank per cycle. The approximate water turnover rate in the exposure tanks was 2.4 times per day. The maximum fish loading in each test tank throughout the study was about 1.3 g/L and the maximum fish loading was 0.5 g/L of water passing through the tank in 24 h. Excess food and fecal matter were removed daily. Daily records of diluter operations were maintained throughout the studies. Nominal exposure concentrations (ng/L) were 0 (control), 0.115, 0.231, 0.463, 0.925, and 1.85 for TCDD; and 0 (control), 1.3, 2.7, 5.3, 10.6, and 21.3 for TCDF. Water temperature in the exposure tanks was maintained at 12 ± 1°C.

The combined effluents from the diluter system were recycled through two columns containing activated charcoal to remove TCDD and TCDF from solution. GC-MS and radiometric analyses were used to monitor the effluent for TCDD and TCDF.

Toxicants

Monsanto Company (St. Louis, MO) supplied the TCDD and TCDF used in the studies. The [^{3}H]TCDD (99+% pure; 22% unlabeled, 42% monotritiated and 36% ditritiated) used had a specific activity of 2.81×10^5 dpm/ng (0.128 μCi/ng) as determined by radiometric and GC-MS analyses. The TCDF provided by Monsanto was originally obtained from KOR, Inc. (Cambridge, MA), and was 98+% pure as determined by GC-MS.

Preparation of stock solutions

All glassware used to prepare stock solutions was rinsed several times with reagent-grade solvents. Carrier solvent for the compounds was acetone (Baker-analyzed). The [^{3}H]TCDD was diluted with acetone to a concentration of 36 ng/L. The stock solution was analyzed by GC-MS and by liquid scintillation radiometric analysis. Toxicants were delivered by an automatic pipetting system (Micromedic) that provided 0.05 ml/L or less of acetone to each exposure concentration. The TCDF was diluted with acetone to a measured concentration of 407 ng/L. This stock solution was used throughout the study and was delivered to exposure tanks by Micromedic pipetting systems. The acetone concentration delivered to each tank was 0.05 ml/L or less.

Water chemistry

In an effort to reduce the number of instruments coming in contact with the toxicants, we performed routine water chemistry only on the control chambers of both compounds, and only once during the exposure phase and once during the depuration phase. Alkalinity was measured by potentiometric titration with 0.02 N H_2SO_4 to pH 4.5, and hardness was titrated with EDTA according to standard methods [17]. We used an Orion

Table 1. Concentration of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in exposure water as measured by radiometric and GC-MS analyses

Day	Measurement	TCDD nominal concentration (pg/L)					
		0	115	231	463	925	1,850
1	pg/L (^{3}H)[a]	1.2	31	62	130	280	527
	pg/L (GC-MS)	—[b]					—[b]
7	pg/L (^{3}H)[a]	1.4	41	78	169	359	705
	pg/L (GC-MS)	<25[c]					840
14	pg/L (^{3}H)[a]	1.1	34	69	146	298	606
	pg/L (GC-MS)	<15[c]					730
21	dpg/L (^{3}H)[a]	0.7	41	87	200	466	970
	pg/L (GC-MS)	<15[c]					1,220
28	pg/L (^{3}H)[a]	1.3	44	99	234	507	1,135
	pg/L (GC-MS)	<20[c]					1,400
$\bar{x}$ pg/L (^{3}H) ± SD		1.1	38 ± 5	79 ± 15	176 ± 42	382 ± 101	789 ± 256
$\bar{x}$ pg/L (GC-MS) ± SD		<15[c]					1,048 ± 315

[a]Measured by radiometric analyses for [^{3}H]TCDD. Conversion of dpm/L to pg/L (^{3}H) based on specific activity of 2.81×10^5 dpm ^{3}H/ng TCDD.

[b]Not determined.

[c]None detected (less than minimal detectable limits).

digital pH meter to measure pH, a Sybron/Barnstead Model pM-70CB conductivity bridge to measure conductivity and a Varian Model 3700 gas chromatograph to measure ammonia. Water chemistry determinations were as follows: hardness, 153 ppm; alkalinity, 88 ppm; pH, 7.7; conductivity, 215 μohms; un-ionized ammonia, 0.0013 mg/L; and dissolved oxygen, 65 to 85% saturation.

Analyses of exposure water

During the exposure phase of the study, samples for GC-MS analysis were extracted from the TCDD control and highest exposure concentrations and from all TCDF exposure concentrations on days 0, 7, 14, 21, and 28. On each day immediately following the date of sample collection for GC-MS, we took samples for radiometric TCDD analyses from all exposure chambers. Radiometric analyses of all water extracts were conducted at Battelle Laboratories. Water from replicate *A* was sampled on days 0, 7 and 21, and water from replicate *B* on days 1, 14, and 28. On day 7 of the depuration period, the TCDD control and highest concentrations were measured radiometrically, and the TCDF control and highest concentrations were sampled for GC-MS analysis. On day 7 of the depuration phase, only 92 pg/L TCDD was measured in water from the highest TCDD exposure chamber, and 0.56 ng/L TCDF in the highest TCDF exposure chamber. The TCDD and TCDF exposure concentrations measured throughout the exposures are shown in Tables 1 and 2.

Water samples of a volume necessary to provide an adequate amount of analyte were collected from the diluter tanks with solvent-washed glassware and transferred directly to a glass separatory funnel. The water sample was then spiked with the appropriate internal standard solution containing $[^{13}C_{12}]$2,3,7,8-TCDD and $[^{13}C_{12}]$2,3,7,8-TCDF at 4.0 pg/μl in acetonitrile. The water sample was extracted three times with 50-ml portions of methylene chloride (CH_2Cl_2) and the extracts were passed through a column (about 2 × 6 cm) of anhydrous, granular sodium sulfate to break emulsions and remove suspended water. The extract was then rotary-evaporated to a low volume and transferred with three or four portions of CH_2Cl_2 to a glass ampoule, blown to dryness with nitrogen and flame-sealed.

The sample was removed from the opened ampoule with four 1.5-ml portions of 20% CH_2Cl_2 in hexane onto a dual column arrangement of 2 × 0.5 cm 40% H_2SO_4 on silica gel (SA-SG) in the first column and 15 mg Amoco PX-21 activated carbon dispersed in 150-mg glass fibers (CGF) [18]. The efficiency of transfer of $[^3H]$TCDD from these ampoules in the presence of solid residues was determined to exceed 99%. The SA-SG column was then discarded and the CGF column slightly pressurized to move the sample entirely onto the carbon adsorbent. We applied 15 ml CH_2Cl_2 to the CGF column at about 2 ml/min under pressure, and discarded the eluate.

The analyte, either $[^3H]$TCDD or TCDF, was recovered from the CGF by back-flushing with 15 ml toluene. The toluene was removed by rotary evaporation in a waterbath at 65 to 70°C under a 9.8-cm vacuum (sample taken just to dryness).

At this point, we added 2-(4-biphenyl)-6-phenylbenzoxazole (PBBO) to perform radiometric analyses on each sample or aliquots thereof containing $[^3H]$TCDD. The quench curve for counting efficiency was determined by the sealed tritium standard (HAV3612), corrected for decay, as the reference point, and replicate analyses of samples of $[^3H]$TCDD at various quench values. We used the equation, $\text{dpm} = \text{cpm}/0.85 \times S$, where dpm is disintegrations per minute, cpm is counts per minute and S is the quench value.

Table 2. Concentration (ng/L) of 2,3,7,8-tetrachlorodibenzofuran (TCDF) as measured by GC-MS in exposure water during a 28-d chronic toxicity study with rainbow trout

	TCDF nominal concentration (ng/L)					
Day	0	1.3	2.7	5.3	10.6	21.3
1	0.02	0.38	0.70	1.40	3.20	6.60
7	<0.06	0.33	0.91	1.98	3.84	9.04
14	<0.029	0.44	0.86	1.56	3.82	7.97
21	<0.025	0.37	0.93	1.93	4.19	10.4
28	0.017	0.52	1.10	2.10	4.60	9.9
$\bar{x} \pm$ SD	<0.02	0.41 ± 0.07	0.90 ± 0.14	1.79 ± 0.30	3.93 ± 0.52	8.78 ± 1.53

We applied the sample to alumina (Bio-Rad AG4 acid alumina, 3.5 ml = 3.65 g activated at 190°C) packed in a 5-ml graduated pipet with solvent reservoir using multiple washings of hexane totaling 5.0 ml. The column was then washed with 10 ml 5% CH_2Cl_2 in hexane (discarded) and the analyte recovered with 10 ml 20% CH_2Cl_2/hexane. The sample was evaporated just to dryness by rotary evaporation and transferred with three 1-ml portions of CH_2Cl_2 to a conical vial. The solvent was gently removed under a stream of nitrogen. The sample was then dissolved in a minimum of 5 μl *o*-xylene in preparation for GC-MS analysis.

We carried out the GC-MS analysis on a Finnigan 4023 quadrupole mass spectrometer (EI mode at 35 eV), using a 30 m × 0.25 mm DB-5 (0.25 μm) column (J&W Scientific, Inc., Rancho Cordova, CA) and helium carrier gas at about 35 cm/s. The temperature program was 120°C, hold 1 min, increase 20°C/min to 210°C, 5°C/min to 270°C and 4.5°C/min to 300°C. Selected ions monitored were m/z 304, 306, and 308 summed for 2,3,7,8-TCDF; m/z 316, 318 and 320 summed for [$^{13}C_{12}$]2,3,7,8-TCDF; m/z 320, 322, 324 and 326 summed for [^{3}H]2,3,7,8-TCDD; and m/z 332, 334, and 336 summed for [$^{13}C_{12}$]2,3,7,8-TCDD. We calibrated the internal standard solutions by preparing calibration mixtures of these standards with quantitative standards of native 2,3,7,8-TCDD and 2,3,7,8-TCDF prepared at the NFCRC and 2,3,7,8-TCDD solution as a U.S. Environmental Protection Agency (EPA) quality assurance material (Ref. No. 20603; EPA, Las Vegas, NV). We assumed equal integrated GC-MS responses for the molecular ions of native and [^{3}H]2,3,7,8-TCDD. The level of tritiation of the [^{3}H]2,3,7,8-TCDD computed from the molecular ion abundances measured by GC-MS gave a mole fraction of tritium of 27.3% and a specific activity of 2.15×10^5 dpm/ng. We calculated the specific activity, using the GC-MS–determined concentration and measured activity, to be $2.81 \pm 0.07 \times 10^5$ dpm/ng (triplicate analyses).

Collection of fish for residue analyses

Fish for whole-body TCDD and TCDF residue analyses were collected during the exposure period on days 0 (prior to exposure), 7, 14, 21, and 28, and on day 56 (after 28 d of depuration). When we removed fish from the exposure tanks for residue analyses on day 7, we removed unequal numbers from different tanks to reduce the number of fish remaining in all tanks to 42, and thus reduce the biomass and avoid potential overloading in the exposure tanks.

Fish for residue analyses were collected randomly from the exposure tanks for each toxicant. Individual weights and lengths were measured for fish collected on day 7 of the exposure and on day 28 of the depuration phase. Fish collected on other sampling days were weighed but not measured for length. All fish were blotted dry before they were weighed and were then wrapped in hexane-rinsed aluminum foil, placed in labeled screw-topped glass vials and stored at −10°C until residue analyses were begun.

GC-MS determinations of TCDD and TCDF in fish

Analyses of fish samples were performed by the method of Smith et al. [19]. The GC-MS conditions and spiking procedures were as described above for the analysis of the water samples.

Sample extracts that required radiometric analysis for [^{3}H]TCDD were rotary-evaporated and brought to 10.0-ml volumes; an appropriate aliquot (usually 1.00 ml) was then taken for scintillation counting. The quench values for the aliquots of the fish extracts were uniformly near the minimum (*S* values of 0.65), as observed for analytical standards. Negative and positive control samples were routinely included in the radiometric determinations of [^{3}H]TCDD and established so that there was no procedural background contribution in these determinations.

The internal standard procedure for GC-MS determinations of both [^{3}H]TCDD and TCDF provided internal quality control for overall accuracy of quantitation. In all reported determinations of these analytes, the criteria attained were relative GC retention time (±1 scan number in 1,160 or ±0.001 relative retention units) and correct ion abundances of the three or four molecular ion cluster members (±10% of theoretical value). The limit of quantitation was five times the signal-to-noise ratio and the limit of detection was three times the signal-to-noise ratio. The molecular ion cluster for [^{3}H]TCDD was significantly distorted from that produced by the native populations of ^{35}Cl and ^{37}Cl. Relative ion abundances of m/z 320, 324, and 326 were 24, 75, 100 and 70%, respectively. This pattern remained constant throughout the study, indicating no significant exchange of hydrogen for tritium in TCDD during the exposure. This observation also demonstrated no significant background of native 2,3,7,8-TCDD in any of the samples, because the presence of native dioxin would have had an easily discernible effect on this pattern. Procedural background controls showed no 2,3,7,8-TCDD (limit of quantitation, less than 0.006 ng/g) by radiometric analysis and no TCDF (limit of quantitation, less than 0.06 ng/g) by GC-MS. The limit of quantitation for [^{3}H]TCDD was also less than 0.06 ng/g by GC-MS.

Analyses of fish food were carried out by the same procedure used for fish samples, and analyses of [^{3}H]TCDD and TCDF stock solutions were performed by direct dilution before analysis.

We computed percent recoveries of [^{13}C]TCDD and [^{13}C]TCDF internal standards by the less precise external standard technique, using the responses of the [^{13}C]TCDD and [^{13}C]TCDF internal standards; the recoveries of [^{13}C]TCDF and [^{13}C]TCDD, respectively, are listed here according to the various matrices: stock solutions, 71 ± 30% and 71 ± 33%; exposure water, 134 ± 55% and 109 ± 52%; fish, 101 ± 37% and 117 ± 46%; all matrices combined, 112 ± 51% and 105 ± 47%.

Determination of total concentration of [^{3}H]TCDD species in fish by biological material oxidation procedure

Determinations of total body burden of [^{3}H]TCDD residues in fish, as opposed to extractable residue, were made on homogenate aliquots of individual fish by the method of total burn, followed by liquid scintillation radiometric analysis of the combustion products. A Harvey Biological Materials Oxidizer (Model OX-100, R. J. Harvey Instrument Corp., Hillsdale, NJ) and a Harvey tritium cocktail (lot No. DC02) were used in the procedure. The combustion/trapping efficiency was 84% with triplicate analyses of a [^{14}C]PCB standard. Cryogenic traps and dry ice and methanol were used to trap the tritiated water produced in the combustion. The combustion/trapping efficiency observed for a standard of [^{3}H]TCDD was 89 ± 3% for spiked fish tissue. The scintillation counting efficiency when the tritium cocktail was used was 37%, and radioactivity was calculated from scintillation analysis using the equation, dpm = cpm/0.64 × S, after subtraction of 50 cpm background.

Samples that had previously been weighed, wrapped in filter paper and aluminum foil and stored in the freezer were transferred along with the approximately 1-cm^{2} pieces of filter paper to the quartz combustion boats. Before combustion of samples, we ran a series of blanks and spikes to ensure that performance was satisfactory. Each sample was combusted twice into the cryogenic trap, which contained about 0.5 ml residual methanol. The glass elbow connecting the trap and oxidation chamber was heated with a hot air gun during the procedure to prevent loss by condensation. The condensed residue was transferred from the trap to a scintillation vial with three 5-ml portions of the cocktail. We then washed the trap thoroughly three times with methanol, leaving about 0.5 ml to aid in the next trapping. Because previous tests had indicated that carryover between sample combustions was a potential problem, blank combustions were performed after each sample and control. Scintillation analysis of the blanks showed that carryover was negligible.

Observation of fish for behavioral responses

The behavioral responses of rainbow trout were assessed daily during the TCDD and TCDF exposures. A checklist of behavioral reactions modified from Drummond et al. [20] was used to systematically document and characterize abnormal responses. The responses included coloration, activity (hyperactive, lethargic), excitability by external stimuli (hyperactive, unresponsive), location in aquaria, mode of swimming (head-up, frequent sinking and rising, swimming on side, swimming on back, free swimming), feeding, and morphological observations (bent spine, fin erosion). Observations were made each day by the same observer at the time of feeding.

An aberrant behavioral reaction was recorded when at least one fish in a given treatment responded in a manner that obviously differed from that of controls. Although no attempt was made to quantify the number of fish responding abnormally, an overall measure of the onset, duration and sequence of behavioral changes was made from the systematic daily observations.

Statistical analyses

Daily mortality was analyzed by one-way analysis of variance on the arc-sin transformed values. Differences among means were determined using Fisher's least significant difference (LSD) procedure [21].

Growth as measured by weight or length was analyzed by analysis of variance, including the effects of treatment, replicate within treatment, day, treatment × day, and replicate (treatment × day). Since the replicates, not the individual fish, were the experimental unit, replicate within treatments was used as the error term for testing the effect of treatment, and replicate (treatment × day) was used as the error term for testing the effects of day and treatment × day. We deter-

mined differences among means by calculating a t statistic, using the standard error of the difference for a split-plot design. For growth of TCDD-exposed fish during the depuration phase, we tested the control and lowest exposure concentration groups for equal population means, using a two-sample t test adjusted for unequal variance where appropriate [21].

The cumulative number of days on which fish showed abnormal behavior, from the time of induction to the day of depuration, was analyzed by simple regression against concentration, to provide an estimate of the behavioral responses to chemical exposure.

The BIOFAC computer program [22] was used to estimate the bioconcentration kinetics for TCDD and TCDF. Data from only the exposure phase in each study were used to estimate the kinetics because the number of fish residue samples available during the depuration phase was not adequate. In addition, the fish were held in their original exposure test tanks during the depuration phase, which resulted in the presence of the toxicants in the water because they desorbed from the glass aquaria. Because water concentration measurements and sufficient fish to sample during the depuration phase were not available, we were unable to use data from the depuration phase to estimate rate constants for the toxicants.

To estimate the 56-d LC50 value for TCDD, we computed a multiple-regression model to determine the relationship between percent mortality (arc-sin transformation) to concentration and time of exposure. The linear statistical model contained the effects of linear concentration (CL), days of exposure linear (DL), concentration quadratic (CQ), and day of exposure quadratic (DQ): CL * DL, CL * DQ, CQ * DL and CQ * DQ [21]. We used a quadratic function relationship to estimate the concentration of TCDD at a constant mortality (50%) and period of exposure (56 d).

RESULTS AND DISCUSSION

Mortality

TCDD induced significant mortality in rainbow trout within 14 d of exposure in the highest exposure concentration (789 pg/L), and there was a trend toward increased mortality in fish exposed to 176 and 382 pg/L (Table 3). After 28 d of exposure, significant mortality was evident in the three highest exposure concentrations; the no observed effect concentration (NOEC) was 79 pg/L. Although no mortality was observed, fish in the 38 and 79 pg/L exposure groups were obviously stressed, as judged by reduced growth and behavioral responses. Only rainbow trout in the control group and the three lowest exposure concentrations were observed during the 28-d depuration phase of the study; fish in the two highest exposure concentrations were excluded because the survivors were few and obviously stressed. Significant mortality continued to occur throughout the depuration period in fish previously exposed to 38, 79, and 176 pg/L. There was no apparent recovery in the fish during the 28-d depuration period in clean

Table 3. Cumulative mortality (%) in rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzodioxin (TCDD) for 28 d followed by a 28-d depuration period

	Mean TCDD exposure concentration (pg/L)						
Phase and day	0	38	79	176	382	789	F value
Exposure							
7	5	0	1	4	6	10	1.79
14	5	1	1	13	17	33[a]	5.48[b]
21	5	3	9	36[a]	46[a]	74[a]	28.02[b]
28	5	6	18	50[a]	73[a]	85[a]	27.51[b]
Depuration							
7	5	12	64[a]	85[a]	—[c]	—[c]	9.33[b]
14	5	22	78[a]	95[a]	—	—	30.49[b]
21	7	33	83[a]	95[a]	—	—	28.63[b]
28	7	45[a]	83[a]	95	—	—	27.72[b]

[a]Significantly different from controls by least-significant-difference multiple means comparison test ($p < 0.05$).

[b]Significant treatment effect (one-way analysis of variance; $p < 0.05$).

[c]Exposure groups not part of depuration phase.

water. The NOEC of TCDD, based on mortality throughout the exposure and depuration phases, was less than the lowest exposure concentration of 38 pg/L (parts per quadrillion).

Further insight into the NOEC was inferred from the background concentration of 1.1 pg/L of TCDD detected by radiometric analyses in the control group throughout the study. This low background was probably due to volatilization of TCDD and translocation within the diluter system. Mortality in the control group was 5% during the exposure phase and most of the depuration phase. We suggest from these observations that the NOEC was between 1.1 and 38 pg/L. However, the minimal detectable limits for TCDD in water by GC-MS were not adequate to confirm the 1.1 pg/L detected by radiometric analyses.

A 56-d LC50 of 46 pg/L was calculated from the combined mortality data for the exposure and depuration phases. The surface response curve describing the relation among daily mortality, time and exposure concentrations is shown in Figure 1. The quadratic equation describing this relation was used to derive the 56-d LC50.

Significant mortality was induced by TCDF in rainbow trout within 14 d at exposure concentrations of 3.93 and 8.78 ng/L (Table 4). No additional significant mortality occurred throughout the 28-d exposure phase. During the depuration phase, additional mortality occurred only in fish exposed to 8.78 ng/L. The NOEC throughout the exposure and depuration phases was 1.79 ng/L.

Growth

Growth as measured by the weight of the fish was significantly decreased by all TCDD concentrations after 28 d of exposure (Table 5). There were trends of decreased growth within 14 d of exposure, but significant effects in all concentrations were not observed until 28 d of exposure. During the 28-d depuration phase, growth was measured in fish from only the control and the lowest exposure concentration because of the excessive mortality in the higher TCDD exposure concentrations. There was a significant decrease in growth in the fish exposed to 38 pg/L after the 28-d depuration phase. Fish exposed to 38 pg/L TCDD did not grow during the depuration phase, whereas the weight of fish in the control group exhibited an 80% increase. The NOEC of TCDD on growth during the exposure and depuration phases was less than the lowest exposure concentration of 38 pg/L.

TCDF exposure concentrations of 1.79, 3.93 and 8.78 ng/L significantly decreased the growth of rainbow trout within 28 d of exposure (Table 6). There were trends toward decreased growth

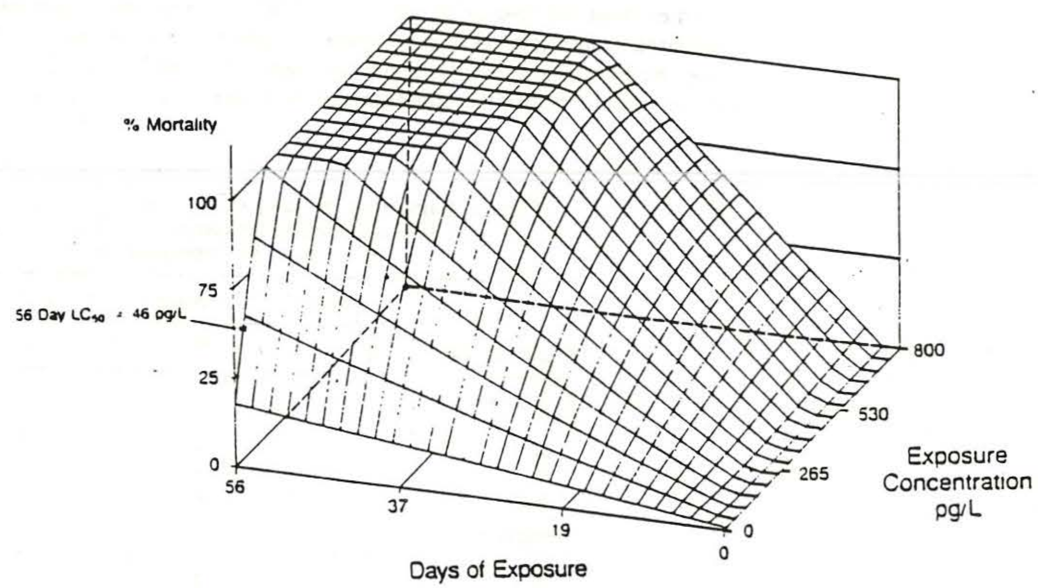


Fig. 1. Surface response describing the relation among daily mortality, time of exposure during the 28-d exposure and 28-d depuration phases, and TCDD exposure concentrations. The quadratic relation was used to derive a 56-d LC50 value of 46 pg/L TCDD for rainbow trout.

Table 4. Cumulative mortality (%) in rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d followed by a 28-d depuration period

Phase and day	Mean TCDF exposure concentration (ng/L) 0	0.41	0.90	1.79	3.93	8.78	F value
Exposure							
7	0	1	1	2	2	12	2.54
14	0	1	3	3	16[a]	22[a]	4.51[b]
21	0	2	5	3	18[a]	23[a]	3.73[b]
28	0	2	6	3	18[a]	28[a]	4.49[b]
Depuration							
7	0	2	6	3	20[a]	37[a]	6.53[b]
14	0	2	6	3	22[a]	46[a]	8.56[b]
21	0	2	6	3	22[a]	46[a]	8.56[b]
28	0	2	6	3	22[a]	46[a]	8.56[b]

[a]Significantly different from controls by least-significant-difference multiple means comparison test ($p < 0.05$).
[b]Significant treatment effect (one-way analysis of variance; $p < 0.05$).

Table 5. Weight (g) of rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzodioxin (TCDD) for 28 d followed by a 28-d depuration period

Phase and day	Mean TCDD exposure concentration (pg/L) 0	38	79	176	382	789
Exposure[a]						
7	0.37	0.36	0.38	0.33	0.36	0.33
14	0.41	0.39	0.42	0.33	0.35	0.40
21	0.48	0.35[b]	0.40	0.39	0.39	0.44
28	0.61	0.53[b]	0.47[b]	0.49[b]	0.45[b]	0.42[b]
Depuration[c]						
28	1.1	0.54[b]	—[d]	—[d]	—[d]	—[d]

Weights are expressed as the mean of 7 to 22 observations.
[a]Analysis of variance used for testing the effects of exposure concentration and time; $F = 2.43$ (time × exposure), $p < 0.03$.
[b]Significantly different from control group (t test; $p < 0.05$).
[c]Fish weight in depuration phase analyzed by t test adjusted for unequal variances.
[d]No measurements made.

after 21 d of exposure but the decrease observed was significant only in the group exposed to 3.93 ng/L. Decreased growth was evident in fish exposed to 0.90 ng/L or more after the 28-d depuration phase. The NOEC for TCDF based on growth during the exposure and depuration phases was 0.41 ng/L. This was the most sensitive response to TCDF.

Behavioral responses

Exposure to TCDD and TCDF induced behavioral impairments that became progressively worse over time and with increasing concentration. The two highest concentrations of TCDD caused behavioral changes within two weeks of exposure that included lethargic swimming, feeding inhibition, and lack of response to external stimuli, for example, waving of hand above aquaria (Fig. 2). Similar changes were evident in all groups exposed to TCDD by the end of the 28-d exposure, whereas the behavior of the controls remained normal. Although significant mortality did not occur in the two lowest exposure concentrations during 28 d of exposure, the fish were seriously stressed, as evidenced by an abnormal head-up swimming posture and confinement to the bottom of the aquar-

Table 6. Weight (g) of rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d followed by a 28-d depuration period

	Mean TCDF exposure concentration (ng/L)					
Phase and day	0	0.41	0.90	1.79	3.93	8.78
Exposure[a]						
7	0.33	0.35	0.37	0.36	0.35	0.32
14	0.39	0.40	0.43	0.42	0.31	0.41
21	0.55	0.47	0.45	0.50	0.39[b]	0.44
28	0.59	0.59	0.53	0.48[b]	0.50[b]	0.46[b]
Depuration[c]						
28	1.1	0.91	0.85[b]	0.80[b]	0.79[b]	0.71[b]

Weights represent the mean of 8 to 24 observations.
[a]Analysis of variance used for testing the effects of exposure concentration and time; $F = 4.37$ (time × exposure), $p < 0.05$.
[b]Significantly different from controls (t test; $p < 0.05$).
[c]Analysis of variance used for testing the effect of exposure concentration; $F = 5.73$ (exposure), $p < 0.03$.

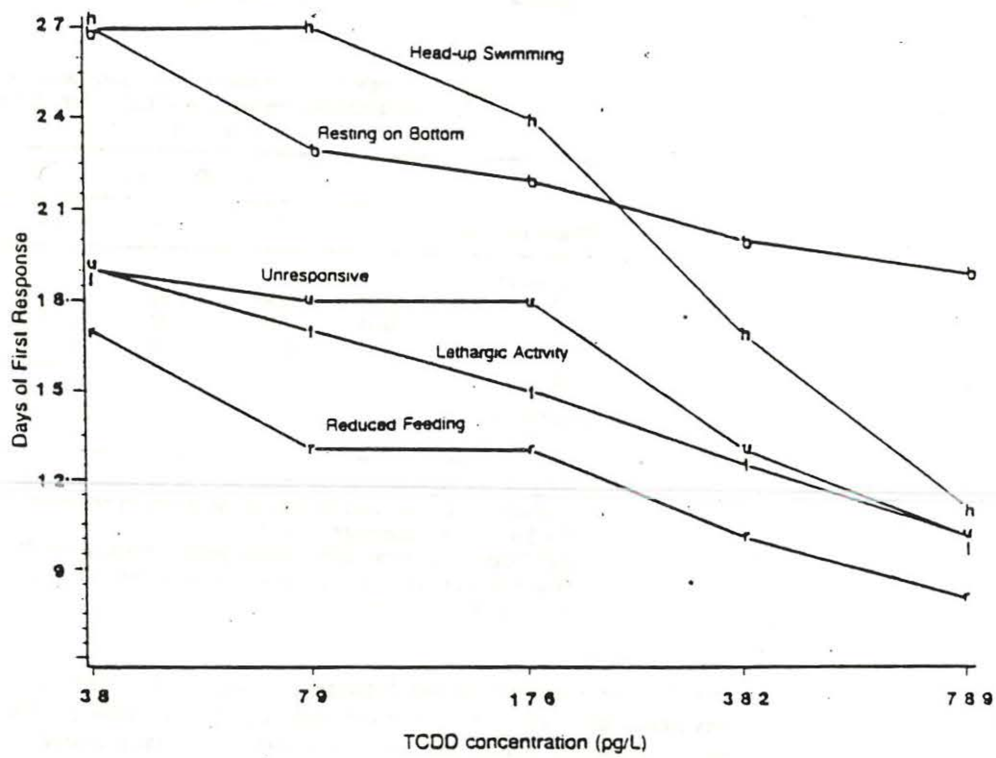


Fig. 2. Days of TCDD exposure required to induce behavioral changes in rainbow trout during a 28-d exposure.

ia. The feeding inhibition and other behavioral changes were not reversed during the 28-d depuration period.

Behavioral reactions similar to those observed in the TCDD exposure were observed in fish exposed to TCDF; however, the responses were of lesser magnitude (Fig. 3). Lethargy, unresponsiveness to external stimuli and diminished feeding

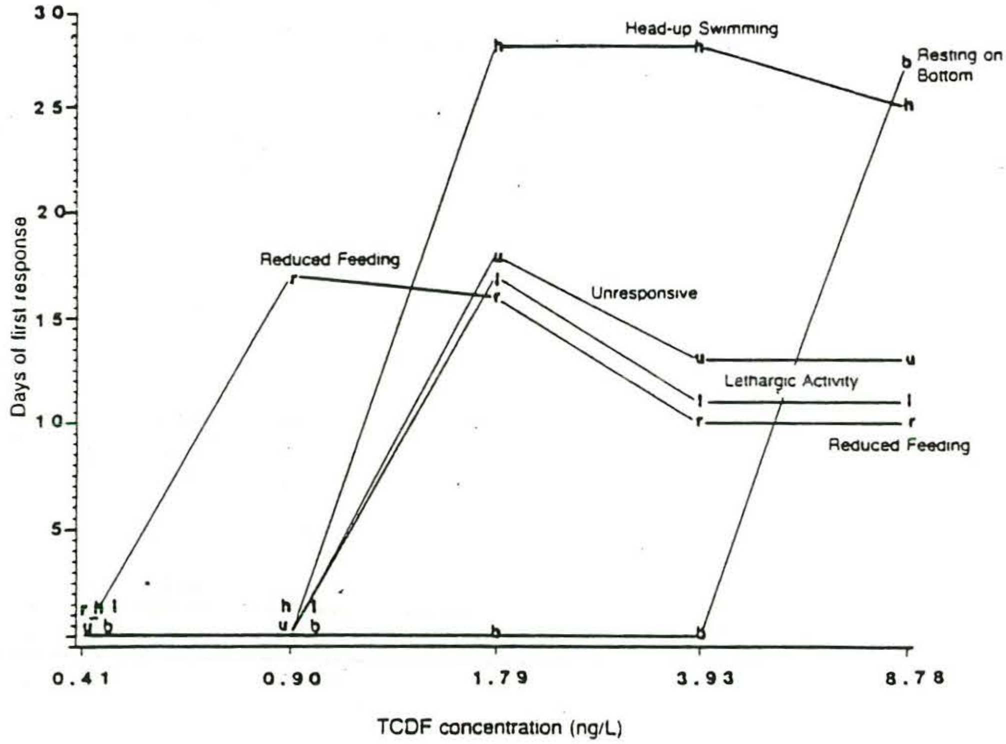


Fig. 3. Days of TCDF exposure required to induce behavioral changes in rainbow trout during a 28-d exposure.

reactions increased significantly in the three highest exposure groups. Recovery of behavioral function was evident in all but the two highest treatment groups by the end of the 28-d depuration period.

Neither TCDD nor TCDF induced observable responses in coloration or morphological characteristics such as scoliosis or lordosis; however, fin erosion was observed in fish in the lowest TCDD exposure concentration at the end of the depuration phase. In addition, exposure to both TCDD and TCDF induced observable, unique characteristics in fecal appearance. The two highest exposure concentrations of each toxicant induced long, stringy faces within the last several days of the 28-d exposure phase.

Bioconcentration

The BCFs for TCDD and TCDF differed greatly during the 28 d of continuous exposure. Whole-body residues throughout the exposure phase were in the low end of a 0.41 to 15.41 ng/g range for TCDD (Table 7). The greater the exposure concentration, the higher were the whole-body residues of TCDD during the 28-d exposures. The measured BCF for TCDD ranged from 8,558 to 28,664 during the exposure and did not appear to reach steady-state equilibrium in any of the exposure concentrations during the 28-d exposure (Table 8). The GC-MS analyses for whole-body TCDD levels agreed closely with the whole-body radiometric determinations for [^{3}H]TCDD. This similarity suggests that the ^{3}H label on the TCDD molecule was not being exchanged, and that the ^{3}H detected in the fish tissue was associated with the parent TCDD molecule. This similarity also indicates that organic extracted [^{3}H]TCDD was not being appreciably metabolized during the exposure and depuration phases. However, as judged by the results of total combustion of fish samples, it appears that about 30% of the ^{3}H label was associated with polar compounds that could have been TCDD metabolites.

Since it was apparent that a steady-state equilibrium for TCDD bioconcentration had not been reached after 28 d of exposure, we used the BIOFAC computer program [22] to estimate the bioconcentration kinetics for TCDD based only on data from the exposure phase. The estimated BCF at steady-state equilibrium was relatively consistent in fish from different exposure concentrations; the

Table 7. Whole-body residues of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout continuously exposed for 28 d followed by a 28-d depuration phase

	Mean TCDD exposure concentration (pg/L)				
Phase and day	0	38	176	382	789
Exposure					
0	[<0.02][a]				
7	0.012[a]	0.41[b] (0.05) [0.38]	1.68[b] (0.15)	3.44[b] (0.20)	6.75[b] (0.37) [6.78]
14	0.022[c]	0.77[b] (0.06) [0.71]	2.81[b] (0.18)	6.22[b] (0.67)	11.67[b] (0.68) [12.3]
21	0.023[d]	0.99[e] (0.03) [0.96]	3.87[b] (0.14)	10.10[e] (1.42) [11.3]	15.41[e] (0.86) [17.6]
28	0.027[a] [<0.02]	0.98[b] (0.05) [0.93]	4.52 (0.41)	10.95[b] (0.87) [10.8]	ND
Depuration					
28	0.22[a]	0.74[b] (0.11) [0.78]	ND	ND	ND

Values (ng/g) represent the mean (with standard deviation in parentheses) of individual fish analyzed radiometrically for [^{3}H]TCDD. Values in brackets represent GC-MS analyses performed on a pooled sample of fish, expressed as ng/g.
ND, not determined.
[a]One observation.
[b]Six observations.
[c]Two observations.
[d]Four observations.
[e]Eight observations.

Table 8. Measured bioconcentration factor (BCF)[a] for 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout exposed continuously for 28 d

	Measured TCDD exposure concentration (pg/L)			
Days of exposure	38	176	382	789
7	10,736	9,551	9,005	8,558
14	20,131	15,966	16,282	14,790
21	25,947	21,977	26,439	19,510
28	25,789	25,670	28,664	ND

[a]BCF = $(C_t/C_w) \times 1{,}000$. ND, not determined.

estimated BCF at 90% steady-state equilibrium ranged from about 37,000 to 86,000 (Table 9). Fish exposed to 382 pg/L showed somewhat different kinetics in that the estimated BCF, time to reach steady-state equilibrium and half-life were greater than in the other exposure concentrations. The relatively low K_2 value, compared with K_2 values from other exposure groups, suggested that metabolic effects may have been reducing the elimination of TCDD.

Ideally, the BCF should be estimated in fish not showing toxicity-induced responses. Inasmuch as the fish exposed to the lowest TCDD concentration of 38 pg/L showed the least toxic responses during the 28-d exposure, we suggest that the predicted BCF of 39,000 is probably the most relia

Table 9. Estimated bioconcentration kinetics[a] of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout exposed to TCDD for 28 d

	TCDD exposure concentrations (pg/L)			
Kinetic parameter	38	176	382	702[b]
K_1, uptake rate constant (d^{-1})	1,852 (132)[c]	1,543 (69)	1,337 (61)	1,591 (53)
K_2, depuration rate constant (d^{-1})	0.047 (0.01)	0.041 (0.005)	0.015 (0.005)	0.043 (0.005)
BCF-K_B	39,000 (9,400)	37,560 (5,032)	86,000 (25,000)	36,637 (4,290)
Time to reach 90% steady state (d)	49 (11)	56 (7)	149 (43)	53 (6)
Elimination half-life, $t_{1/2}$ (d)	15 (3)	17 (2)	48 (13)	16 (2)

[a]Estimated kinetics using BIOFAC [22].
[b]Mean of TCDD measurements at days 1, 7, 14 and 21.
[c]Values in parentheses represent standard deviations.

estimate. The range in BCF we observed was substantially greater than the BCF of 7,000 to 9,270 previously reported in the literature [16,23,24]. Results from our study were perhaps better estimates of the equilibrium BCF because we used a continuous exposure in flowing water for a longer period at lower exposure concentrations. Based on the water solubility of 7.9 ng/L for TCDD [25], the predicted BCF would be about 467,000 if the regression equation, log BCF = 2.791 − 0.564 log S [26], were used; it would be about 1,000,000 if the regression equation, log BCF = 3.41 − 0.508 log S [27], were used.

We suggest from our experimental data that the overall bioconcentration from water to fish is probably much less than the theoretical estimation. The obvious toxicity-induced effects of TCDD, as well as potential influences on membrane transport and other metabolic functions, could account for the observed BCF being less than the theoretical predictions.

The estimated elimination half-life ($t_{1/2}$) from the BIOFAC ranged from 15 to 17 d among exposure concentrations, except for the estimated half-life of 48 d in fish exposed to 382 pg/L. Adams et al. [24] reported an elimination half-life of 15 d, and Branson et al. [16] reported a half-life of 58 d. In the fish exposed to 38 pg/L for 28 d and then held during the 28-d depuration phase, the whole-body residues did not decrease sufficiently to support an estimated half-life in the range of 15 to 17 d (Table 7). The whole-body residues decreased from 0.93 (±0.05) to 0.74 (±0.11) ng/g during the 28-d depuration phase. Excessive mortality in the other TCDD exposure concentrations precluded our obtaining experimental data on elimination in fish exposed to higher concentrations.

The uptake and depuration of TCDF were measured in fish exposed to 0.41 and 3.93 ng/L. In contrast to TCDD kinetics, TCDF uptake reached an apparent steady-state equilibrium after only 7 d of exposure (Table 10). Whole-body residues of TCDF did not increase after 7 d of exposure in fish exposed to 0.41 and 3.93 ng/L. In fish exposed for 28 d, the measured BCF was 6,049 at 0.41 ng/L and 2,455 at 3.93 ng/L (Table 11). The estimated bioconcentration kinetics of TCDF are shown in Table 12. Rainbow trout apparently were able to readily eliminate or metabolize TCDF. The whole-body residues in fish held during the 28-d depuration phase suggested a very short elimination half-life for this compound. Although TCDD and TCDF are structurally very similar, their bioconcentration kinetics and toxicities were found to be very different.

Table 10. Whole-body residues of 2,3,7,8-tetrachlorodibenzofuran (TCDF) in rainbow trout continuously exposed for 28 d followed by a 28-d depuration phase

	Mean TCDF exposure concentration (ng/L)		
Phase and day	0	0.41	3.93
Exposure			
0	<0.06		
7	0.17	1.63 (0.89)	11.9 (2.88)
14	0.12	1.80 (0.62)	9.30 (2.26)
21	0.19	1.05 (0.44)	10.7 (2.24)
28	0.22	2.48 (1.32)	9.65 (1.30)
Depuration			
28	<0.06	0.09 (0.06)	0.54 (0.08)

Values represent the mean (with standard deviation in parentheses) of four observations performed on individual fish, expressed as ng/g wet weight.

Table 11. Measured bioconcentration factors (BCF)[a] for 2,3,7,8-tetrachlorodibenzofuran (TCDF) in rainbow trout exposed continuously for 28 d

Days of exposure	TCDF exposure concentration (ng/L) 0.41	3.93
7	3,976	3,028
14	4,390	2,366
21	2,561	2,730
28	6,049	2,455

[a] $BCF = (C_t/C_w) \times 1{,}000$.

CONCLUSIONS

We conclude that TCDD and TCDF – especially TCDD – are extremely toxic to rainbow trout. A relative comparison of TCDD and TCDF chronic toxicities with those of several other organochlorine compounds demonstrated that TCDD is more than 10,000 times as toxic to fish as either endrin or toxaphene, and that TCDF is about 1,000 times more toxic than either of these insecticides (Table 13). Results from previous toxicity studies with fish by Helder [10,11], Miller et al. [12] and Adams et al. [24] demonstrated the toxicity of TCDD to be in the low ng/L range. However, we have shown that our lowest TCDD exposure concentration of 38 pg/L induced significant adverse effects on survival, growth, and behavioral responses. Results from our studies are perhaps more adequate estimates of TCDD toxicity because we used continuous exposure techniques for a longer time than had been used in previous studies. For similar reasons, we believe the BCF for TCDD derived from our studies is a more accurate estimate of the bioconcentration potential than are the estimates reported by Branson et al. [16] and Adams et al. [24]. Although we showed that TCDD was ex-

Table 12. Estimated bioconcentration kinetics[a] for TCDF in rainbow trout exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d

Kinetic parameter	TCDF exposure concentration (ng/L) 0.41	3.93
K_1 uptake rate constant (d^{-1})	1,228 (1,191)	6,852 (8,037)
K_2 depuration rate constant (d^{-1})	0.28 (0.30)	2.60 (3.04)
BCF-K_B	4,449 (6,481)	2,640 (4,379)
Time to reach 90% steady state (d)	8 (9)	0.90 (1.04)
Elimination half-life, $t_{1/2}$ (d)	3 (3)	0.27 (3.1)

Values in parentheses represent standard deviations.
[a] Estimated kinetics using BIOFAC [22].

Table 13. Chronic no effect concentrations (μg/L) for growth and survival of freshwater fish exposed to various organochlorine chemicals

Chemical and fish species	Days of exposure	Survival	Growth[a]	Source
Aroclor 1254, brook trout	118	9.0	9.0	[28]
Chlorodecone, fathead minnows	120	>0.31	>0.31	[29]
Pentachlorophenol (ultrapure), fathead minnows	90	>139	>139	[30]
Toxaphene, brook trout	90	>0.50	0.38	[31]
Toxaphene, channel catfish	90	0.096	0.20	[32]
Endrin, bluntnose minnows	30	0.1	0.1	[33]
TCDD, rainbow trout	56	<0.000038	<0.000038	This study
TCDF, rainbow trout	56	0.00179	0.00041	This study

[a] Change in weight of fish.

tremely toxic to rainbow trout, even our lowest exposure concentration was too high to derive a NOEC.

Acknowledgement – We are grateful to the many people from the Fish and Wildlife Service (FWS), Battelle and Monsanto who assisted in conducting these studies. We especially thank Mr. Dave Zumwalt for his efforts in designing the specialized diluter exposure system, and Mr. Zumwalt and Mr. George Holroyd for their outstanding efforts in constructing and calibrating the system. We appreciate the excellent advice and assistance of Dr. Mark Ellersieck and Ms. Linda Sappington in analyzing the data, and the technical assistance of Mr. Rick Archeski in analyzing the behavioral data. We give special thanks to Dr. Paul Eschmeyer, Editorial Section, Office of Information Transfer, FWS, Fort Collins, Colorado, for his review of the manuscript and for editorial advice.

REFERENCES

1. **Olie, K., M.v.d. Berg** and **O. Hutzinger.** 1983. Formation and fate of PCDD and PCDF from combustion processes. *Chemosphere* 12:627–636.
2. **Firestone, D.** 1972. Determination of polychlorodibenzo-*p*-dioxins and related compounds in commercial chlorophenols. *J. A.O.A.C.* 55:85–92.
3. **Ballschmiter, K., W. Zoller, C. Scholz** and **A. Nottrodt.** 1983. Occurrence and absence of polychlorodibenzofurans and polychlorodibenzodioxins in fly ash from municipal incinerators. *Chemosphere* 12: 585–594.
4. **Petty, J.D., D.L. Stalling, L.M. Smith** and **J.L. Johnson.** 1983. Occurrence and potential impact of PCDF's and PCDD's in aquatic ecosystems. In D.D. Hemphill, ed., *Trace Substances in Environmental Health* – XVII. University of Missouri Press, Columbia, MO, pp. 96–102.
5. **Crummett, W.B.** 1982. Environmental chlorinated dioxins from combustion: The trace chemistries of fire hypothesis. In O. Hutzinger, R.W. Frei, E. Merian and F. Pocchiari, eds., *Chlorinated Dioxins and Related Compounds Impact on the Environment.* Pergamon Press, Elmsford, NY, p. 261.
6. **Ryan, J.J., P.-Y. Lan, J.C. Pilon** and **D. Lewis.** 1983. 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and 2,3,7,8-tetrachlorodibenzofuran residues in Great Lakes commercial and sport fish. In G. Choudhary, L.H. Keith and C. Rappe, eds., *Chlorinated Dioxins and Dibenzofurans in the Total Environment.* Butterworth, Boston, MA, pp. 87–97.
7. **Columbia National Fisheries Research Laboratory.** 1983. Impacts of contaminants on early life stages of striped bass. In P.M. Mehrle and J.L. Ludke, eds., *Progress Report.* U.S. Fish and Wildlife Service, Columbia, MO.
8. **Belton, T.J., R. Hazen, B.E. Ruppel, K. Lockwood, R. Mueller, E. Stevenson** and **J.J. Post.** 1985. A study of dioxin contamination in select finfish, crustaceans, and sediments of New Jersey Waterways. Office of Science and Research, New Jersey Department of Environmental Protection, Trenton, NJ.
9. **U.S. Food and Drug Administration.** 1981. Correspondence from FDA Commissioner Dr. Arthur Hall Hayes, Jr., to Governor Milliken of Michigan concerning the public health significance of TCDD contaminant "levels of concern" for finfish in Great Lakes. 26 August.
10. **Helder, T.** 1980. Effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on early life stages of the pike (*Esox lucius* L.). *Sci. Total Environ.* 14:255–264.
11. **Helder, T.** 1981. Effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on early life stages of rainbow trout (*Salmo gairdneri*, Richardson). *Toxicology* 19: 101–112.
12. **Miller, R.A., A.N. Logan** and **C.L. Hawkes.** 1979. Toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in aquatic organisms. *Environ. Health Perspect.* 5: 177–186.
13. **Cooper, K.R., J. Schell, P. Kahn** and **M. Gallo.** 1986. The effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on the development and survival of the Japanese medaka (*Oryzias latipes*). *Toxicologist* 6:27 (Abstract).
14. **Kleeman, J.M., J.R. Olson, S.M. Chen** and **R.E. Peterson.** 1986. Metabolism and disposition of 2,3,7,8-tetrachlorodibenzodioxin in rainbow trout. *Toxicol. Appl. Pharmacol.* 83:391–401.
15. **Kleeman, J.M., J.R. Olson, S.M. Chen** and **R.E. Peterson.** 1986. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin metabolism and disposition in yellow perch. *Toxicol. Appl. Pharmacol.* 83:402–411.
16. **Branson, D.R., I.T. Takahashi, W.M. Parker** and **G.E. Blau.** 1985. Bioconcentration kinetics of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in rainbow trout. *Environ. Toxicol. Chem.* 4:779–788.
17. **American Public Health Association, American Water Works Association** and **Water Pollution Control Federation.** 1980. *Standard Methods for the Examination of Water and Wastewater*, 15th ed. American Public Health Association, Washington, DC.
18. **Smith, L.M.** 1981. Carbon dispersed in glass fibers as an adsorbent for contaminant enrichment and fractionation. *Anal. Chem.* 53:2152–2154.
19. **Smith, L.M., D.L. Stalling** and **J.L. Johnson.** 1984. Determination of part-per-trillion levels of dibenzofurans and dioxins in environmental samples. *Anal. Chem.* 56:1830–1842.
20. **Drummond, R.A., C.L. Russom, D.L. Geiger** and **D.L. DeFoe.** 1986. Behavioral and morphological changes in fathead minnow, *Pimephales promelas*, as diagnostic endpoints for screening chemicals according to mode of action. In *Aquatic Toxicology and Hazard Assessment: Ninth Symposium.* American Society for Testing and Materials, Philadelphia, PA, pp. 415–435.
21. **Snedecor, G.W.** and **W.C. Cochran.** 1967. *Statistical Methods*, 6th ed. Iowa State University Press, Ames, IA.
22. **Blau, G.E., W.B. Neely** and **D.R. Branson.** 1975. Ecokinetics: A study of the fate and distribution of chemicals in laboratory ecosystems. *AIChE J.* 21: 854–861.

23. **Isensee, A.R.** 1978. Bioaccumulation of 2,3,7,8-tetrachlorodibenzo-para-dioxin. *Ecol. Bull.* **27**:255–262.
24. **Adams, W.J., G.M. DeGraeve, T.D. Sabourin, J.D. Cooney** and **G.M. Mosher.** 1986. Toxicity and bioconcentration of 2,3,7,8-TCDD to fathead minnows (*Pimephales promelas*). *Chemosphere* **15**:1503–1511.
25. **Adams, W.J.** and **K.M. Blaine.** 1986. A water solubility determination of 2,3,7,8-TCDD. *Chemosphere* **15**:1397–1400.
26. **Kenaga, E.E.** and **C.A.I. Goring.** 1980. Relationship between water solubility, soil sorption, octanol-water partitioning, and concentration of chemicals in biota. In J.G. Eaton, P.R. Parrish and A.C. Hendricks, eds., *Aquatic Toxicology.* STP 707. American Society for Testing and Materials, Philadelphia, PA, pp. 78–115.
27. **Chiou, C.T., V.H. Freed, D.H. Schmedding** and **R.L. Kohnert.** 1977. Partition coefficients and bioaccumulation of selected organic chemicals. *Environ. Sci. Technol.* **11**:475–478.
28. **Mauck, W.L., P.M. Mehrle** and **F.L. Mayer.** 1978. Effects of the polychlorinated biphenyl Aroclor 1254 on growth, survival, and bone development in brook trout (*Salvelinus fontinalis*). *J. Fish. Res. Board Can.* **35**:1084–1088.
29. **Buckler, D.R., A. Witt, Jr., F.L. Mayer** and **J.N. Huckins.** 1981. Acute and chronic effects of Kepone and mirex on the fathead minnow. *Trans. Am. Fish. Soc.* **110**:270–280.
30. **Cleveland, L., D.R. Buckler, F.L. Mayer** and **D.R. Branson.** 1982. Toxicity of three preparations of pentachlorophenol to fathead minnows: A comparative study. *Environ. Toxicol. Chem.* 1:205–212.
31. **Mayer, F.L., P.M. Mehrle** and **W.P. Dwyer.** 1975. Toxaphene effects on reproduction, growth, and mortality of brook trout. EPA-600/3-75-013. U.S. Environmental Protection Agency, Duluth, MN.
32. **Mayer, F.L., P.M. Mehrle** and **W.P. Dwyer.** 1977. Toxaphene: Chronic toxicity to fathead minnows and channel catfish, EPA-600/3-77-069. U.S. Environmental Protection Agency, Duluth, MN.
33. **Mount, D.I.** 1962. Chronic effects of endrin on bluntnose minnows and guppies. U.S. Fish and Wildlife Service Research Report No. 58, Washington, DC.

Attachment 9

ASSESSMENT OF THE HUMAN HEALTH RISKS RELATED TO THE PRESENCE OF DIOXINS IN COLUMBIA RIVER FISH

Prepared by:

Russell E. Keenan, Ph.D.
Alan H. Parsons, Ph.D.
Ellen S. Ebert
Pamela D. Boardman, M.P.H.
Steven L. Huntley
Mary M. Sauer, M.S.P.H.

ChemRisk™
A McLaren Company
1685 Congress Street
Stroudwater Crossing
Portland, ME 04102
(207) 774-0012
(207) 774-8263

January 8, 1990

ChemRisk
A McLaren Company

An exposure pathway consists of four necessary elements: a source and mechanism of chemical release into the environment, an environmental transport medium for the released chemical, a point of potential human contact with the environmental medium, and a human exposure route (eg., inhalation, dermal contact, ingestion) at the point contact. Each pathway describes a unique potential mechanism by which a population or an individual may be exposed to a chemical. For each exposure pathway, the environmental fate and persistence of the chemical from the point of discharge to the point of human contact is an important consideration. Many factors such as adsorption onto particulates, sedimentation, and solubility influence the degree of human exposure. These factors are highly variable in the environment. Consequently, a truly valid exposure assessment can only be conducted using site-specific data. To this purpose, a study of the levels of dioxin in the edible portions of Columbia River fish has been conducted. Additionally, the rates of consumption of locally caught fish were estimated.

Columbia River fish sampling

For the purpose of determining accurate species-specific concentrations of dioxin in edible fish fillets, a variety of species of fish were collected from six different sites along the Columbia River system by an independent laboratory and consultant. A total of 680 individual fish were sampled at the six sites. Species collected included top and bottom feeders as well as resident and anadromous populations. Migratory fish sampled included coho salmon, fall chinook salmon (upriver and tule) and summer steelhead trout. Resident species sampled included white sturgeon, largescale sucker, and carp. Results of sampling data are reported below[1].

Fillet TCDD Levels in Columbia River Fish (ppt)

Species	Sampling Site 1	2	3	4	5	6
Coho salmon	0.08	0.10	NS	NS	NS	NS
Fall chinook salmon (Upriver)	0.08	0.09	NS	NS	NS	NS
Fall chinook salmon (Tule)	0.31	0.18	NS	NS	NS	NS
Summer steelhead trout	0.07	0.07	NS	NS	NS	NS
White sturgeon	0.09	0.12	1.09	0.88	1.68	0.55
Largescale sucker	0.32	NS	0.39	0.19	0.22	0.26
Carp	0.79	NS	1.06	1.35	1.46	0.76

At Sites 1 and 2, located downstream of NWPPA pulp and paper mills, the geometric mean concentrations of TCDD in salmon ranged from 0.08 to 0.31 parts per trillion (ppt) and steelhead trout averaged 0.07 ppt. Sturgeon, sucker, and carp collected from sites 1, 2, 3, and 4 had fillet TCDD levels averaging

1 Note: 80% of the anadromous and 45% of all species sampled had nondetectable levels of TCDD. Nondetectable samples were assigned a value equal to one half the limit of detection per EPA protocol. This results in a more conservative estimation of tissue TCDD levels because actual values could equal zero.

DRAFT Attachment 10

ANALYSIS OF THE POTENTIAL POPULATIONS AT RISK FROM THE CONSUMPTION OF FRESHWATER FISH CAUGHT NEAR PAPER MILLS

Craig McCormack
Office of Policy Planning and Evaluation

David Cleverly 202-382-7891 (D.C)
Office of Research and Development

April 23, 1990

INTRODUCTION:

OTS, OSW, and OW have conducted a detailed human and ecological risk assessment of environmental loadings of dioxin from bleached pulp and paper mills. In that analysis only maximum lifetime cancer risk and average lifetime cancer risk to the hypothetically exposed individual was estimated for various exposure scenarios. No estimation of potential population risk, especially to sensitive subgroups, was provided in the analysis. Since draft publication of these results, we have identified populations of Asians, and tribal Native Americans that reside along the banks of the Columbia River in Oregon. The State government indicates that there are eight bleached pulp and paper mills that directly discharge to the Columbia River. The State also indicates that freshwater fish caught from the Columbia river are the main source of animal protein for these people. They consume an average of 100 to 150 grams of fish flesh each day over the course of the year. These individuals are much more likely to catch and consume fish that has been contaminated with dioxin from the effluent discharged from the mills than other populations in the area. The Native Americans number about 15,000, and the Asians number about 30,000 people.

In addition to these subpopulations exposed by diet to dioxin, we have estimated that approximately 610,000 people living in the vicinity of pulp and paper mills have family incomes at or below the poverty level. These individuals are also expected to derive a significant portion of animal protein from both subsistence and sports fishing in rivers near paper mills. Subsistence fishermen consume about 100 grams of fish per day/[1], and sports fishermen consume about 69 grams fish per day/[2].

For purposes of the assessment of potential cancer risk, we have employed monitoring data of dioxin contamination in fresh water fish caught in the vicinity of bleached pulp and paper mills. This was developed by the Environmental Research Laboratory in Duluth Minnesota as part of the National Bioaccumulation Study of freshwater fish in the U.S. The range of detected TCDD equivalent concentration in the edible fish fillet was from 0.1 ppt - 24 ppt. The weighted

average fillet concentration was 6.5 ppt (6.5 pg/gm). For purposes of estimating incremental lifetime cancer risk to the most exposed individual, a fillet concentration of 24 ppt was used. The weighted average dioxin concentration in the fillet of 6.5 ppt was used to derive the approximate average lifetime risk to subsistence and sports fishermen. The average exposure and average lifetime risk was used to estimate the annual cancer incidence in these sensitive subpopulations. In addition a human body weight of 70 kilograms was assumed to compute estimates of excess cancer risk.

CONCLUSIONS:

It is currently not possible to directly measure the association between the chronic dietary intake of dioxin contaminated freshwater fish, and the occurrence of specific forms of cancer in the exposed populations. The epidemiologic studies of these populations with a high dependency for subsistence fishing as a source of dietary animal protein have not been conducted. Therefore we have mathematically estimated lifetime excess cancer risk to the population residing near the Columbia River, as well as to low-income populations living in the vicinity of other mills in the U.S. This analysis is not intended to replace any previous risk assessments involving the human consumption of fish that has been contaminated with dioxin from the effluent discharged from paper mills, but is merely to illustrate that methodologies can be developed to estimate total populations at risk in the U.S.

The following are the results:

	Pop.	MIR(a)	AVG Risk(b)	Cancer Inc.(c)
Native Americans	15,000	8.6×10^{-3}	1.5×10^{-3}	0.33
Asian Americans	30,000	8.6×10^{-3}	1.5×10^{-3}	0.67
Total Risk	45,000	8.6×10^{-3}	1.5×10^{-3}	1.0
Low income families	**610,000**	**5.4×10^{-3}**	**1.0×10^{-3}**	**9.3**

(a) MIR is the maximum individual risk, and is associated with the highest fish consumption rate and the highest dioxin concentration in fish caught near paper mills.

(b) Average lifetime cancer risk is the excess cancer risk based on the average fish consumption rate for subsistence and sports fishermen, and the weighted average dioxin concentration in fish caught near paper mills.

(c)Cancer incidence is the estimated number of cancer cases per year within the

defined exposed population. This was computed using average lifetime risk.

1/ U.S. Environmental Protection Agency (1988). Risk Assessment for Dioxin Contamination Midland, Michigan. Region 5. EPA-905/4-88-005.

2/Estimated consumption by the U.S. Food and Drug Administration, assuming substitution of average U.S. population daily consumption of red meat with fish.

Calculations of Risk

1. Native Americans

Assumptions:

a. MEI consumes 150 gms fish/day.
b. Average consumption is 100 grms fish/day.
c. 70 kilogram person.
d. Lifetime exposure.
e. Max. dioxin concentration in fish fillet = 24 pg/gm.
f. Weighted average dioxin in fish fillet = 6.5 pg/gm.
g. Population of 15,000.
h. Risk Specific Dose of Dioxin = lifetime cancer risk of one in a million is: 0.006 pg/kg/day.

Max. Daily Dose= (150 gms/day X 24 pg/gm) / 70 kg person
= 51.43 pg dioxin/kg/day

MIR ={(51.43 pg/kg/day) / (0.006 pg/kg/day)} X 10^{-6}
MIR = 8.6 X 10^{-3}

Avg. Daily Dose= (100 gms/day X 6.5 pg/gm)/ 70 kg person
= 9.28 pg dioxin/kg/ day

Avg. lifetime risk = {(9.28 pg/day)/(0.006 pg/kg/day)} X 10-6
= 1.5 X 10^{-3}

Annual Cancer Incidence = (Avg risk * population)/ 70 year lifespan
= (1.5 X 10^{-3} * 15,000)/ 70 yrs
= 0.33

2. Asian Americans

Assumptions are the same as with Native Americans. The population size is

MEI = maximally exposed individual

30,000.

Max. Daily Dose = 51.43 pg dioxin/kg/day.
MIR = 8.6 X 10-3

Avg. Daily Dose = 9.28 pg dioxin/kg/day
Avg. lifetime risk = 1.5 X 10^{-3}

Annual Cancer Incidence = (1.5 X 10^{-3} * 30,000)/70 yr lifespan
= 0.67

3. Low income families.

Assumptions:

a. MEI consumes 100 gms fish/day.
b. Average consumption is 69grms fish/day.
c. 70 kilogram person.
d. Lifetime exposure.
e. Max. dioxin concentration in fish fillet = 24 pg/gm.
f. Weighted average dioxin in fish fillet = 6.5 pg/gm.
g. Population of 610,000.
h. Risk Specific Dose of Dioxin = lifetime cancer risk of one in a million is: 0.006 pg/kg/day.

Max Daily Dose = (100 gms/day) X (24 pg dioxin/gm)/ 70 kg person
= 34.28 pg dioxin/kg/day

MIR = {(34.28 pg/kg/dy)/(0.006 pg/kg/dy)} X 10^{-6}
= 5.7 X 10^{-3}

Avg. Daily Dose = (69 gms/day) X (6.5 pg/gm)/70 kg person
= 6.41 pg dioxin/kg/day

Avg. lifetime risk = { (6.41 pg/kg/dy)/(0.006 pg/kg/dy)} X 10-6
= 1.0 X 10^{-3}

Annual Cancer Incidence ={ (1.0 X 10^{-3}) * (610,000)}/ 70 year lifespan
=9.3

The Bottom Line:

• The "Forest through the trees" is that the environmental loadings of dioxin from the mills may result in high levels of risk to humans.

• The analysis of the regulatory options suggests that this particular industrial source category fits the mold for a regulatory pollution prevention initiative through use of the CWA, TSCA, and RCRA.

* could require substantial reduction in the overall use of chlorine
* BACT seems to be oxygen delignification

OREGON
INSIDER
A BIWEEKLY DIGEST OF ENVIRONMENTAL NEWS

Inside the Dioxin Standard: Is it Defensible?

■ The Environmental Quality Commission (EQC) will decide Nov. 2 whether to hold public hearings on a complex proposal to update the state's water quality standards. The proposal covers an enormous number of topics including a new "anti-degradation standard" to protect pristine waterways, a new "wetlands" definition, and new standards for dissolved oxygen, bacteria, toxic pollutants, particulate matter and bacteria (see Issue 20).

Tucked somewhere in the middle of the package, the Department of Environmental Quality (DEQ) has proposed to keep unchanged the current and seemingly incomprehensible water quality standard for dioxin: 0.013 parts per quadrillion (ppq). In addition, the agency has for the first time proposed a standard limiting the amount of dioxin that can accumulate in fish tissue. Both proposals are sure to draw the attention of the pulp and paper industry and environmentalists.

Industry representatives have long questioned the scientific underpinnings of the dioxin standard. They have even challenged the assertion that dioxin poses any threat to human health or the environment, comparing it to broccoli in one study. On the other hand, environmentalists see a standard that leaves completely unregulated hundreds of closely related toxic organo-chlorine compounds that are discharged from bleach kraft pulp mills every day. Based only on protecting human populations from cancer, they also see a standard that ignores documented impacts on fish and wildlife and fails to address non-cancerous affects on human health such as reproductive interference and immune system suppression.

Each side contends that the standard for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) — the only compound regulated by DEQ's dioxin standard — should be changed in some way. For now, DEQ has decided to keep the standard as it is.

The standard "answers" a very narrow question for DEQ and the public: How much 2,3,7,8-TCDD can exist in the water column without creating more than a 1-in-a-million cancer risk?

The standard does not regulate the amount of dioxin in river bottom sediments, where a seemingly significant percentage of these insoluble compounds settle. It does not take into account the natural loss, or "attenuation," of dioxin through breakdown and binding with particles suspended in the water column. And, since compliance with the standard is measured down river at the edge of the "mixing zone," it isn't even used to directly regulate the amount of dioxin coming out of pulp mill discharge pipes.

There are significant gaps in the scientific understanding of this toxin and in the regulatory mechanism by which it is controlled. While it is impossible to resolve the many questions surrounding dioxin, it is not particularly difficult to understand the guts of the standard and how the federal government came up with the result of 0.013 parts per quadrillion.

CONTENTS

An Understandable Formula

For all the rhetoric, battling experts, and discussions of "linearized multistage models," "LD_{50} values" and all the rest, the standard is surprisingly understandable. The Environmental Protection Agency developed the dioxin standard using a relatively simple formula that includes six factors:

$$\text{Dioxin Standard} = \frac{\text{RISK} \times \text{WT}}{[\text{WCR} + (\text{BCF} \times \text{FCR}) \times \text{CPF}]}$$

The Six Factors

RISK: The cancer risk society is willing to tolerate from dioxin.

WT: The weight of the average adult.

WCR: The amount of water ingested by the average person each day — called the water consumption rate.

BCF: The extent to which fish concentrate dioxin in their tissues by swimming in contaminated water — called the bio-concentration factor.

FCR: The amount of fish ingested by the average person each day — called the fish consumption rate.

CPF: The chemical's cancer potency, a measure of how harmful the toxin really is — called the cancer potency factor.

The Overall Debate

Agency officials, industry representatives and environmentalists seem to agree that the formula itself is scientifically defensible. The debate rages over what numbers go into the formula and to many broader issues surrounding dioxin regulation.

EPA/DEQ Numbers

Through laboratory tests and simple assumptions, EPA assigned values to each of these factors, plugged them into a formula, and came up with the dioxin standard. DEQ adopted all of EPA's recommended values. With estimates of potential compliance costs running in the hundreds of millions of dollars and predictions of disastrous human health and environmental impacts, there is a surprisingly high degree of "play" in the numbers used to calculate the final standard. As a result, experts on both sides have been free to tweak the

THE EPA/DEQ NUMBERS:

RISK	1-in-a-million
WT	70 kilograms*
WCR	2 liters/day
BCF	5,000
FCR	6.5 grams/day*
CPF	156,000

* 6.5 grams per day is about ¼ of an ounce of fish. 70 kgs is about 155 pounds.

OREGON INSIDER (ISSN 1043-7142) is published biweekly (twenty-four times a year) as a news service of the Oregon Environmental Foundation, 2637 SW Water Avenue, Portland, Oregon 97201 (503) 222-2252. The Foundation is a non-profit corporation dedicated to education and research. Executive Editor: Peter A. Ravella, OSB No. 86264, Staff Writers: Jeff Bernstein & Sarah McCoy. Business Manager: Greg Tozian. Advisory Board Members: Roy Hemmingway, Consultant; Margaret Kirkpatrick, Attorney, Stoel, Rives, Boley, Jones & Grey; Judy Roumpf, Publisher, Resource Recycling magazine; Connie Taylor, Associate, HartCrowser; Dan Saltzman, President, Environmental Management Solutions and Diane Dimon Snow, Assistant to Earl Blumenauer. Subscription Rates: $245 per year including first-class delivery, $135 for private, non-profit 501(c)(3) organizations. Multiple subscription rates available. Letters to the Editor and comments welcome at above address.

numbers to better fit their view of the relative risks and benefits of dioxin regulation.

Three of the six factors are generally accepted and attract little attention. These are the water consumption rate, body weight, and the acceptable risk (RISK) determination.

THE "ACCEPTED" NUMBERS

WCR - 2 liters/day

Water Consumption Rate (WCR). Because of how the formula works, this factor has virtually no affect on the final standard and consequently draws little attention. If DEQ were to eliminate drinking water as a route of dioxin exposure altogether — and plug in a "0" for the WCF — the final standard would not change.

WT - 70 kilograms

Body Weight Factor (WT). EPA used 70 kilograms for the body "weight" factor. At about 155 pounds, this seems to be a pretty good approximation of the average adult's weight. The dioxin standard would be stricter if the agency plugged in a smaller number for body weight. For example, had EPA used 50 kilograms — about 110 pounds — the final dioxin standard would be .009 PPQ instead of .013 PPQ.

All else being equal, people weighing less than 155 pounds, such as children and women would, on average, face a slightly greater risk of cancer than their heavier counterparts under the .013 PPQ standard.

RISK - 1-in-a-million

Acceptable Cancer Risk (RISK). There is no magic behind DEQ's decision to base the state's dioxin standard on a 1-in-a-million cancer risk. It is not mandated by federal or state law; it is a policy decision. According to Lydia Taylor, administrator of the Water Quality Division, all DEQ water quality standards have been based on this risk level since 1987.

1-in-10-million?

Reasonable people differ whether it would be appropriate to set environmental regulatory policy on a less demanding cancer risk limit. John Bonine, a professor of environmental law at the University of Oregon, questioned whether the general population should be subjected to any greater cancer risk for the sake of industry profits. "EPA has developed guidance for dioxin based on a 1-in-10-million cancer risk. Oregon is free to adopt it but hasn't," he said.

A standard based on a 1-in-10-million cancer risk would be ten times tougher than the current one, or .0013 PPQ.

1-in-10,000?

According to Doug Morrison, environmental counsel for the Northwest Pulp & Paper Association, using a 1-in-a-million cancer risk level can be overly protective. Morrison said it would be statistically sound to accept cancer risks as high as 1-in-100,000 or 1-in-10,000 for certain sub-populations — such as Native Americans, Asians and recreational fisherman who eat more river fish — because there are fewer than 1 million in the group. "You can allow a higher risk factor for these smaller groups and still not cause any additional cancers," he said.

Other States Vary

At least one other state has decided to accept greater risks. Maryland's dioxin standard is based on a 1-in-100,000 cancer risk and is 1.2 PPQ, about 100 times less stringent than Oregon's.

DEQ Uses 1-in-a-million

Because DEQ's Water Quality Division has uniformly set its standards based on a 1-in-a-million cancer risk, it seems unlikely that the state would follow Maryland's lead. The EQC has made it an agency-wide goal to apply a uniform risk level to all regulatory programs, but that level has not been defined, (see DEQ 1990 "Strategic Plan."

THE "CONTROVERSIAL" NUMBERS

The remaining three factors – fish consumption (FCR), cancer potency (CPF), and bio-concentration (BCF) – have attracted the most debate for a couple of reasons. Not only do these factors have the greatest impact on the final standard, but the information on them is less developed. The bio-concentration and cancer potency numbers are based on laboratory studies that remain open to interpretation in the scientific community. Definitive surveys on consumption of Columbia River fish have not been done.

FCR: Who Does the Standard Protect?

Fish Consumption Rate (FCR). The debate over this factor is not complicated. Because different people eat different amounts and kinds of fish, a simple question arises: What single number best represents the public's average fish consumption? The answer may be, "There isn't one."

EPA's Number

In adopting the dioxin standard, DEQ accepted EPA's estimate that the average person consumes 6½ grams of freshwater or estuarine fish per day. That's a little less than one-quarter of an ounce per day, or about 5 pounds of fish and shellfish per year. According to Gene Foster, DEQ's expert on the dioxin standard, EPA based its estimate on a limited nationwide market survey of consumer buying habits.

Complete Data is Unavailable

"Complete fish consumption data has not been compiled specifically for the Columbia River system – where the pulp mills discharge their effluent – or for the fish most commonly consumed," said Foster. With the help of the Columbia River Intertribal Fish Commission, EPA is studying the diets of Native Americans along the river. Results could be available by year's end.

Accounting for Sub-Groups

Foster said differences between identifiable sub-groups cannot be overlooked when compiling fish consumption data. Native Americans – particularly those living along the river – Asians, commercial and recreational fisherman, and low-income subsistence fisherman all eat more fish than the general population.

FCR Range: 6.5 to 150 g/day

According to a preliminary risk assessment done by EPA this Summer, members of some sub-groups along the Columbia consume as much as 100 to 150 grams or about 3½ to 5¼ ounces of fish per day. "These rates are not off the wall," added Foster.

Industry says 13 - 16 g/day

Even the Northwest Pulp and Paper Association (NWPPA) – an industry trade group – acknowledges that EPA's 6.5 g/day figure is too low. The NWPPA estimates that recreational fisherman and Native Americans eat a little more than 13 and 16 grams of fish per day, respectively.

Most Agree 6.5 g/day is Low

The table at right shows how the dioxin standard would change if higher fish consumption numbers were plugged into the formula. No one claims that the average fish consumption rate in the Northwest is less than the 6.5 g/day. While

HOW MUCH FISH DO YOU EAT?

Grams Per Day	No. of 6 oz. Meals / Wk.	New Standard*
6.5	.2	0.013
10	.4	0.089
25	1.0	0.0035
50	2.0	0.0017
75	3.0	0.0012
100	4.0	0.0009
150	6.0	0.0006

* This is how the standard would change if DEQ used a higher FCR.

individuals may consume as much as 150 g/day, the overall average for the population would be lower.

BCF: Inadequate Science

Bio-concentration Factor (BCF). Dioxin in the environment tends to concentrate in living organisms, but in different ways and in different amounts. This factor quantifies the amount of dioxin fish concentrate in their tissues by swimming in contaminated water. Surprisingly, it does not take into account dioxin entering the fish through the food chain, just absorption through the skin.

Simplistic Studies

Based on simplistic laboratory experiments, EPA concluded that some fish concentrate 5,000 times as much dioxin in their tissues as is found in the water column. As with all other factors, DEQ adopted EPA's conclusion rather than conduct its own experiments.

Food Chain Ignored

Environmentalists argue a BCF of 5,000 grossly underestimates the amount of dioxin in fish tissue and therefore, the amount ingested by humans. "This is a significant oversight in the standard," said Bonine. "Scientists have documented dioxin accumulation in fish through the food change -- called "bio-accumulation" -- and it is a more important route of exposure than absorption through the skin," he said.

BCF Could Go Higher

Agency officials, industry representatives, and environmentalists generally agree that the BCF should be higher. The debate is over how much higher. Studies conducted for the NW Pulp & Paper Association indicate the BCF for sturgeon ought to be 10,600, over twice as high as the number EPA plugged into the formula.

BCF for Non-Resident Fish at Issue

"We acknowledge that our effluent is responsible for elevated dioxin levels in local, resident fish populations near our discharge pipes, said Llewellyn Matthews, executive director of the NWPPA. "We are not convinced that pulp mill effluent contributes to dioxin levels found in non-resident fish such as salmon. There are other sources of dioxin," she said.

HOW MUCH DIOXIN DO FISH ACCUMULATE?

BCF Values	New Standard*
10,000	0.0069
25,000	0.0027
50,000	0.0013
75,000	0.0009
100,000	0.0006
150,000	0.0004

* This is how the standard would change if DEQ used a higher BCF.

BCF Range: 5,000 to 150,000

According to Bill Diamond, director of EPA's Water Quality Criteria and Standards Division, EPA studies suggest the bio-concentration factor could range as high as 159,000.

Environmentalists have even argued the BCF could be as high as 500,000 for some species, if contamination of the food chain is taken into account.

DEQ Leans to 50,000

DEQ seems to be leaning toward a moderate increase in the bio-concentration factor. "The conclusions on this factor are very crude at this point," said Foster. "My guess is it will settle in somewhere around 50,000 to 60,000." The table at right shows how the dioxin standard would change if a higher bio-concentration factors were used. According to Foster, DEQ is planning to conduct field studies to develop a more accurate BCF for Columbia River fish.

CPF: How Toxic is Dioxin?

Cancer Potency Factor. Most of the debate has focused on this factor, which indicates dioxin's human cancer-causing potential. All arguments by industry and the environmental community regarding dioxin's dangerousness are subsumed in this factor. A closer look at this factor reveals that even if the industry's lowest cancer potency number is plugged into the formula, the dioxin

standard is still less than 1 part per quadrillion.

EPA selected a CPF of 156,000 mg/kg/day. The higher the CPF, the more dangerous the chemical, and the lower the water quality standard.

The Kociba Study . . .

The federal agency based its CPF on a single, two-year rat liver study completed in 1978 by Dr. R.J. Kociba. Since then, industry representatives and some members of the scientific community have challenged the Kociba study. Critics point out that the model used to develop the CPF is too simplistic. They argue Dr. Kociba improperly counted "precancerous liver tumors," failed to incorporate a "no observable affect level" in the test, and made other errors.

Under Attack

Dr. Robert Squire, a John Hopkins researcher and participant in the original study, recently reevaluated Dr. Kociba's data and concluded that the CPF was too high, possibly by a factor of 10 or more. EPA and DEQ acknowledge that legitimate questions surround the Kociba study but they are not prepared to change the CPF yet.

Other Agencies Use Lower CPFs

Other federal agencies use cancer potency factors much lower than EPA's. The U.S. Food and Drug Administration uses a CPF of 17,500 and the federal Center for Disease Control uses 36,000. According to Lydia Taylor, the administrator of DEQ's Water Quality Division, it would not be appropriate for DEQ to regulate dioxins based strictly on these cancer potency factors. "FDA is required to take economics into account when developing their cancer potency factor and we are not," she said.

Industry Wants State Review

The NWPPA has repeatedly urged DEQ to conduct its own review of dioxin's cancer potency. "The upshot is we believe they have over estimated the cancer potency of dioxin and that the states should do their own independent analysis of this factor," said Matthews.

The Washington Department of Health — with help from University of Washington researchers — has undertaken its own study of dioxin's cancer potency. EPA also has a study underway but Oregon does not.

DEQ May Respond

"We will be looking at the cancer potency factor when the new data is available from EPA, but for now we are satisfied with the value we are using," said DEQ's Foster.

CPF Range: 6,700 to 250,000

The range of CPF values seems to be between 6,700 and 250,000. The NWPPA says 6,700 to 9,700 is justified based on the Squire re-analysis and other studies. Environmentalists have challenged the objectivity of the Squire re-analysis and argue that there is no compelling reason to lower the CPF. They also assert that the CPF could be as high as 250,000.

HOW POTENT IS DIOXIN?

CPF Values	New Standard*
6,700	0.321
9,700	0.222
17,500	0.123
36,000	0.059
250,000	0.008

* This is how the standard would change if DEQ used a lower CPF.

DEQ Leans to 15,000

According to Foster, some studies suggest that the CPF could be as low as 15,000. If such a CPF were used, the dioxin standard would be about 0.12 PPQ, or about 10 times less strict than the current standard.

The table at right shows how the dioxin standard would change if lower CPF values were plugged into the formula. None of the new standards exceeds a single part per quadrillion.

PULLING IT TOGETHER

How Does the Standard Change?

The large table on page 8 shows how the dioxin standard changes as the various parameters are "tweaked" one at a time. It also shows what happens if the controversial factors were all changed at the same time, rather than independently of each other. With the help of industry, the environmental community and DEQ, four new dioxin standards were developed -- two "NWPPA Numbers," the "Bonine Numbers" and the "DEQ Lean To."

Industry's Scenario

NWPPA Numbers. These numbers were provided by Doug Morrison, an attorney for the NW Pulp and Paper Association. If DEQ were to assume a fish consumption rate of 13.4 grams per day, a bio-concentration factor of 10,600 and a cancer potency factor of 6,700, the final dioxin standard would be .073 PPQ, about 5 times less strict than the current standard but still less than 1 PPQ. If the CPF were 9,700 -- the NWPPA's upper end estimate -- the final standard would be .050 PPQ.

Environmentalists' Scenario

Bonine Numbers. As an "exercise in number crunching," John Bonine agreed to provided his estimates for the factors: a fish consumption rate of 100 grams per day to protect Native Americans; a body weight of 50 kilograms -- about 110 pounds -- to better protect women and children; a risk factor of 1-in-10-million; and a bio-concentration factor of 50,000. Based on these assumptions, the dioxin standard would be 0.0000021 PPQ or 0.0021 parts per quintillion.

Bonine is actively engaged in the dioxin debate, representing the Northwest Coalition for Alternatives to Pesticides (NCAP) in litigation over DEQ's dioxin regulations.

FOUR POSSIBLE STANDARDS

Source of Values	New Standard*
NWPPA Numbers	.050
NWPPA Numbers	.073
Bonine Numbers	.0000021
DEQ 'Lean To'	.0037

* This is how the standard would change if EPA used the unofficial values provided by industry, environmentalists and DEQ.

DEQ's 'Lean To' Scenario

DEQ 'Lean To'. This scenario was developed with DEQ's help but does not reflect the agency's position on the dioxin standard. These numbers used are values the agency may "lean to" if the standard is eventually reviewed. The values are a fish consumption rate of 25 grams per day (about 1 fish meal per week), a bio-concentration factor of 50,000, and a cancer potency factor of 15,000 (over 10 times smaller than EPA's current CPF of 156,000, and smaller than any CPF employed by other federal agencies). Based on these assumptions, the final dioxin standard would be .0037 PPQ, or about 3½ times more strict than the current standard.

CONCLUSION

No Silver Bullets

All parties to the controversy acknowledge that the .013 PPQ dioxin standard is based on rough guesses and uncertain science.

Whether DEQ's dioxin standard is too strict, or not strict enough, depends on each individual's personal sense of comfort with levels of acceptable risk, and the economics of reaching the standard. As Dr. Donald Barnes, Director of the

TWEEKING THE NUMBERS: A LOOK AT HOW THE STANDARD CHANGES

	Fish Consumpt (FCR)	Water Consumpt (WCR)	Body Weight (WT)	Accepted Risk (RISK)*	Bioconcentration (BCF)	Cancer Potency (CPF)*	Final Standard
DEQ's Standard	6.5 (g/day)	2 (l/day)	70 (kg)	1.00E-06	5,000	156,000 (mg/kg/day)	.013 PPQ
	10	2	70	1.00E-06	5,000	156,000	.0089 PPQ
Tweeking	25	2	70	1.00E-06	5,000	156,000	.0035 PPQ
the	50	2	70	1.00E-06	5,000	156,000	.0017 PPQ
FCR	75	2	70	1.00E-06	5,000	156,000	.0012 PPQ
	100	2	70	1.00E-06	5,000	156,000	.0009 PPQ
	150	2	70	1.00E-06	5,000	156,000	.0006 PPQ
	6.5	2	70	1.00E-06	10,000	156,000	.0069 PPQ
Tweeking	6.5	2	70	1.00E-06	25,000	156,000	.0034 PPQ
the	6.5	2	70	1.00E-06	50,000	156,000	.0013 PPQ
BCF	6.5	2	70	1.00E-06	75,000	156,000	.0009 PPQ
	6.5	2	70	1.00E-06	100,000	156,000	.0006 PPQ
	6.5	2	70	1.00E-06	150,000	156,000	.0004 PPQ
	6.5	2	70	1.00E-06	5,000	6,700	.321 PPQ
Tweeking	6.5	2	70	1.00E-06	5,000	9,700	.222 PPQ
the	6.5	2	70	1.00E-06	5,000	17,500	.123 PPQ
CPF	6.5	2	70	1.00E-06	5,000	36,000	.059 PPQ
	6.5	2	70	1.00E-06	5,000	250,000	.008 PPQ
NWPPA Numbers	13.4	2	70	1.00E-06	10,600	9,700	.050 PPQ
	13.4	2	70	1.00E-06	10,600	6,700	.073 PPQ
Bonine Numbers	100	2	50	1.00E-07	150,000	156,000	.0000021
DEQ's 'Lean To'	25	2	70	1.00E-06	50,000	15,000	.0037 PPQ

*NOTE: The RISK FACTOR is expressed in Lotus 1-2-3 scientific notation. A 1.00E-06 notation means a 1-in-a-million risk and 1.00E-07 means 1-in-10-million.

Standard Unlikely to Exceed 1 PPQ

EPA's Science Advisory Board, told the EQC this summer, "When it comes to dioxin, there are a lot of uncertainties; there are no silver bullet answers."

Whatever else is decided, a few conclusions can be drawn. First, no single factor will be changed in isolation. Both DEQ and EPA are committed to a full review all the factors, not just the just the cancer potency, bio-concentration, or fish consumption numbers. Second, even if adjustments are made, it appears the final standard will remain below a single part per quadrillion, far below the detectable limits of today's instruments. Third, under all the scenarios presented, it appears the Columbia River will remain "water quality limited," forcing the mills to make expensive improvements to control dioxin.

Status & References

If approved by the EQC Nov. 1, eight public hearings on DEQ's entire water quality regulatory package, including the dioxin standard, will be held between Jan. 14 and Jan. 22 (watch *OI Calendar* for details). For more information, contact Eugene Foster (DEQ) at 229-6982. References: ORS 468.735, OAR 340-41 Table 20 (proposed water quality standards for toxic substances).

AIR QUALITY

Advisory Committee to Recommend Few Changes to Protect Wilderness Area Visibility

■ After some 18 months of work, it appears a Department of Environmental Quality (DEQ) advisory committee will recommended few if any significant changes in the way the agency protects visibility and other "air quality related values" in wilderness areas. Even though the group will recommend adding some new wilderness areas to the program, it will be years before that occurs.

Low Priority

"This is a slow moving process — it's not on the front burner," said John Core, visibility program coordinator and liaison to the advisory committee.

The recommendations are being developed as part of a federally-mandated review of the state "Visibility Protection Program." The VPP is supposed to protect air quality related values such as scenic vistas, air chemistry, aquatic biology and even sensitive plants in certain designated wilderness areas.

Triennial Review Underway

First completed in 1986, the VPP was approved by the Environmental Protection Agency in 1987. The program is unique because it requires air pollution control measures even where air quality is generally very high. The idea is to "preserve, protect, and enhance" the pristine air quality often found in wilderness areas, national parks, national seashores and similar areas.

DEQ appointed a 15-member Visibility Protection Advisory Committee last April to help review the program. The group includes representatives of the public, federal land management agencies, timber and agricultural industries, environmentalists and the tourism industry.

Field & Slash Burning at Issue

The primary threat to air quality in these areas is smoke from grass seed industry field burning, forest industry slash burning, and natural forest fires. The VPP restricts field and slash burning during certain months so smoke does not interfere with recreational uses.

Twelve Areas Protected Now

Some of Oregon's most noteworthy attractions are among the 12 wilderness areas currently protected under the program. These include Crater Lake National Park, Mt. Hood Wilderness Area, and popular wilderness areas near Bend. Designated "Class I," these areas receive the greatest air quality protection under the Clean Air Act and DEQ regulations.

Two Questions

There are two general questions before the committee. First, should DEQ expand the VPP to include areas set aside as wilderness since 1977? Second, should DEQ change the way visibility and other related values are protected?

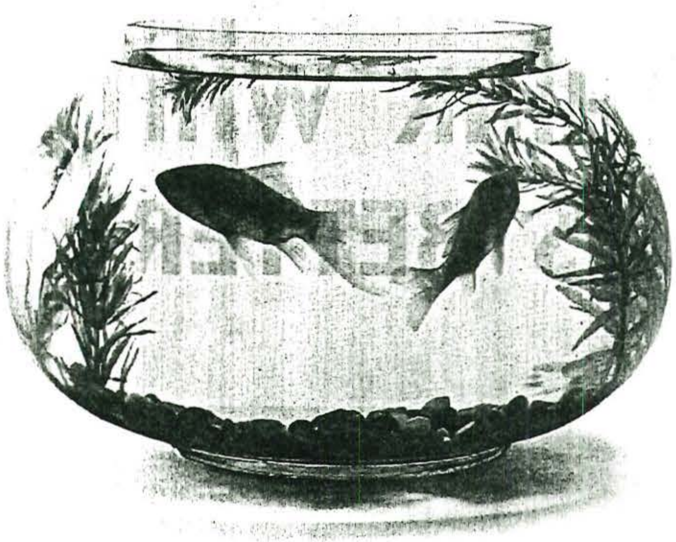
[illegible]

[illegible]

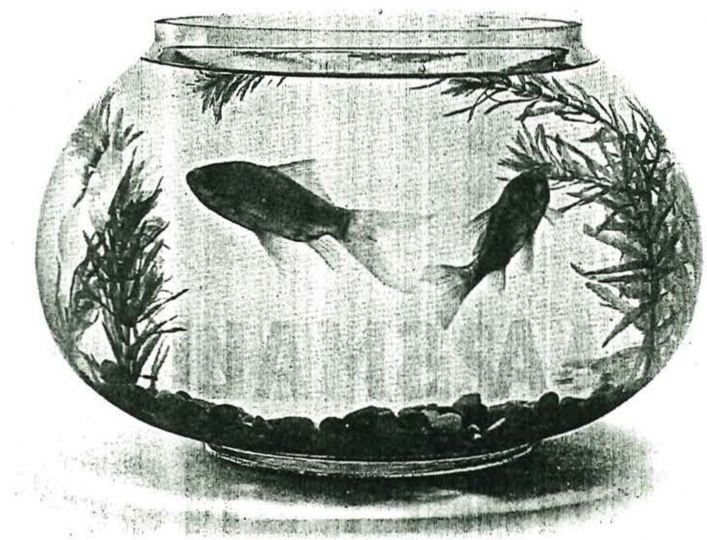
IF YOU THINK WHITER IS BETTER...

GREENPEACE

...THINK AGAIN.

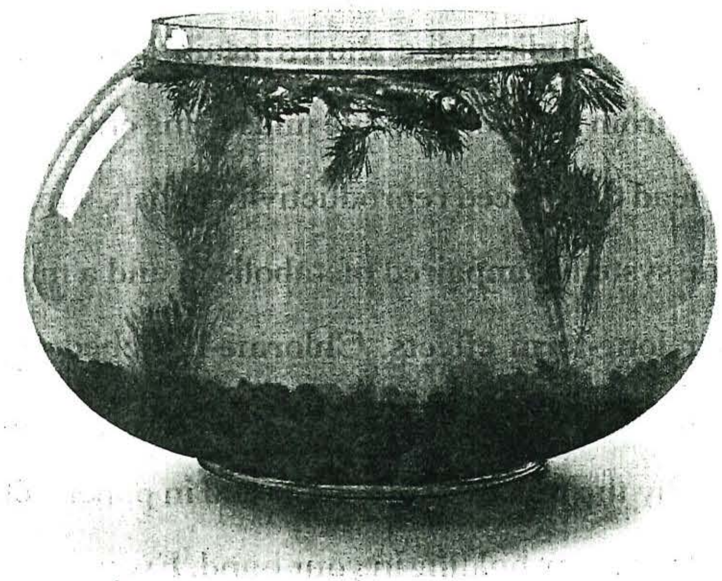


This paper is white. It was bleached with oxygen.



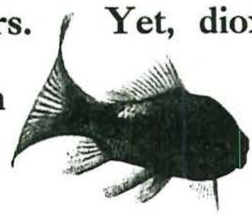
This paper is whiter. It was bleached with chlorine.

A SMALL
DIFFERENCE
TO YOU...

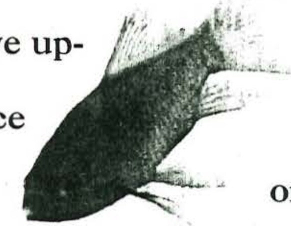


...MAKES A
BIG DIFFERENCE
TO OTHERS.

Chlorine-bleached pulp is bad for the environment. There can be no doubt about that. Studies have shown again and again that effluents from kraft or sulphite mills using chlorine technology lead to reduced reproductivity in fish, suppressed immune systems, impaired metabolism, and a multitude of other long-term effects. Chlorine-bleached paper is also bad for you. Many of the chlorinated poisons discharged by the mills will also be found in paper - like the page you are now holding in your hand. Even dioxin, one of the most toxic chemicals ever produced, is likely to be present in this chlorine-bleached paper. Dioxin has been proven to leach from bleached paper products, such as milk cartons and coffee filters. Yet, dioxin is only the tip of the iceberg when it comes to organochlorine pollution from pulp and paper mills. Up to 1,000 different chemicals can be found in the effluent of mills employing chlorine-bleaching. Many of these cause cancer or genetic damage and are persistent and accumulate in the environment. On average, pulp mills discharge around 35 tons of toxic organochlorines every single day.

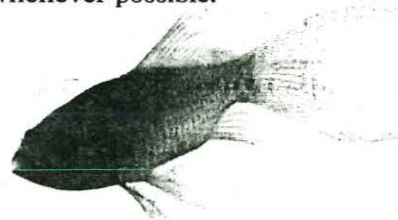


Even those mills that already have upgraded their process to reduce formation of the most notorius organochlorine, dioxin, will still discharge between 10 and 20 tons of other chlorinated poisons every single day. These discharges must stop now. The page you are now reading was printed on sulphite pulp bleached with oxygen-based agents. Such chlorine-free bleaching technology is readily available and must be employed immediately by mills using the sulphite process. Chlorine-free bleaching technology available for kraft mills will yield a cream-colored pulp. That brightness is entirely sufficient for most purposes, particulary since kraft pulp is mainly used in paper products that need to be strong, not white, such as packaging, stationery or envelopes.



THINK TWICE BEFORE YOU BUY WHITE, AND SUPPORT GREENPEACE IN ITS DEMANDS FOR

- Complete elimination of all chlorine-based bleaching chemicals.
- Use of the right fiber for the right product, i.e. the use of off-white kraft and off-white sulphite pulp, or completely unbleached pulp whenever possible.



CHLORINE-FREE BY 1993!

For more information about different pulp and paper making technologies and their impact on the environment, please ask us for the Greenpeace Guide to Paper.

DIOXINS, FURANS AND PCBs: THE TRUE STORY

TOXICS

GREENPEACE

Dioxins, furans and PCBs have become some of the most controversial chemicals of modern society. Dioxin in particular has been labelled the most toxic chemical ever produced by man. More than $1 billion has been spent so far on dioxin research[1], yet at the same time, industry and government officials insist that not enough evidence on the toxicity exists to justify elimination of the sources.

This paper explores some of the myths and facts surrounding these environmentally dangerous chemicals and explains why the scientific debate has become of an increasing political nature.

What Are 'Dioxins'

The term 'dioxins' usually refers to a whole chemical family with 75 individual members, which more correctly should be termed chlorinated dibenzo-p-dioxins. The most toxic member of this family is 2,3,7,8-Tetra-Chloro-Dibenzo-p-Dioxin, often abbreviated as 2,3,7,8-TCDD.

Often, the term 'dioxins' also includes a closely related chemical family called chlorinated dibenzofurans. The most toxic among the 135 known furans is 2,3,7,8-Tetra-Chloro-Dibenzo-Furan (TCDF), which is one tenth as toxic as the corresponding dioxin, TCDD.

Of the 210 dioxins and furans, twelve are extremely toxic and are commonly referred to as the 'Dirty Dozen'. Their individual toxicity is ranked by comparing them to 2,3,7,8-TCDD via internationally agreed upon Toxic Equivalence Factors (TEFs). Box 1 (next page) shows the chemical structures of dioxins and furans, and their toxicity ranking.

PCBs are another chemical family closely related to dioxins. Due to their similar chemical structure, some PCBs can act through exactly the same pathways in organisms as dioxins, but are much less potent. However, due to their chemical nature, PCBs are inevitably contaminated with furans and dioxins, and will form these more toxic chemicals during fires.

How Toxic Are Dioxins [2]

a) Extreme Ability to Kill

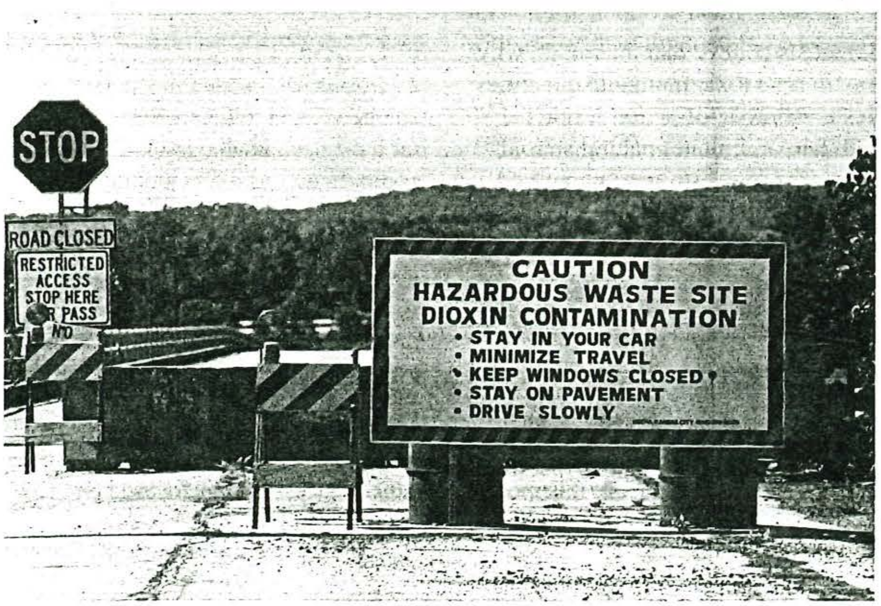
Dioxin TCDD is the most toxic man-made chemical ever tested on laboratory animals. Acutely lethal doses are measured in micro-grams per kilogram animal weight, in the parts per billion range. [2e] Though the lethal dose varies considerably from species to species, dioxin has been found to be extraordinarily toxic to all species tested.

Characteristic of lethal dioxin exposure is the 'wasting syndrome': animals seem to waste away, and eventually die, without displaying any overt pathological symptoms. The exact reason why dioxin can cause death in these minute quantities is not yet known.[2e]

b) Extremely Bio-Accumulative

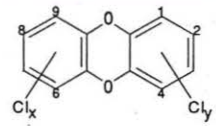
Dioxins are some of the most persistent and bio-accumulative man-made chemicals released into the environment. While dioxins can be broken down under certain conditions, in particular when exposed to intensive sunlight, they cannot be broken down once absorbed by soil or dust. When they enter the food-chain, they will bio-magnify, often to levels many thousands of times higher than their surroundings.[2d,3]

It is this combination of dioxin's extreme toxicity and its bio-magnification in the environment that makes Greenpeace believe that there can be no safe level of dioxin emissions.

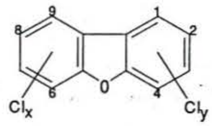


INTERNATIONAL TOXICITY EQUIVALENCY FACTORS (I-TEFS)

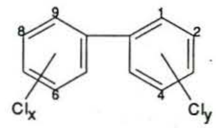
	I – TEF
2,3,7,8-TCDD	1
1,2,3,7,8-PeCDD	0.5
1,2,3,4,7,8-HxCDD	
1,2,3,7,8,9-HxCDD	0.1
1,2,3,6,7,8-HxCDD	
1,2,3,4,6,7,8-HpCDD	0.01
OCDD	0.001
2,3,7,8-TCDF	0.1
2,3,4,7,8-PeCDF	0.5
1,2,3,7,8-PeCDF	0.05
1,2,3,4,7,8-HxCDF	
1,2,3,7,8,9-HxCDF	
1,2,3,6,7,8-HxCDF	0.1
2,3,4,6,7,8-HxCDF	
1,2,3,4,6,7,8-HpCDF	
1,2,3,4,7,8,9-HpCDF	0.01



chlorinated dibenzo—p—dioxins



chlorinated dibenzofurans



chlorinated byphenyls (PCBs)

Box 1

c) Long-Term Toxicity: The Dioxin-Receptor

More worrisome than the high acute toxicity are the more insidious long-term effects of exposure to sub-lethal doses of dioxin. Daily doses 1,000 times below the lethal dose, the parts per trillion range, cause profound delayed effects in mammals, such as cancer, damage to the immune system, and reproductive failure.[2e]

Concentrations in water another 1,000 times lower, the parts per quadrillion range, can still cause a wide variety of toxic effects in fish, e.g. in rainbow trout.[3]

Scientists believe that the reason why dioxin is so toxic in minute quantities lies in its mode-of-action inside the cell. Dioxin imitates natural steroid hormones (e.g. estrogen) in our bodies. Dioxin fits into a protein receptor, which normally responds to these steroid hormones. The receptor then transports the dioxin directly into the cell nucleus, where it interacts with basic cell chemistry.[2a]

The 'dioxin-receptor' has been identified in laboratory animals as well as in humans. One can compare this mode-of-action with dioxin acting as a key to the receptor-lock. Some individual dioxins and furans fit better into the receptor than others; PCBs do not fit as well. 2,3,7,8-TCDD fits best into this receptor and consequently is the most toxic.

d) Chloracne

The disfiguring skin disease chloracne is often erroneously referred to as the only human health effect positively linked to dioxin exposure, and is often down-played in its severity. Yet, chloracne is always accompanied by other health effects, such as chronic weakness in the legs, severe pain in the joints, headaches, pronounced fatigue and irritability, and often lasts for decades, as several studies on occupationally exposed workers show.[2b]

e) Cancer

2,3,7,8-TCDD is the most potent carcinogen tested to date.[2] Researchers so far have been unable to clarify whether dioxin acts as a co-carcinogen or whether it suppresses the immune response to other carcinogens. Yet given the fact that other carcinogens are plentiful in our polluted environment, that question can be of academic interest only.

Does Dioxin Cause Cancer in Humans?

Much discussion has focused on whether 2,3,7,8-TCDD is a human carcinogen. Some evidence exists to support such a claim, but there are also indications that this discussion has not been without bias.

One of the best analyzed groups of exposed humans are chemical workers who produced 2,4,5-T (Agent Orange). The West German chemical company BASF experienced an explosion in 1953, which exposed workers to relatively high doses of dioxin TCDD. Many of the workers subsequently suffered from chloracne.

At the 1989 International Symposium on dioxin and its toxic effects, West German scientist F. Rohleder presented a re-analysis of these exposed BASF workers and found significantly elevated levels of respiratory cancer and cancer of the digestive system. [4]

Most disturbingly, Rohleder found that earlier studies, paid for by BASF itself, were fraudulent: non-exposed workers had been deliberately added to the 'exposed' cohort, and truly exposed workers, some of whom were displaying chloracne, had been deliberately excluded from the study.

Evidence that PCBs may be carcinogenic in humans is also mounting. A cancer study by the Cincinnati National Institute for Occupational Safety and Health found that Westinghouse workers in Bloomington, Indiana experienced a more than two-fold increase in mortality from brain cancer and a four-fold increase in deaths from skin cancer.[5]

The Shortcomings of Epidemiology

The reason clear proof of dioxins' and PCBs' carcinogenicity in humans does not exist, and may never exist, lies in some important short-comings of any epidemiological study: the humans investigated are exposed to many more toxic influences than just dioxin, and it will always be possible to point the finger at other factors possibly causing the disease. This poses an ethical dilemma, since it is impossible to raise humans in controlled environments such as a laboratory.

Further, epidemiological studies carried out so far rarely have verified the actual exposure of the presumed exposed versus the unexposed control group. That fact is probably the single most important reason why the findings of epidemiological studies carried out so far contradict each other so much.

Recently it has become possible to determine actual dioxin body burdens through analysis of blood serum, and some exposed cohorts investigated earlier, e.g. Vietnam Veterans and occupationally exposed workers, are being re-analyzed. However, individuals in these cohorts who have died since the original study was conducted are invariably excluded from these new studies.

f) Reproductive Effects

More subtle than chloracne or cancer are other health effects such as reproductive failure. It is striking that reproductive failure has been observed in all animal species tested, be it fish, bird or mammal. It is therefore highly likely that reproductive failure also occurs in humans exposed to dioxin.[2c]

Most disturbing are laboratory experiments on primates such as rhesus monkeys, whose reproductive systems were found to be extremely sensitive to dioxins when administered in minute doses on a daily basis. Researchers found a serious decrease in sperm count in exposed males, and an inability to conceive or carry the pregnancy to term in exposed females.[2d,6]

Some evidence of such reproductive failure in humans already exists. Jock Ferguson, a Canadian reporter who investigated health effects in occupationally exposed workers, once interviewed three Hooker Chemicals workers, all of whom suddenly came to realize that none had fathered children.[7] Why is it that incidences like these are always dismissed immediately as anecdotal evidence, and are not followed up in a formal investigation, e.g. an epidemiological study, whereas negative findings are always promoted as certainty?

Other reproductive effects observed in laboratory animals include stillbirths and birth defects. Dioxin has been linked to spina bifida, anencephaly (absence of brain) and cleft palate.[2]

g) Suppression of the Immune System

Perhaps most frightening of all are the effects dioxin has on the immune system. The thymus, a gland that is of utmost importance to the immune system, is one of the main targets of dioxin. It has been shown in laboratory animals that one of the first signs of dioxin poisoning is thymic atrophy.[d]

The human thymus develops at 9 weeks of gestation and disappears at puberty, at the age of 10 to 12. It seems that the thymus is not required for the maintenance of effective immune function in adults, since human T lymphocytes have a life-span of 15 – 20 years, and there is little replacement for them during adult life.[2d]

But what about children, and even worse, what does thymic atrophy do to nursing babies?

h) Behavioral Changes in Offspring and Minimum Effect Levels

A number of health effects have been noted at doses comparable to those producing cancer. Very few of the studies, however, have produced clear No Observable Effect Levels. This is particularly true of long-term studies in rodents and rhesus monkeys.[2e]

The available evidence suggests that No Observable Effect Levels for some of the immunologic and reproductive effects in rhesus monkeys are well below 1 ng/kg/day. [6] Behavioral changes in the offspring, for example, were observed in rhesus monkeys when exposed to dioxin levels in the diet as low as 0.12 parts per trillion.[6a]

Box 2 shows how these Minimum Effect Levels for immunotoxic, reproductive and carcinogenic effects, as observed in various animal species, compare to the average daily intake of nursing babies in the western industrialized world.[2d,8]

Dioxins in Human Milk

An average breast-fed baby in industrialized countries already ingests up to 100 times more dioxin than the World Health Organization (WHO) deems tolerable for a healthy adult.[8] The margin of safety, that is the difference between the levels of dioxin we expose our babies to and those that we know will cause adverse effects in laboratory animals, is on the order of ten to non-existent. Babies in heavily contaminated areas are already exposed to dioxin levels that are certain to induce toxic effects in laboratory animals.

Aside from dangerously high levels of dioxins and furans, mother's milk also contains other toxic chlorinated chemicals, such as PCBs, hexachlorobenzene, and polychloronaphthalenes to name a few. Yet no research has been done on the likely synergistic effects of these compounds.

Further, some scientists believe that exposure in utero from transplacental migration may have important effects on brain development, and thus may

Minimum Effect Levels and Tolerable Daily Intake of Dioxin, expressed in equivalents of 2, 3, 7, 8-TCDD (TEQ), compared to the Average Daily Intake by a nursing baby in industrialized countries. (2d,8)

EFFECTS	MEL (lab.tests) ng/kg bw/day	ADI (nursing baby) ng/kg bw/day
immunotoxic	6 (guinea pig)	
reproductive	0.12 (primates)	around 0.1
carcinogenic	10 (rats)	
	TDI pg/kg bw/day	**ADI pg/kg bw/day**
Sweden	1 – 5	
Canada	10	
USEPA	0.006	100
USFDA	0.06	
WHO	1	

Box 2

wood articles become very significant sources of dioxin when burnt in wood stoves or incinerators.

Municipal incinerators are another very significant but completely avoidable source of dioxins. They not only generate vast amounts of dioxin-laden ash but also emit dioxins into the atmosphere where they can be transported over long distances, e.g. to the Arctic. The disposal of toxic incinerator ash has become a highly publicized problem since export schemes to Panama and other developing nations were exposed by Greenpeace.

Incinerators should be eliminated for other environmental reasons as well. Incinerators are not compatible with recycling systems, since comprehensive recycling systems eliminate cheap fuel from the waste stream, e.g. paper or plastics, thus eliminating the economic viability of incinerators.

Copper reclamation plants and hospital waste incinerators are also major dioxin sources due to the burning of PVC (polyvinylchloride) and PVDC (polyvinylidene-chloride) waste. Copper wires are coated with PVC, and many hospital disposable items are made of these chlorinated plastics, as are many disposable household products.

Many West German cities, e.g. Bielefeld, Munich, Aachen and others, have now banned the use of PVC material in public buildings to protect the public and fire fighters from dioxin formed during fires. The Danish government is actively pursuing a phase-out of all PVC articles, and is presently researching a feasible time-table.

The Swedish government is pushing for a phase-out of chlorinated solvents, due to the risks they pose to ground water supply, their effects in the lower atmosphere, and the associated waste disposal problems.

The pulp and paper industry as well as certain branches of the metallurgical industry are significant sources of dioxin due to the use of raw chlorine. Chlorine gas reacts with wood compounds or carbon electrodes to form dioxins. European governments are researching and implementing new production processes that would ban the use of chlorine and thus the generation of dioxin as well as other toxic organochlorines.

It is clear that eliminating these sources of dioxin means eliminating a much larger portion of toxic chemicals from our environment. This makes a lot of sense from an environmental point of view, because dioxins never come alone, but are always accompanied by other toxic organochlorines.

Dioxin indeed is only the tip of an iceberg of environmentally dangerous organochlorines and other organohalogens; and successfully eliminating modern society's dioxin sources will inevitably mean eliminating this iceberg, which is exactly the reason environmentalists are becoming more and more vocal in this matter. To Greenpeace, dioxin is a symbol of whether we want to deal with our pollution or whether we want to continue our self-destructive lifestyle.

SOURCE	ELIMINATION STRATEGY
a) PRODUCTION OF ORGANOCHLORINES, e.g.	
* chlorophenols and chlorobenzenes	ban production and use immediately
b) COMBUSTION OF ORGANOCHLORINES, e.g.	
* car exhaust, leaded gas	don't add org. chlorine scavengers (use unleaded gas)
* municipal waste incinerators	comprehensive recycling
* hazardous waste incinerators	waste reduction/elimination and use other destruction methods
* copper reclamation	eliminate PVC coating
* steel recycling	no chlorinated rubber/plastics to be used in car or machinery
c) USE OF CHLORINE GAS, e.g.	
* pulp and paper industry	less bleaching and bleaching with oxygen/ H202
* zinc/magnesium smelters	use chlorine-free process

Box 3

The Politics – Whose Interests Are At Stake?

Obviously, when the entire organohalogen production is being questioned, some very powerful interest groups want to have a say. Much is at stake, both in terms of liability law suits and lost profits.

It would be naive to think that the chlorine- and organochlorine-producing industry, e.g. PVC and chlorinated solvents or pesticide producers, have had no influence on the colour of dioxin science. Other vested parties to name include the incineration lobby, the pulp and paper industry and the metallurgical industry. Even defense departments are involved in the discussion, due to the use of Agent Orange in Vietnam and elsewhere.

The result: instead of devoting research efforts toward eliminating the sources, finding alternative products or production technologies, and safe methods of dealing with the existing wastes, the public is being deluged with attempts to linguistically detoxify dioxin, via media releases, information brochures and widely publicized risk assessments.

Risk assessments, in particular, can at best only be viewed as pseudo-scientific exercises, because they do not take into account:

- total exposure from all possible sources
- synergistic effects
- effects on the next generation, for example through contaminated human milk
- all possible health effects, rather than selected health effects only, e.g. certain forms of cancer.

be of even more concern than postnatal exposure through mother's milk. [9]

Scientists will never be able to prove a link between health effects at a later stage in life to any toxic chemicals present in mother's milk or to exposure to these toxins in utero, simply because babies do not grow up in controlled environments such as a laboratory.

Who is at Risk?

Obviously, the human baby is of most concern when it comes to human health effects. But what about the entire environment? Despite all the money spent and all the papers published, we know very little about dioxin's effect on an entire ecosystem. It seems likely that animals and birds with a fish-based diet will suffer most.

The Baltic gray seal is a case in point. In the mid-seventies it was found that only 20 percent of the mature female gray seals were fertile.[10] This is commonly thought to be caused by PCBs in the Baltic food chain; and PCBs, as we know, react through the same protein receptor as dioxins.

Fertility is not the only effect linked to PCBs in the seals' diet: over 75% of the seals found dead in recent years have been found to have intestinal ulcers and kidney damage. Roughly half the female gray seals also had uterine tumors. Often, even the living display these same diseases. Interestingly, when seals are raised with a diet of less contaminated fish caught outside the Baltic, the seals are able to reproduce. Yet, this fact is often excluded in discussions about toxic effects of PCBs and dioxins, and seldom mentioned in official government or industry brochures.

Clearly, the solution to such environmental problems cannot be to place Baltic seals or beluga whales or fish-eating birds into a sanctuary and feed them less contaminated fish. Neither can the solution be to forbid breast-feeding. It is essential, then, to prevent any further build-up of these insidious chemicals in the food chain. This can only be achieved by immediate elimination of all sources of dioxins.

The Sources and Elimination Strategies

While the production of PCBs was finally outlawed worldwide, and the worry now is how to eliminate existing PCB wastes, dioxins and furans seem to come from many different and ongoing sources. Yet there is an obvious common denominator to these sources: modern society's use of chlorine.

It is often claimed that dioxin is a naturally occurring toxin, produced in forest fires and wood stoves. This theory, first introduced by Dow Chemical scientists as the 'Trace Chemistry of Fire' theory [11], has been convincingly disclaimed by at least three separate studies:

a) the Czuczwa study, which investigated contamination of Great Lakes sediments, found that dioxin levels were virtually non-existent prior to the Second World War, which coincides with the beginning of large-scale production and combustion of organochlorines.[12]

b) the Inuit mummy study, in which A. Schector investigated tissue of two 400-year-old mummies. Only minor amounts of the less toxic but very persistent octa-chlorodibenzo-p-dioxin (OCDD) were found. [13]

c) the Chilean mummy study, in which W.V. Lignon analyzed tissue of nine Chilean mummies for dioxins and furans. Again, only minor amounts of OCDD were found.[14]

All three studies conclude that rising dioxin levels are intimately linked to modern industrialized society. Box 3 lists strategies to eliminate major industrial sources of dioxin, all of which are connected with the use of elemental chlorine as well as the production and combustion of chlorinated organic chemicals (organochlorines).

Elemental chlorine does not exist in Nature, and Nature does not produce organochlorines on a large scale either, with the exception of some very simple molecules, such as methylchloride or dichloromethane.

Many of the industrial dioxin sources are easy to eliminate.

Chlorophenols, for example, are already banned in many European countries. Sweden actually experienced a decline of dioxin levels in human milk after banning both pentachlorophenol and chlorophenol-based herbicides.

Both Canada and the United States actively resist such a ban, and chlorophenols are still used for wood preservation (utility poles and railway ties) and as a fungicide on lumber destined for export. Once treated, these

Conclusions and Greenpeace Demands

Enough research exists to prove that dioxin is extremely toxic and persistent, and that levels in our environment and in human milk are increasing. Given that many health effects occur from exposure to even minute quantities over time, and that widespread contamination of our environment and the build-up of these chemicals in the food chain has already led to dangerously high levels in human milk and in marine mammals, all energy must be devoted toward preventing any further releases of dioxins into the environment.

The elimination of man-made dioxin sources would go hand-in-hand with the elimination of a much larger group of environmentally dangerous organochlorines, which would be extremely desirable from an overall environmental point of view. Elimination of all dioxin sources would mark a turning point in our dealings with pollution control, since a holistic approach would have to include the phase-out of an entire class of anthropogenic chemicals presently discharged in large quantities into the environment.

In 1983, after two years of research, the Ministers' Expert Advisory Committee on Dioxins stated that [15]:

"Regardless of arguments about the significance of species differences in sensitivity, the validity of risk assessments, and other uncertainties which may take years to resolve, it is quite clear that dioxins are very unpleasant things to have in our environment and the less we have of them the better. It is, in fact, imperative to reduce dioxin exposure to the absolute possible minimum."

Despite these recommendations, the Canadian government has failed to eliminate even such outstanding dioxin sources as pentachlorophenol, but has instead actually added new dioxin sources to the Canadian environment by building further municipal and hazardous waste incinerators.

Greenpeace demands that the Canadian government follow the leadership provided by forward thinking European governments, and:

establish a five-year plan to eliminate all known industrial dioxin sources,

and in particular:

- **ban import and use of chlorophenols immediately;**
- **establish an indefinite moratorium on construction of new municipal and hazardous waste incinerators;**
- **phase out disposable products made of PVC or PVDC;**
- **phase out PVC coating of copper wire;**
- **phase out chlorinated solvents;**
- **eliminate the use of chlorine in the pulp and paper industry and metallurgical industry;**
- **establish a mass-balance of chlorine and organochlorines in Canada; i.e. determine the amount of chlorine gas and organochlorines produced, and their fate in the environment. This mass balance should extend to other halogens and organohalogens;**
- **commission a feasibility study on phase-out of all production and use of organochlorines.**
- **Fund research to find clean production technologies and alternatives to chlorinated products, as well as safe methods of destroying the existing piles of dioxin and other chlorinated waste.**

This paper was researched and written by Renate Kroesa, M.Sc., Toxic Project Co-ordinator.

REFERENCES

1) Report from Conferences, the 5th Int'l Dioxin Symposium, Bayreuth, 1985; Chemosphere, 1986, 15, N1-2.

2) This entire section is based on the following five overview reports/books published on the toxicology of dioxin. All reports/books give an excellent overview and provide many detailed references to the interested reader.
   a) 'Human Health Aspects of Exposure to PCDDs and PCDFs'; UAREP, Bethesda, Maryland, June 1988 (funded by the American Paper Institute).
   b) 'The Chemical Scythe', by Alistair Hay; Plenum Press 1982.
   c) 'A Cancer Risk-Specific Dose Estimate for 2,3,7,8-TCDD'; US-EPA/600/6-88/007Ab, June 1988, plus Appendices A-F.
   d) 'Dioxins in the Environment' by the UK Dept of the Environment; Pollution Paper No. 27, 1989.
   e) S.A. Skene et al, Human Toxicol, 1989, 8, 173-203.

3) P.M. Mehrle et al, Environmental Toxicology and Chemistry, 1988, 7, 47-62.

4) F. Rohleder, Presentation to the 9th Int'l Dioxin Symposium, Toronto, 1989.

5) T. Sinks, Presentation to the 7th Int'l Symposium on Epidemiology in Occupational Health, Tokyo, 1989.

6) a) R.E. Bowman et al, Neurotoxicology, 1986, 7, 637-650.
   b) J.R. Allen et al, Toxicology and Applied Pharmacology, 1979, 48, A180.
   c) J.R. Allen et al, Bulletin of Environmental Contamination and Toxicology, 1979, 21, 463-469.

7) 'Who do you believe?', Jock Ferguson; Chemosphere, 1985, 14 791-796.

8) PCBs, PCDDs and PCDFs in Breast Milk: Assessment of Health Risks; WHO, Regional Office for Europe; EH 29 (1988).

9) W.R. Swain; Aquatic Toxicology, 1988, 11, 357-377.

10) Monitor 1988, Sweden's Marine Environment - Ecosystems Under Pressure; National Swedish Environmental Protection Board.

11) a) R.R. Bumb et al (Dow Chemical), Science, 1980, 210, 385.
   b) Nestrick et al (Dow Chemical), Chemosphere, 1983, 12, 617-626.

12) J.M. Czuczwa, R.A. Hites, Chemosphere, 1986, 15, 1417-1420.

13) a) A. Schector et al, Chemosphere, 1988, 17, 627.
   b) A. Schector et al, poster at the 9th Int'l Dioxin Symposium, Toronto, 1989.

14) W.V. Ligon et al (General Electric), Environ. Sci. Technol. 1989, 23, 1286-1290.

15) Report of the Joint Health and Welfare Canada/ Environment Canada Advisory Committee on Dioxins, November 1983.

GREENPEACE

Founded in Canada, 1971
Fondé au Canada, 1971

Vancouver

1726 Commercial Drive,
Vancouver
British Columbia
Canada V5N 4A3
✆ 604 253-7701
FAX 604 253-0114

Toronto

578 Bloor Street West
Toronto, Ontario
Canada M6G 1K1
✆ 416 538-6470
Fax 416 538-6479

Montréal

2444 Notre-Dame Ouest
Montréal (Québec)
Canada H3J 1N5
✆ 514 933--0021
Fax 514 933-1017

Press Gang Printers - a feminist worker-controlled collective

SAT., JUNE 8, 1991

The Register-Guard

ALTON F. BAKER, Publisher, 1927-1961
ALTON F. BAKER Jr., Editor and Publisher, 1961-1982
EDWIN M. BAKER, Publisher, 1982-1987

ALTON F. BAKER III, Editor and Publisher
FLETCHER LITTLE, General Manager
ALLAN A. GEMMELL, Finance Director

PATRICK A. YACK, Managing Editor
DON ROBINSON, Editorial Page Editor
HENNY WILLIS, Associate Editor
JACKMAN WILSON, Associate Editor

An Independent Newspaper

The Register-Guard's policy is the impartial publication in its news pages of all news and statements on news. On this page, the editors offer their opinions on events of the day and matters of importance, endeavoring to be candid but fair and helpful in the development of constructive community policy. A newspaper is a CITIZEN OF ITS COMMUNITY.

No retreat on dioxin

Meeting state standards limiting dioxin pollution will be difficult and expensive for the pulp and paper industry. But it's hard to muster much sympathy for two mills in Oregon that are complaining about the standards when a third, Pope & Talbot's mill near Halsey, already has a plan to comply with the dioxin rules. If one can do it, the others can.

Dioxins are chemicals created as byproducts of certain chemical and industrial processes, including paper bleaching. Some dioxins are highly toxic; one is the most powerful known carcinogen. The federal Environmental Protection Agency studied fish living downstream from pulp and paper mills nationwide and found that dioxin had accumulated in their tissues.

The EPA told the states to regulate mills' dioxin emissions. Oregon's Department of Environmental Quality obliged by requiring that water downstream from pulp and paper mills contain no more than 0.013 parts per quadrillion of dioxin. That small a portion of the United States' total land area is one-tenth of a square inch — a fact that illustrates both the strictness of the DEQ standard and the potency of the deadliest dioxin.

Last year, Pope & Talbot reached an agreement with the DEQ that will allow it to meet the state's standard. Improving current industrial processes will reduce dioxin emissions by about 60 percent. By 1993 the mill expects to meet the 0.013 parts per quadrillion standard. And in concert with an expansion project, Pope & Talbot intends to change its paper-bleaching process so that by 1997 it will be able to triple its production and still meet the state standard.

The two companies that operate Oregon's other two bleached-pulp mills, James River II Inc. and Boise Cascade Corp., haven't kept up with Pope & Talbot. Instead, they're urging the DEQ to loosen its regulations and allow them to put 177 times as much dioxin in the Columbia River as is permitted under the 0.013 parts per quadrillion standard.

#1

The two companies argue that dioxins are not as carcinogenic as was once believed. One of the scientists who did the original evaluations has now concluded that dioxins pose only a small threat to human and animal health, they say. The companies accuse the DEQ of forcing them to spend tens of millions of dollars to meet a standard that is based on an exaggerated assessment of the dioxin threat.

The DEQ, however, is not directly responsible for determining whether dioxin is dangerous. That determination has been made by the federal EPA, which told the states to limit dioxin discharges to levels that would cause fewer than one cancer case among a million people. Oregon's standard is in response to that order, and complaints about its scientific basis should be directed to the EPA, not the DEQ.

#2

Even if there are doubts about the magnitude of the health risk posed by dioxins, it's plain that some hazard exists. Barring a conclusive finding that would allow the EPA to downgrade its assessment of the danger from dioxin, a cautious approach offers the best protection for human health and river-dwelling fish and wildlife. At least one pulp and paper mill intends to grow and prosper while meeting the standard that recognizes the wisdom of caution. The other two should be expected to do the same.

While one Oregon mill is moving toward papermaking methods that produce less dioxin and two others are dragging their heels, the pulp and paper industry in other parts of the world is moving away from dioxin-producing processes altogether. The elimination of dioxin should be the industry's goal. Pope & Talbot's reductions are welcome but incomplete, and a lack of progress by the other two companies should be unacceptable.

3

JAMES RIVER CORPORATION
P.O. Box 2218, Richmond, VA 23217 (804) 644-5411

RONALD B. ESTRIDGE
Senior Vice President, Group Executive
Technology
(804) 649-4209

May 17, 1991

The Honorable William K. Reilly
Administrator
United States Environmental Protection Agency
Washington, DC 20460

Re: Industrial Toxics Project

Dear Mr. Reilly:

James River Corporation is pleased to participate in EPA's proposed voluntary Industrial Toxics Project.

Our 1995 goals are:

- The 17 high priority chemicals - 50% reduction in annual releases
- Dioxin - 90% reduction in annual releases

In addition to our U.S. operations, these goals include reductions of chloroform and dioxin at our pulp mill in Marathon, Ontario, which is located on Lake Superior. Where possible, pollution prevention methods will be used to reach these goals.

Although we fully intend to meet these goals, we understand that this project is completely voluntary and that the goals are not firm, enforceable requirements under any laws or regulations. Also, there are several concerns about the program which have been communicated by the American Paper Institute in its May 8 letter to you; EPA's prompt attention to these issues will be appreciated.

The Industrial Toxics Project represents a real step forward from the current "command-and-control" approach favored to date by Congress and the Agency. We look forward to a success that will set a new tone for industry/agency cooperation in environmental protection.

Very truly yours,

Ronald B Estridge

Ronald B. Estridge

RBE/kr

cc: The Honorable Linda J. Fisher
Assistant Administrator
Office of Pesticides and Toxic Substances

signed mixing zone, as measured relative to a control point immediately upstream from a discharge when stream temperatures are 58° F. or greater; or more than 0.5° F. increase due to a single-source discharge when receiving water temperatures are 57.5° F. or less; or more than 2° F. increase due to all sources combined when stream temperatures are 56° F. or less, except for specifically limited duration activities which may be authorized by DEQ under such conditions as DEQ and the Department of Fish and Wildlife may prescribe and which are necessary to accommodate legitimate uses or activities where temperatures in excess of this standard are unavoidable and all practical preventive techniques have been applied to minimize temperature rises. The Director shall hold a public hearing when a request for an exception to the temperature standard for a planned activity or discharge will in all probability adversely affect the beneficial uses.

(C) Marine and estuarine waters: No significant increase above natural background temperatures shall be allowed, and water temperatures shall not be altered to a degree which creates or can reasonably be expected to create an adverse effect on fish or other aquatic life.

(c) Turbidity (Jackson Turbidity Units, JTU): No more than a 10 percent cumulative increase in natural stream turbidities shall be allowed, as measured relative to a control point immediately upstream of the turbidity causing activity. However, limited duration activities necessary to address an emergency or to accommodate essential dredging, construction or other legitimate activities and which cause the standard to be exceeded may be authorized provided all practicable turbidity control techniques have been applied and one of the following has been granted:

(A) Emergency activities: Approval coordinated by DEQ with the Department of Fish and Wildlife under conditions they may prescribe to accommodate response to emergencies or to protect public health and welfare.

(B) Dredging, Construction or other Legitimate Activities: Permit or certification authorized under terms of Section 401 or 404 (Permits and Licenses, Federal Water Pollution Control Act) or OAR 141-85-100 et seq. (Removal and Fill Permits, Division of State Lands), with limitations and conditions governing the activity set forth in the permit or certificate.

(d) pH (hydrogen ion concentration): pH values shall not fall outside the following ranges:

(A) Marine waters: 7.0 – 8.5.

(B) Estuarine and fresh waters: 6.5 – 8.5.

(e) Organisms of the coliform group where associated with fecal sources (MPN or equivalent MF using a representative number of samples):

(A) Columbia River from the Highway 5 bridge between Vancouver and Portland to the mouth: A log mean of 200 fecal coliform per 100 milliliters based on a minimum of 5 samples in a 30-day period with no more than 10 percent of the samples in the 30-day period exceeding 400 per 100 ml.

(B) Marine waters and estuarine shellfish growing waters: A fecal coliform median concentration of 14 organisms per 100 milliliters, with not more than 10 percent of the samples exceeding 43 organisms per 100 ml.

(C) Estuarine waters other than shellfish growing waters: A log mean of 200 fecal coliform per 100 milliliters based on a minimum of 5 samples in a 30-day period with no more than 10 percent of the samples in the 30-day period exceeding 400 per 100 ml.

(f) Bacterial pollution or other conditions deleterious to waters used for domestic purposes, livestock watering, irrigation, bathing, or shellfish propagation, or otherwise injurious to public health shall not be allowed.

(g) The liberation of dissolved gases, such as carbon-dioxide, hydrogen sulfide, or other gases, in sufficient quantities to cause objectionable odors or to be deleterious to fish or other aquatic life, navigation, recreation, or other reasonable uses made of such waters shall not be allowed.

(h) The development of fungi or other growths having a deleterious effect on stream bottoms, fish or other aquatic life, or which are injurious to health, recreation, or industry shall not be allowed.

(i) The creation of tastes or odors or toxic or other conditions that are deleterious to fish or other aquatic life or affect the potability of drinking water or the palatability of fish or shellfish shall not be allowed.

(j) The formation of appreciable bottom or sludge deposits or the formation of any organic or inorganic deposits deleterious to fish or other aquatic life or injurious to public health, recreation, or industry shall not be allowed.

(k) Objectionable discoloration, scum, oily sleek, or floating solids, or coating of aquatic life with oil film shall not be allowed.

(l) Aesthetic conditions offensive to the human senses of sight, taste, smell, or touch shall not be allowed.

(m) Radioisotope concentrations shall not exceed maximum permissible concentrations (MCP's) in drinking water, edible fishes or shellfishes, wildlife, irrigated crops, livestock and dairy products, or pose an external radiation hazard.

(n) The concentration of total dissolved gas relative to atmospheric pressure at the point of sample collection shall not exceed one hundred and ten percent (110%) of saturation, except when stream flow exceeds the 10-year, 7-day average flood. However, for Hatchery receiving waters and waters of less than 2 feet in depth, the concentration of total dissolved gas relative to atmospheric pressure at the point of sample collection shall not exceed one hundred and five percent (105%) of saturation.

(o) Total Dissolved Solids: Guide concentrations listed below shall not be exceeded unless otherwise specifically authorized by DEQ upon such conditions as it may deem necessary to carry out the general intent of this plan and to protect the beneficial uses set forth in rule 340-41-202:

(A) Columbia River – 500.0 mg/l;

(B) All other Fresh Water Streams and Tributaries – 100.0 mg/l;

340-41-205(2)(p)

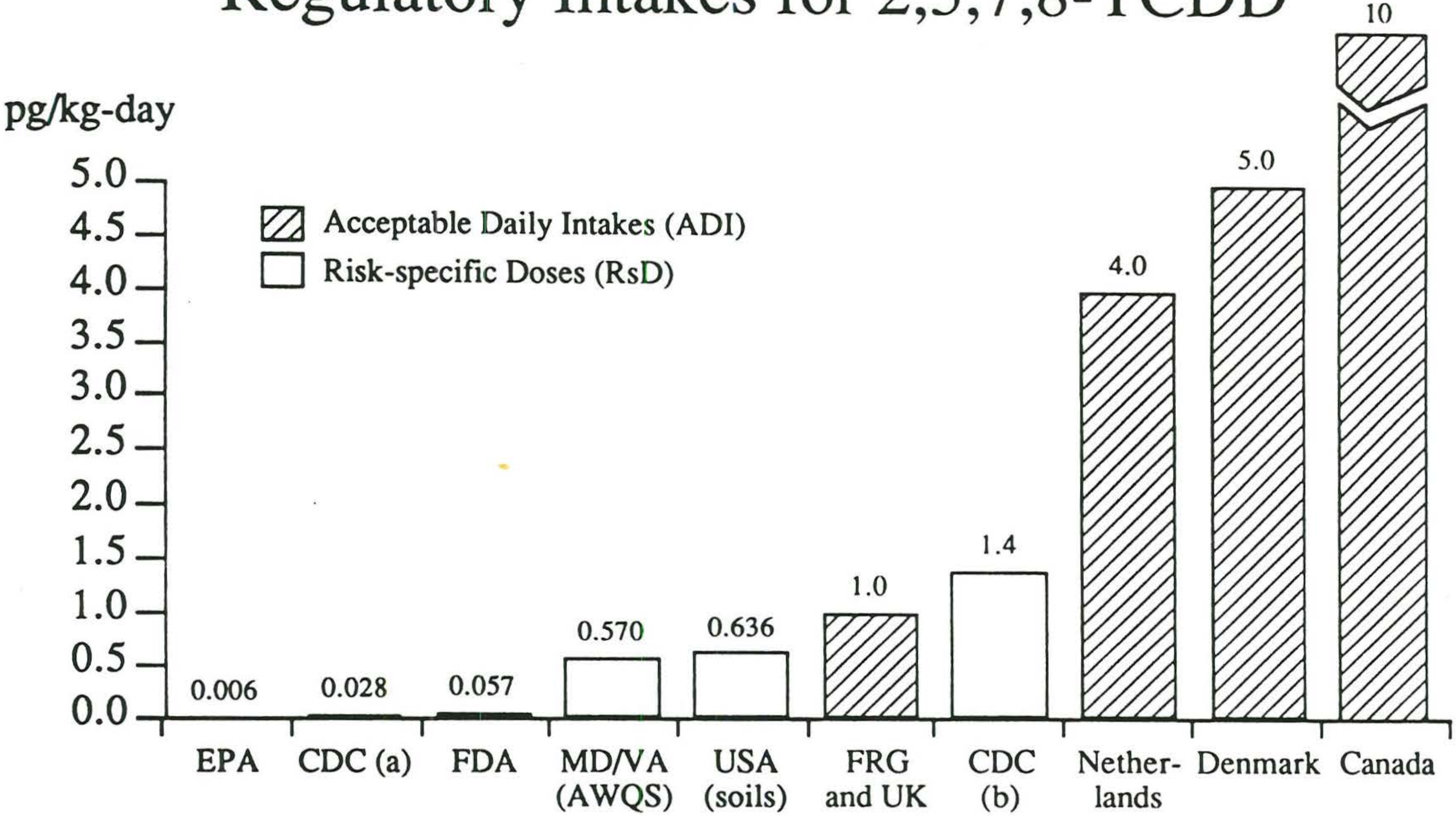
(p) Toxic Substances:

(A) Toxic substances shall not be introduced above natural background levels in the waters of the state in amounts, concentrations, or combinations which may be harmful, may chemically change to harmful forms in the environment, or may bioaccumulate to levels that adversely affect public health, safety, or welfare; adquatic life; or other designated beneficial uses.

(B) Levels of toxic substances shall not exceed the most recent criteria values for organic and inorganic pollutants established by EPA and published in Quality Criteria for Water (1986). A list of the criteria is presented in Table 20.

(C) The criteria in paragraph (B) of this subsection shall apply unless data from scientifically valid studies demonstrate that the most sensitive designated beneficial uses will not be adversely affected by exceeding a criterion or that a more

Regulatory Intakes for 2,3,7,8-TCDD



CDC(a) most conservative figure of range
CDC(b) least conservative figure of range

Pathology Working Group (PWG, 1990)

Membership

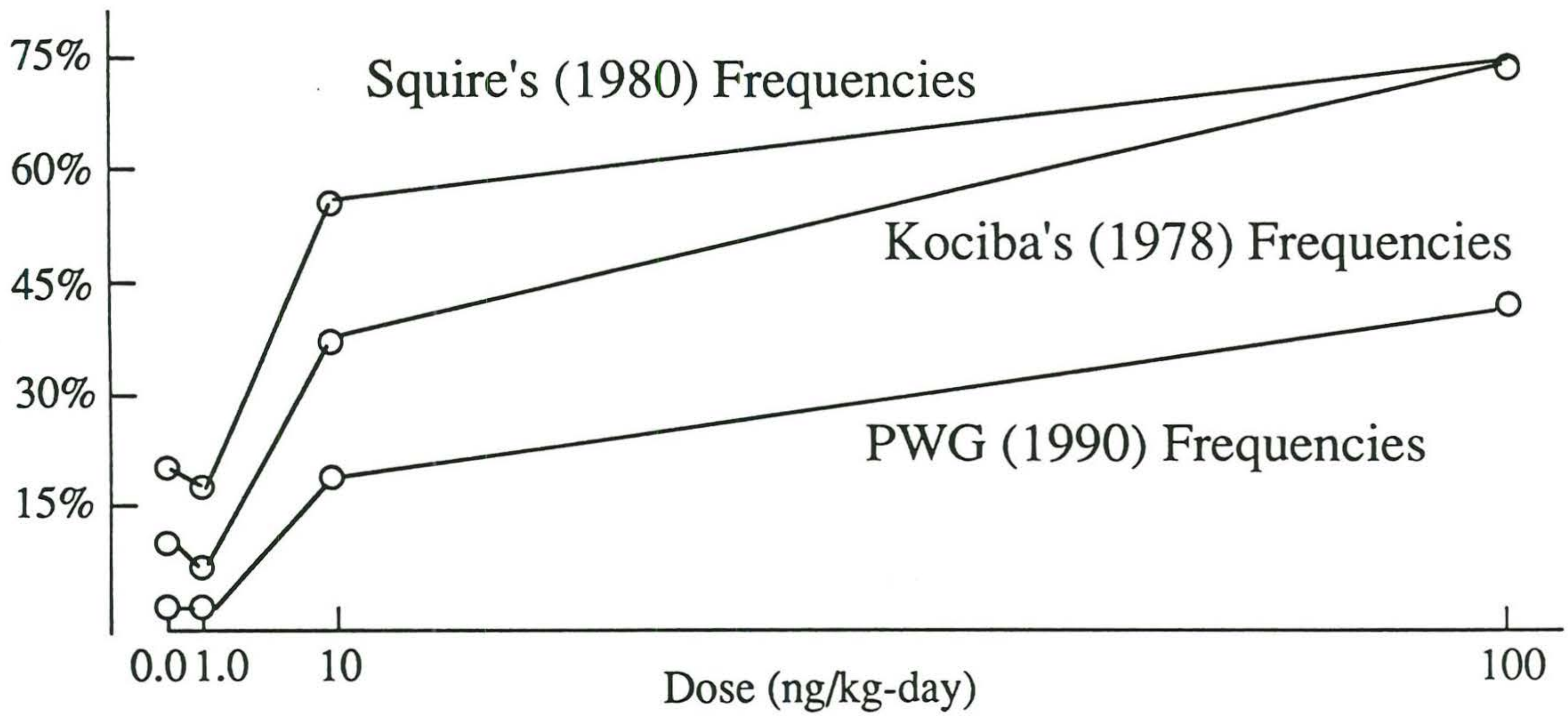
- Dr. Robert Sauer (Pathco)
- Dr. Robert Maronpot (NTP)
- Dr. Paul Newberne (Boston Univ.)
- Dr. James Popp (CIIT)
- Dr. Gerald Ward (NCI)
- Dr. W. Ray Brown (Res. Path. Serv.)

Observers

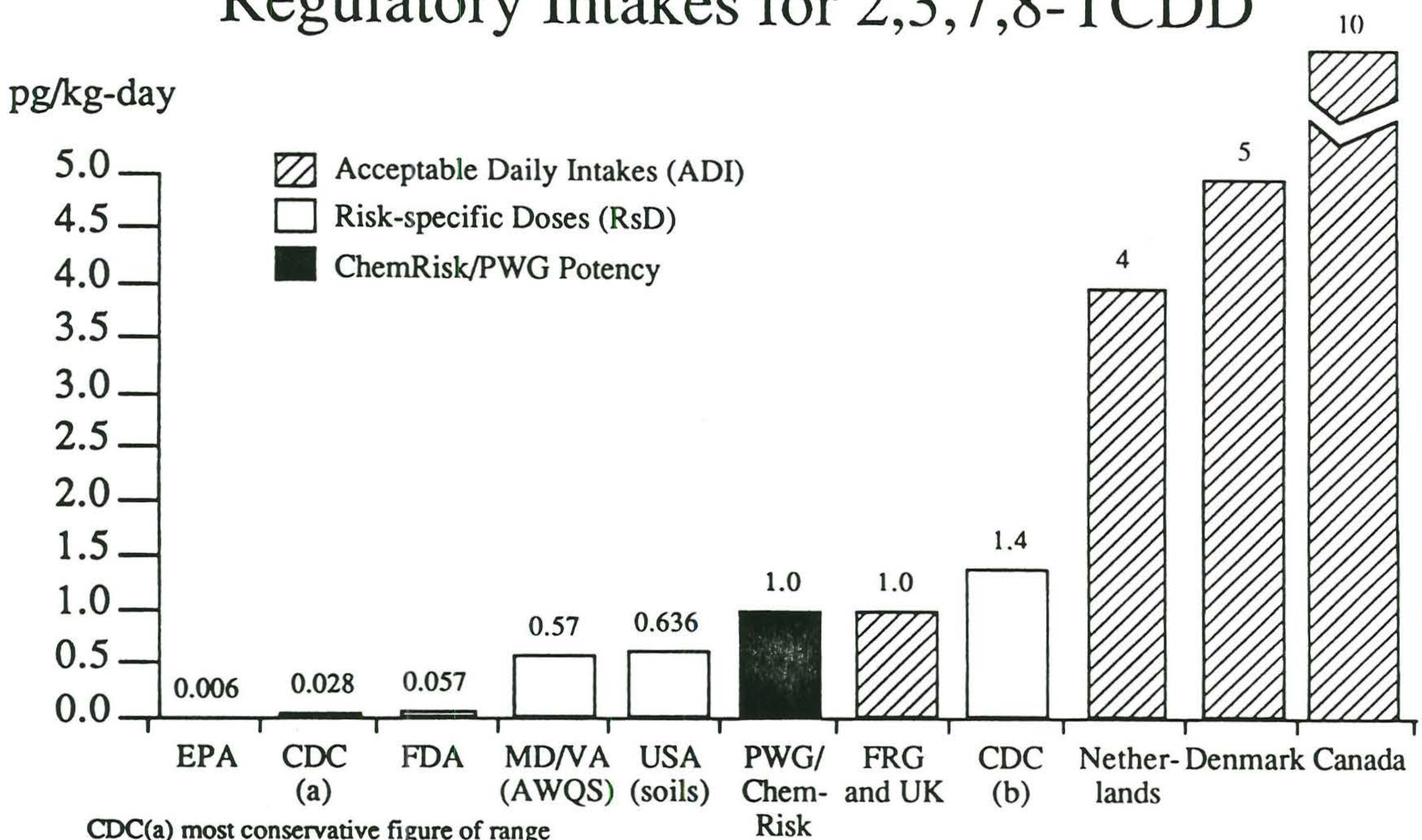
- Dr. R.A. Squire (Johns Hopkins)
- Dr. R.W. Moch (FDA)
- Dr. D. Singh (EPA)
- Dr. A. Chiu (EPA)

– 1980 EPA Evaluation –

The Observed Frequencies of Hepatocellular "Neoplastic Nodule" or Carcinoma in Female Sprague-Dawley Rats Reported by Kociba et al. (1978), Squire (USEPA, 1985) and PWG (1990)

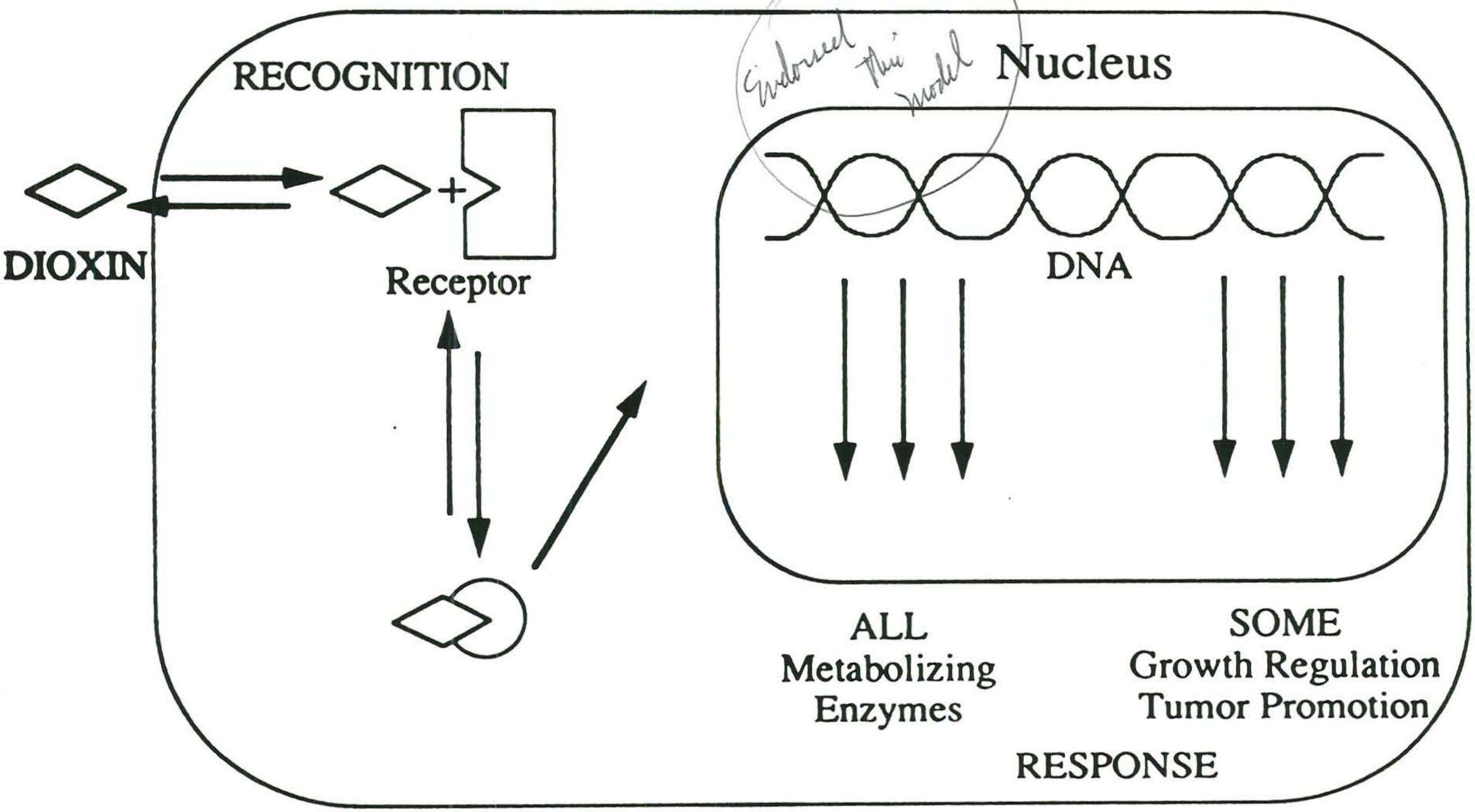


Regulatory Intakes for 2,3,7,8-TCDD



CDC(a) most conservative figure of range
CDC(b) least conservative figure of range

Mechanism of Dioxin Action on Target Cells



Is 1-10 pg/kg-day health protective?

RSD (10^{-5}) based on PWG (1990)/ChemRisk (1990)

- 1 pg/kg-day

ADI for chronic reproductive effects

- 13 pg/kg-day

RfD for carcinoma/adenoma

- 10 pg/kg-day

TDI for receptor-mediated induction

- 10 pg/kg-day

ADI for carcinoma

- 20-80 pg/kg-day

RfD for immunotoxic effects

- 60 pg/kg-day

RfD for acute reproductive effects

- 300 pg/kg-day

Scientific evidence supports that a dose of 1 to 10 pg TCDD/kg-day is health-protective.

OSPIRG
The Oregon State Public Interest Research Group
1536 SE 11th Portland, Oregon 97214 (503) 231-4181, FAX: (503) 231-4007

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 13 1991
OFFICE OF THE DIRECTOR

To the Environmental Quality Commission
Comments of
Quincy Sugarman, Environmental Advocate for the
Oregon State Public Interest Research Group
in opposition to
Petition to Amend Water Quality Standard for Dioxin (TCDD)
6-14-91

Thank you for accepting these written comments on the petition to amend Oregon's ambient water quality standard for dioxin. My name is Quincy Sugarman, and I am an environmental advocate for the Oregon State Public Interest Research Group. OSPIRG is a statewide consumer and environmental research and advocacy organization with 35,000 members. We are opposed to the proposed amendments to the state standard for dioxin and urge you to deny the petition to do so.

General Background Information

The petition before you is to re-examine the state's ambient water quality standard for 2,3,7,8-dibenzo-p-dioxin (2,3,7,8-TCDD or dioxin). This chemical is a by-product of certain manufacturing processes, including the chlorine-based bleaching of pulp in pulp and paper mills. These mills release dioxins, and other chemicals, in their effluent that goes into Oregon's rivers.

Dioxins bioaccumulate in organisms at the higher end of the food chain, such as certain fish, birds of prey and humans. TCDD is a potent carcinogen in laboratory animals, and exposure to it has been linked to other chronic diseases. The state Department of Environmental Quality has enacted water quality standards to reflect its potential harm. DEQ ambient standards of .013 parts per quadrillion (ppq) are designed to limit dioxin discharges to levels that would cause fewer than one cancer case per million people.

No Weakening of State Standards

OSPIRG is opposed to weakening of the state standard for 2,3,7,8-TCDD. The current standard is strict, and it reflects real concern for the potency of the chemical concerned. It is a feasible standard as well. The Pope & Talbot pulp mill in Oregon has been working with DEQ to devise technological ways that it can meet this standard. Pope & Talbot expects to meet the standard by 1993.

By maintaining this tough standard in rules, Oregon sends an important message to dioxin-producing industries that toxic

discharges must be reduced or eliminated to protect the public health and environment in Oregon. To reduce their discharges to this limit, industry is trying improved, more efficient bleaching technologies. Alternatively, particular facilities may try bleaching pulp without chlorine, a technique that eliminates all organochlorine discharges.

Industry should be moving to eliminate the use of chlorine and therefore eliminate all the organochlorine toxics that such use creates. Raising the allowable limit of dioxin to be discharged constitutes a step backward in protecting the quality of Oregon's environment.

Pollution Prevention

Statewide we need to protect the quality of Oregon's rivers, by preventing further contamination. In 1989 OSPIRG worked in the state legislature for passage of the Oregon Toxics Use Reduction Act. This is one of the first laws in the country to focus on reducing pollution at the front-end of the process, by encouraging industry to reduce the initial use of toxic chemicals to prevent later pollution problems.

Tough standards for discharges of potent toxics, like dioxin, also encourage reducing the use of toxic chemicals. Pollution prevention, through toxics use reduction, reduces risks to public environmental health and reduces later expensive cleanup costs.

On June 8, 1991, the Eugene Register-Guard editorialized on this subject saying "a cautious approach offers the best protection for human health and river-dwelling fish and wildlife. At least one pulp and paper mill intends to grow and prosper while meeting the standard that recognizes the wisdom of caution. The other two should be expected to do the same."

We urge you to deny this petition and to preserve the ambient water quality standard currently in rules. Thank you for accepting my comments.

OSPIRG
The Oregon State Public Interest Research Group
1536 SE 11th Portland, Oregon 97214 (503) 231-4181, FAX: (503) 231-4007

To the Environmental Quality Commission
Comments of
Quincy Sugarman, Environmental Advocate for the
Oregon State Public Interest Research Group
in opposition to
Petition to Amend Water Quality Standard for Dioxin (TCDD)
6-14-91

Thank you for accepting these written comments on the petition to amend Oregon's ambient water quality standard for dioxin. My name is Quincy Sugarman, and I am an environmental advocate for the Oregon State Public Interest Research Group. OSPIRG is a statewide consumer and environmental research and advocacy organization with 35,000 members. We are opposed to the proposed amendments to the state standard for dioxin and urge you to deny the petition to do so.

General Background Information

The petition before you is to re-examine the state's ambient water quality standard for 2,3,7,8-dibenzo-p-dioxin (2,3,7,8-TCDD or dioxin). This chemical is a by-product of certain manufacturing processes, including the chlorine-based bleaching of pulp in pulp and paper mills. These mills release dioxins, and other chemicals, in their effluent that goes into Oregon's rivers.

Dioxins bioaccumulate in organisms at the higher end of the food chain, such as certain fish, birds of prey and humans. TCDD is a potent carcinogen in laboratory animals, and exposure to it has been linked to other chronic diseases. The state Department of Environmental Quality has enacted water quality standards to reflect its potential harm. DEQ ambient standards of .013 parts per quadrillion (ppq) are designed to limit dioxin discharges to levels that would cause fewer than one cancer case per million people.

No Weakening of State Standards

OSPIRG is opposed to weakening of the state standard for 2,3,7,8-TCDD. The current standard is strict, and it reflects real concern for the potency of the chemical concerned. It is a feasible standard as well. The Pope & Talbot pulp mill in Oregon has been working with DEQ to devise technological ways that it can meet this standard. Pope & Talbot expects to meet the standard by 1993.

By maintaining this tough standard in rules, Oregon sends an important message to dioxin-producing industries that toxic

discharges must be reduced or eliminated to protect the public health and environment in Oregon. To reduce their discharges to this limit, industry is trying improved, more efficient bleaching technologies. Alternatively, particular facilities may try bleaching pulp without chlorine, a technique that eliminates all organochlorine discharges.

Industry should be moving to eliminate the use of chlorine and therefore eliminate all the organochlorine toxics that such use creates. Raising the allowable limit of dioxin to be discharged constitutes a step backward in protecting the quality of Oregon's environment.

Pollution Prevention

Statewide we need to protect the quality of Oregon's rivers, by preventing further contamination. In 1989 OSPIRG worked in the state legislature for passage of the Oregon Toxics Use Reduction Act. This is one of the first laws in the country to focus on reducing pollution at the front-end of the process, by encouraging industry to reduce the initial use of toxic chemicals to prevent later pollution problems.

Tough standards for discharges of potent toxics, like dioxin, also encourage reducing the use of toxic chemicals. Pollution prevention, through toxics use reduction, reduces risks to public environmental health and reduces later expensive cleanup costs.

On June 8, 1991, the Eugene Register-Guard editorialized on this subject saying "a cautious approach offers the best protection for human health and river-dwelling fish and wildlife. At least one pulp and paper mill intends to grow and prosper while meeting the standard that recognizes the wisdom of caution. The other two should be expected to do the same."

We urge you to deny this petition and to preserve the ambient water quality standard currently in rules. Thank you for accepting my comments.

OSPIRG
The Oregon State Public Interest Research Group
1536 SE 11th Portland, Oregon 97214 (503) 231-4181, FAX: (503) 231-4007

**To the Environmental Quality Commission
Comments of
Quincy Sugarman, Environmental Advocate for the
Oregon State Public Interest Research Group
in opposition to
Petition to Amend Water Quality Standard for Dioxin (TCDD)
6-14-91**

Thank you for accepting these written comments on the petition to amend Oregon's ambient water quality standard for dioxin. My name is Quincy Sugarman, and I am an environmental advocate for the Oregon State Public Interest Research Group. OSPIRG is a statewide consumer and environmental research and advocacy organization with 35,000 members. We are opposed to the proposed amendments to the state standard for dioxin and urge you to deny the petition to do so.

General Background Information

The petition before you is to re-examine the state's ambient water quality standard for 2,3,7,8-dibenzo-p-dioxin (2,3,7,8-TCDD or dioxin). This chemical is a by-product of certain manufacturing processes, including the chlorine-based bleaching of pulp in pulp and paper mills. These mills release dioxins, and other chemicals, in their effluent that goes into Oregon's rivers.

Dioxins bioaccumulate in organisms at the higher end of the food chain, such as certain fish, birds of prey and humans. TCDD is a potent carcinogen in laboratory animals, and exposure to it has been linked to other chronic diseases. The state Department of Environmental Quality has enacted water quality standards to reflect its potential harm. DEQ ambient standards of .013 parts per quadrillion (ppq) are designed to limit dioxin discharges to levels that would cause fewer than one cancer case per million people.

No Weakening of State Standards

OSPIRG is opposed to weakening of the state standard for 2,3,7,8-TCDD. The current standard is strict, and it reflects real concern for the potency of the chemical concerned. It is a feasible standard as well. The Pope & Talbot pulp mill in Oregon has been working with DEQ to devise technological ways that it can meet this standard. Pope & Talbot expects to meet the standard by 1993.

By maintaining this tough standard in rules, Oregon sends an important message to dioxin-producing industries that toxic

discharges must be reduced or eliminated to protect the public health and environment in Oregon. To reduce their discharges to this limit, industry is trying improved, more efficient bleaching technologies. Alternatively, particular facilities may try bleaching pulp without chlorine, a technique that eliminates all organochlorine discharges.

Industry should be moving to eliminate the use of chlorine and therefore eliminate all the organochlorine toxics that such use creates. Raising the allowable limit of dioxin to be discharged constitutes a step backward in protecting the quality of Oregon's environment.

Pollution Prevention

Statewide we need to protect the quality of Oregon's rivers, by preventing further contamination. In 1989 OSPIRG worked in the state legislature for passage of the Oregon Toxics Use Reduction Act. This is one of the first laws in the country to focus on reducing pollution at the front-end of the process, by encouraging industry to reduce the initial use of toxic chemicals to prevent later pollution problems.

Tough standards for discharges of potent toxics, like dioxin, also encourage reducing the use of toxic chemicals. Pollution prevention, through toxics use reduction, reduces risks to public environmental health and reduces later expensive cleanup costs.

On June 8, 1991, the Eugene Register-Guard editorialized on this subject saying "a cautious approach offers the best protection for human health and river-dwelling fish and wildlife. At least one pulp and paper mill intends to grow and prosper while meeting the standard that recognizes the wisdom of caution. The other two should be expected to do the same."

We urge you to deny this petition and to preserve the ambient water quality standard currently in rules. Thank you for accepting my comments.

VICTOR M. SHER (WSB# 16853)
TODD D. TRUE (WSB# 12864)
REBECCA E. TODD (WSB# pending)
Sierra Club Legal Defense Fund
216 First Avenue S., Suite 330
Seattle, Washington 98104
(206) 343-7340

BEFORE THE ENVIRONMENTAL QUALITY COMMISSION
OF THE STATE OF OREGON

In the Matter of the Petition of James River II, Inc. and Boise Cascade Corporation to Amend Subparagraph (2)(p)(B) of Oregon Administrative Rules Chapter 340, Division 41, Sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965.	MEMORANDUM IN OPPOSITION TO THE PETITION FOR RULE AMENDMENT

I. Introduction

This Memorandum in Opposition to the Petition for Rule Amendment is submitted by the Sierra Club Legal Defense Fund, Inc. on behalf of the American Oceans Campaign, the Campaign for Puget Sound, the Dioxin/Organochlorine Center, Friends of the Earth, National Audubon Society, Puget Sound Alliance, the Washington Environmental Council, and the Washington Toxics Coalition.[1] These organizations are non-profit environmental groups dedicated to and actively working toward the preservation and protection of water resources and all life dependent on them.

---

[1] American Oceans Campaign, 4007 Latona Avenue NE Seattle, WA 98105; Campaign for Puget Sound, P.O. Box 2807 Seattle, WA 98111-2807; Dioxin/Organochlorine Center, 1247 Willamette Street Eugene OR 97401; Friends of the Earth, 4512 University Way NE Seattle WA 98105; National Audubon Society, P.O. Box 462 Olympia, WA 98502; Puget Sound Alliance, 4516 University Way NE Seattle WA 98105; Washington Environmental Council, 5200 University Way NE Seattle WA 98105; and the Washington Toxics Coalition, 4516 University Way NE Seattle WA 98105.

In specific, the organizations seek to reduce and eliminate entirely the discharge of toxic organochlorines to the waters of the Pacific Northwest, including 2,3,7,8 tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD), commonly known as dioxin.[2]

We strongly oppose the Petition for Rule Amendment and urge the Environmental Quality Commission to deny the Petition. We are a group of national, regional, and Washington State environmental groups concerned about the water quality of the Pacific Northwest, Oregon, and the water resources shared by Oregon, Washington, and Idaho. The Columbia River receives much of the region's pulp and paper mill organochlorine discharge and for many hundreds of miles is a shared resource and border for Oregon and Washington.[3] The ambient water quality standard for 2,3,7,8-TCDD in Oregon necessarily affects these shared ecosystems and the livelihood and recreation of those living in both states. We are also concerned with the precedential implications that the Petition for Rule Amendment may have nationwide and for the Pacific Northwest.

---

[2] "Dioxin" as it refers to 2,3,7,8-TCDD is actually a misnomer. Dioxins are a family of approximately 75 separate chlorinated organic compounds, each of which is characterized by the existence of two oxygen atoms connecting two chlorinated benzene rings.

[3] The interdependence of the Pacific Northwest states with regard to the Columbia River has been recognized by the formation by Oregon and Washington of the Bistate Commission for the Columbia River, and the basin-wide protection strategies for the River established by the Environmental Protection Agency [EPA], including the establishment of Total Maximum Daily Loadings and Individual Control Strategies pursuant to the Federal Water Pollution Control Act, 33 U.S.C. §§ 1313(d) and 1314(l), respectively.

2,3,7,8-TCDD is a known human carcinogen, teratogen, and immunosuppressant.[4] Other types of damage caused by 2,3,7,8-TCDD include skin disorders, reproductive disorders, hormonal and metabolic effects, developmental defects, damage to the liver, kidney and thymus, wasting syndrome, neurobehavioural effects, and learning disabilities.[5] Furthermore, 2,3,7,8-TCDD is

---

[4] Some pertinent papers regarding this include:

Fingerhut, Marilyn A., William E. Halperin, David A. Marlow, Laurie A. Piacitelli, Patricia A. Honchar, Marie H. Sweeney, Alice L. Greife, Patricia A. Dill, Kyle Steenland, and Anthony J. Suruda, Cancer Mortality in Workers Exposed to 2,3,7,8 Tetrachlorodibenzo-p-dioxin, The New England Journal of Medicine 324: 212-218 (1991).

Schwartz, E., A Proportionate Mortality Ratio Analysis of Pulp and Paper Mill Workers in New Hampshire, British Journal of Industrial Medicine 45:234-238 (1988).

Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 (1989).

Skene, S.A., I.C. Dewhurst, and M. Greenberg, Polychlorinated Dibenzo-p-dioxins and Polychlorinated Dibenzofurans: The Risks to Human Health: A Review, Human Toxicology 8:173-203 (1989).

[5] Some pertinent papers regarding this include:

Bowman, R.E., S.L. Schantz, M.L. Gross, and S.A. Ferguson, Behavioral Effects in Monkeys Exposed to 2,3,7,8-TCDD Transmitted Maternally During Gestation and for Four Months of Nursing, Chemosphere 18:235-242 (1989).

Fish and Wildlife Service, Dioxin Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review, Biological Report 85, May 1986.

Jacobson, Joseph L., Sandra W. Jacobson, and Harold E.B. Humphrey, Effects of In Utero Exposure to Polychlorinated Biphenyls and Related Contaminants on Cognitive Functioning in Young Children, Journal of Pediatrics 116:38-45 (1990).

Larsson, Ake, T. Andersson, L. Forlin, and J. Hardig, Physiological Disturbances in Fish Exposed to Bleached Kraft Mill Effluents, Wat. Sci. Tech. 20:67-76, 1988.

McCormack, Craig and David Cleverly, United States Environmental Protection Agency, Analysis of the Potential Populations at Risk From the Consumption of Freshwater Fish Caught Near Paper Mills, Draft Report, April 23, 1990.

Schantz, Susan L., and Robert E. Bowman, Learning in Monkeys Exposed Perinatally to 2,3,7,8 Tetrachlorodibenzo-p-dioxin (TCDD), Neurotoxicology and Teratology 11:13-19, 1989.

bioaccumulative, bioconcentrative, and persistent.[6]

Moreover, while 2,3,7,8-TCDD is the most toxic substance ever identified, and hence the most toxic of the organochlorines, chlorine bleaching pulp and paper production generates tons of chlorinated organics which are toxicologically equivalent to 2,3,7,8-TCDD. In other words, these other organochlorines act within the body and the environment in virtually the same toxicological manner as 2,3,7,8-TCDD. For example, in issuing a recent Fish Consumption Advisory for Lake Roosevelt, the Washington State Department of Health recognized that 90% of the dioxin toxicity is due to 2,3,7,8 tetrachlorodibenzofuran.[7] As one of the leading scientific experts has written,

---

Svensson, Bengt-Goran, Anita Nilsson, Marianne Hansson, Christopher Rappe, Bjorn Akesson, and Staffan Skerving, Exposure to Dioxins and Dibenzofurans Through the Consumption of Fish, The New England Journal of Medicine 116:8-12 (1991).

Swain, Wayland R., Human Health Consequences of Consumption of Fish Contaminated with Organochlorine Compounds, Aquatic Toxicology 11:357-377 (1988).

Tanabe, S., N. Kannan, An. Subramanian, S. Watanabe, and R. Tatsukawa, Highly Toxic Coplanar PCBs: Occurrence, Source, Persistency and Toxic Implications to Wildlife and Humans, Environmental Pollution 47:147-163 (1987).

[6] The toxicokinetic half-life of 2,3,7,8-TCDD in human tissue has been predicted to be approximately 5 to 8 years and the half-life in sediments is even longer. See, Bowman, R.E., S.L. Schantz, N.C.A. Weerasinghe, M.L. Gross, and D.A. Barsotti, Chronic Dietary Intake of 2,3,7,8 Tetrachlorodibenzo-p-dioxin (TCDD) at 5 or 25 Parts Per Trillion in the Monkey: TCDD Kinetics and Dose-Effect Estimate of Reproductive Toxicity, Chemosphere 18:243-252 at 250 (1989), and Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 at 458 (1989).

[7] Washington Department of Ecology, First Progress Report on Ecology's Dioxin/Furan Survey in Lake Roosevelt, Memorandum from Art Johnson, Dave Serdar, and Stuart Magoon to Carl Nuechterlein, August 8, 1990.

it is misleading to consider dioxin as a single entity, and the potential health risks are properly evaluated by taking into account exposures to mixtures of the hundreds of isomers and related compounds in this group.[8]

An approach, therefore, which focuses on the cancer risks from 2,3,7,8-TCDD necessarily underestimates cancer risks from pulp and paper mill effluent[9] and also ignores other arguably more important organismic and ecosystem level impacts from 2,3,7,8-TCDD such as adverse reproductive, developmental, and wildlife effects.

//

//

//

//

//

---

[8] Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 at 456 (1989).

[9] EPA itself recognizes that its cancer risk and attendant water quality standard of .013 ppq vastly underestimate the actual cancer risk suffered by certain sensitive populations. EPA estimates that a Native American adult consuming Columbia River Basin fish in an amount average for Native Americans per day contaminated with 6.5 parts per trillion (ppt) 2,3,7,8-TCDD equivalents exceeds the EPA threshold of concern for reproductive effects by over nine times. See, McCormack, Craig and David Cleverly, United States Environmental Protection Agency, Analysis of the Potential Populations at Risk From the Consumption of Freshwater Fish Caught Near Paper Mills, Draft Report, April 23, 1990.

Furthermore, in calculating the cancer risk and water quality standard for 2,3,7,8-TCDD, EPA assumed a fish consumption rate of only 6.5 grams per day, while actual fish consumption rates are approximately five times higher than this, and Native American fish consumption rates are approximately fifteen times higher. More realistic fish consumption rates, therefore, would make the cancer risk standards five to fifteen times higher, respectively. Id.

II. The Environmental Quality Commission Should Deny the Petition for Rule Amendment.

We strongly urge the Commission to deny the Petition for Rule Amendment filed by James River II and the Boise Cascade Corporation on May 23, 1991. A new rulemaking effort makes little sense in light of the limited resources of the State of Oregon. Indeed, Oregon initially adopted the .013 ppq standard established by EPA's Quality Criteria for Water 1986 with the express realization that the State had insufficient resources to undertake adequately a separate analysis of the health risks of 2,3,7,8-TCDD. As the State continues to suffer from limited resources, it continues to be ill-advisable for the State to undertake the complex analysis of human and environmental health risks from 2,3,7,8-TCDD necessary in deciding the water quality standard.

The adoption of a water quality criterion or standard is a significant task. EPA regulations mandate that every water quality criteria

> must be based on sound scientific rational and must contain sufficient parameters or constituents to protect the designated use. For waters with multiple use designations, the criteria shall support the most sensitive use.

40 C.F.R. § 131.11(b)(1)(1990). To adopt a new water quality standard requires that the rulemaking body employ "scientifically defensible methods" in assuring that the most sensitive uses are protected. 40 C.F.R. § 1313.11(b)(1)(1990) Establishing a new water quality standard for 2,3,7,8-TCDD would be extremely resource intensive, consuming the kind of time and energy that the State of Oregon has already recognized that it lacks.

Furthermore, the issue of the proper water quality standard for 2,3,7,8-TCDD will be debated shortly in another forum. EPA established the Total Maximum Daily Loadings [TMDL] for the Columbia River on February 25, 1991, regarding the total allowable discharge of 2,3,7,8-TCDD into the Basin. We anticipate legal challenges to the TMDL asserting that the .013 ppq standard is inadequate to protect human health and wildlife. In this connection, we believe that the appropriate water quality standard for 2,3,7,8-TCDD is zero, as detailed in Section III below.

Furthermore, from an ecosystem perspective it is nonsensical to allow mills in Oregon to discharge bioaccumulative and persistent organochlorines into the Columbia River Basin at 2.3 ppq, while Idaho and Washington mills comply with the applicable .013 ppq state standards, a difference of orders of magnitude. Fish, endangered Bald Eagles feeding on them, mink, otter, other wildlife, as well as sensitive human populations such as Native Americans, Asian Americans, and subsistence and sport fishers cannot differentiate among the 2,3,7,8-TCDD contamination from Oregon and that from other states. With regard to these especially sensitive groups, the State of Oregon has a duty to protect all of the people that compose the population of the State. While the .013 ppq standard is not adequately protective of either humans and wildlife, the suggested 2.3 ppq standard is even less so.

//

//

At this time and given the limited resources of the State, the most logical and protective course of action for the Commission is to deny the Petition for Rule Amendment.

III. Alternatively, If the Environmental Quality Commission Revisits the Rulemaking Procedure, the Proper Water Quality Standard for 2,3,7,8-TCDD is Zero.

The chlorine bleaching pulp and paper mills insist that new data indicate that the ambient water quality standard for 2,3,7,8-TCDD should be loosened. It is our position, and the position of the best scientific experts in the field, that available data militate for a <u>more stringent and protective</u> standard. These data include human reproductive and developmental effects, the effects on wildlife reliant on contaminated ecosystems, and the bioaccumulation, bioconcentration, and persistence of 2,3,7,8-TCDD in animal tissue and sediments. If the Petition for Rule Amendment is granted, we expect that the Commission will find itself in the midst of an extremely involved and complex dispute, with both sides presenting evidence and expert opinion regarding the proper water quality standard for 2,3,7,8-TCDD.

If the Commission does indeed elect to reopen rulemaking, we anticipate arguing that the standard for 2,3,7,8-TCDD is properly zero, that is, that the Commission should allow no discharges of 2,3,7,8-TCDD at all.

//

//

//

We are not the first to suggest to the State of Oregon that the water quality standard for 2,3,7,8-TCDD should be zero. Over the past several years, the United States Fish and Wildlife Service has consistently advised that because of the long-term health effects on wildlife that 2,3,7,8-TCDD discharges be reduced and eliminated:

> We recommend that the DEQ consider limiting the [pulp and paper mills' National Discharge Elimination System, or NPDES] permit[s] to a discharge of no dioxins...

Letter from the United States Fish and Wildlife Service to the Oregon Department of Environmental Quality dated July 10, 1989. Six months later the Fish and Wildlife reiterated that

> we believe it is appropriate for DEQ to develop a long-term goal that decreases and eventually eliminates the production of dioxin and other chlorinated byproducts.

Letter from the United States Fish and Wildlife Service to the Oregon Department of Environmental Quality dated January 19, 1990.

In recognition of the severity of the organochlorine contamination in the Columbia River Basin, the Fish and Wildlife Service most recently explained that

> considering the longevity of organochlorine compounds and the potential impact of small quantities of dioxins on fish, waterfowl, and endangered species, we recommend that the EPA strive towards limiting NPDES permits to zero discharge of dioxins to the Columbia River Basin.

Letter from the United States Fish and Wildlife Service to Region 10 EPA dated November 21, 1990. The zero discharge standard is the only standard for 2,3,7,8-TCDD that will adequately protect human, wildlife, and environmental health.

There are many technologies available and in use worldwide that reduce and eliminate the use of chlorine or chlorine compounds that are the necessary precursors for all chlorinated organic compounds. Without chlorine or chlorine compounds present in the production process, organochlorines cannot be formed and discharged to the environment. Many European mills and some North American mills currently employ chlorine-free technology in their pulp and paper production. Many if not all the mills in the United States are at the very least exploring ways in which they can reduce their use of chlorine and the subsequent discharge of toxic organochlorines.

Furthermore, the public is becoming increasingly aware of the human and environmental health risks associated with chlorine bleaching and is demanding chlorine-free pulp and paper products. The mill in Lyons Falls, New York is one example of a mill that has converted to a chlorine-free technology and has subsequently experienced an increase in its market share. As consumers increasingly demand chlorine-free paper products, those mills that can supply them are enjoying competitive success in the marketplace.

As has been long recognized elsewhere, there are no functional uses of pulp and paper products that demand the super bright whiteness normally achievable with chlorine bleaching processes. Non-chlorine bleaching renders pulp and paper products that are nearly as bright white as chlorine bleached products. These chlorine-free products are suitable for every use to which pulp and paper products are put today.

Because of the availability of chlorine-free technologies, the complete lack of need for chlorine bleached pulp and paper, and the serious and persistent risks to human and environmental health, if the Commission grants the Petition for Rule Amendment, we anticipate returning to urge the Commission to promulgate an ambient water quality standard of zero for 2,3,7,8-TCDD.

IV. Conclusion

On behalf of the organizations listed above, we offer this Memorandum in Opposition to the Petition for Rule Amendment. We will gladly provide the Commission with any of the data discussed above. As we have not had the opportunity to view all the information submitted by the mills, we are unable to respond directly to their particular scientific or other assertions. Should the Commission like us to provide a more detailed response to their specific claims, we will arrange to procure the mills' lengthy submission and provide a detailed scientific analysis for the Commission's review. That being said, however, we believe that the wisest, most protective, and most efficient course of

//

//

//

//

//

//

//

//

action for the Commission is to deny the Petition for Rule Amendment and we urge the Commission to do so.

Dated this 10th day of June, 1991.

Respectfully submitted,

Victor M. Sher /RET

VICTOR M. SHER

Todd D. True /RET

TODD D. TRUE

Rebecca E. Todd

REBECCA E. TODD

Sierra Club Legal Defense Fund, Inc.
216 First Avenue S. Suite 330
Seattle, WA 98014
(206) 343-7340

Attorneys for American Oceans Campaign, Campaign for Puget Sound, Dioxin/Organochlorine Center, Friends of the Earth, National Audubon Society, Puget Sound Alliance, Washington Environmental Council, and Washington Toxics Coalition.

Sent by telecopy to:

Chair William P. Hutchison, Jr.	(503) 223-5550
Vice Chair Emery N. Castle	(503) 737-1574
Commissioner Henry Lorenzen	(503) 276-3148
Commissioner Carol A. Whipple	(503) 584-2129
Commissioner William W. Wessinger	(503) 229-4689
Director Fred Hansen	(503) 229-6124

cc: Mr. Larry Edelman
Ms. Dana Rasmussen
Mr. Rick Albright
Ms. Adrianne Allen

NORTHWEST ENVIRONMENTAL ADVOCATES

June 10, 1991

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 10 1991
OFFICE OF THE DIRECTOR

Fred Hansen, Director
Oregon Department
of Environmental Quality
811 S.W. Sixth
Portland, OR 97204

Bill Hutchinson, Chair
Oregon Environmental Quality
Commission
Tooze, Shenker Holloway, & Duden
333 SW Taylor St.
Portland, OR 97204

Re: Notice of Consideration of Petition for Rule Amendment
(Water Quality Standard for 2,3,7,8-TCDD)

Dear Fred and Bill:

I am writing to urge the Commission to deny the pulp and paper industry's petition to change the criterion in the water quality standard for dioxin. There are numerous reasons for the Commission not to take up this issue, not the least of which is the fact that the Department recently reevaluated this standard in its most recent "triennial review." In addition, as I am sure you are aware, U.S. EPA is reexamining the criterion.

It would be redundant for the State of Oregon to reevaluate the very same issue that EPA is currently reviewing, and Oregon is certainly less well equipped to do so. It is also premature to second guess the outcome of that evaluation. In fact, EPA Administrator Reilly has urged that regulatory actions based on the existing dioxin criterion proceed as scheduled.

For as many reasons as the pulp and paper industry can come up with to argue for an increase in the allowable limits for dioxin, there are at least an equal number of arguments that the existing standard is not conservative enough. For example, the current criterion is based on a bioconcentration factor of 5,000. Yet studies show that the bioconcentration factor in fish can range up to 156,000. The existing dioxin standard does not take into account the other media by which dioxin contaminates human beings, i.e. inhalation, eating food other than fish. General human background exposure to dioxin compounds (1 to 10 parts per kilogram (equivalent to part per quadrillion) in toxicity equivalent units for all dioxins) is known to already exceed the acceptable daily intake set by EPA for protection against reproductive effects (1 part per quadrillion). In addition there are the synergistic and

additive effects caused by exposure to dioxin in tandem with other toxic pollutants.

Industry is fond of pointing out that the risk to humans from dioxin is far less than to lab rats, for which dioxin is clearly a hazard. Presumably industry would include other 'lower life forms' in its assessment of the hazards of dioxin. This is relevant to the Commission's decision because, whether or not the existing criterion for dioxin adequately protects human beings, it certainly does not take into account the increased effects dioxin has on wildlife. These effects are increased due to the lower body weight and greater consumption of contaminated aquatic life (e.g. fish) by eagles, mink, otter, and other pisciverous wildlife. States' water quality standards are supposed to protect the most sensitive beneficial uses. The Commission should not even consider this or any other petition to change the dioxin standard unless petitioners can demonstrate that a higher level of dioxin contamination will not result in a lower level of protection for the most sensitive uses.

It is an old ploy of industry's to seek to have the rules changed when it doesn't want to meet them. It is inexcusable when government accedes to this. The Commission should enforce the standards it has adopted, not bend them when the going gets tough for a segment of industry which has had the benefit of over-polluting public waters for many years.

Sincerely,

Eugene Rosolie for

Nina Bell
Executive Director

cc: Emery N. Castle
Henry Lorenzen
Carol Whipple
William W. Wessinger

GREENPEACE

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 10 1991
OFFICE OF THE DIRECTOR

7 June, 1991

Oregon Environmental Quality Commission
c/o Oregon DEQ Director's Office
811 S.W. 6th Avenue
Portland, OR 97204

Director
Oregon Department of Environmental Quality
811 S.W. 6th Avenue
Portland, OR 97204

Dear Commissioners and Director:

We understand that James River, Inc. and Boise Cascade Corp., along with several co-petitioners have asked the Commission and the DEQ to amend the state's ambient water quality standard for 2,3,7,8-TCDD from a current level 0.013 ppq to 2.3ppq.

We wish to offer comments regarding the wisdom of honoring such a petition that we hope you will make part of the public record in this decision.

INADEQUATE PUBLIC NOTICE

First we must question the lack of public notification involved in this pending decision. We have, on more than one occasion, asked to be placed on the DEQ notification list for any water quality actions the Department has pending, particularly with respect to pulp mills.

Our requests have to date been ignored, and we find that the only way to obtain a copy of a notice or a draft permit is to hear of its existence from a third party and then to call the DEQ to request a copy be sent us. Nor have we received word of final decisions regarding permits or any response to permit comments we have offered. To say that this archaic and haphazard method of public notice is deficient is an understatement. It is certainly not consistent with the mandate for public participation inherent in EPA's having delegated the water quality program to the state of Oregon.

That the petitioners themselves have the temerity to suggest they have identified all interested parties as the few listed in item 2 of the Commission Chair's notice, is absurd. A gutting of the state's water quality standard for the most potent chemical known to mankind is not something to be decided privately after consultation with just a few individuals.

Even the more narrow decision the Commission intends to make about whether or not to initiate a rulemaking that could potentially weaken the standard should have received broader notice, e.g. tribal governments, fishing interests, the state health department and those state and federal agencies charged with protecting wildlife (e.g. the U.S. Fish and Wildlife Service).

THRESHOLD MODEL CITED BY PETITIONERS AS FAVORING THE WEAKENING OF A STANDARD HAS NOT BEEN PEER REVIEWED

We remind the Commission that the much touted theory regarding a supposed threshold mechanism for 2,3,7,8-TCDD has not yet been peer reviewed. The forum in which it was first advanced, at a Banbury conference last fall, has itself become known for the controversy it created among attendees (see attachment 1). No version of the theory has yet been published in the scientific literature, and the theory has been challenged by other dioxin scientists (see attachments 2, 3).

EPA's own review of it's dioxin standard is still underway and far from finalization, and any attempt by the state of Oregon to presuppose EPA's conclusions would be ill-advised. EPA Administer William Reilly himself warned against second guessing the Agency's dioxin review, advising that in the interim state governments should go on with business as usual.

There is also new evidence coming from other quarters that tends to refute the threshold theory cited so enthusiastically by the petitioners. Abstracts for two papers to be presented at this fall's dioxin symposium are attached which argue against reliance on such a theory (see attachment 4).

Moreover, a paper by Sargent, et al published in a recent issue of Carcinogenesis (see attachment 5) suggests alarmingly that even non-planar PCB's can act by a mechanism identical to that of coplanar compounds such as 2,3,7,8-TCDD, and that exposure to mixtures resulted in superadditive effects. The authors further state that humans already are exposed to levels at which adverse effects would certainly be occurring. This in turn suggests why the epidemiology concerning exposure to 2,3,7,8-TCDD is at best equivocal, except in very exaggerated doses, as was indeed the case for a recently published NIOSH study (see attachment 6).

EVIDENCE CITED BY PETITIONERS REGARDING BIOCONCENTRATION IN FISH AND FISH CONSUMPTION RATES DIFFERS DRAMATICALLY FROM THAT OFFERED BY MORE CREDIBLE SOURCES

Petitioners suggest that the prevailing way of estimating bioconcentration (BCF) factors in fish used to calculate the current standard should be scrapped, and that a different (less conservative) method for estimating BCF's should be substituted. The method they suggest yields a number in the same ballpark as

the existing one. Yet there is much evidence from EPA's lab in Duluth to suggest that fish are far better at taking up and storing dioxin than the 5000 factor now in use supposes (see attachments 7, 8), and the Agency has requested funds in its 1992 budget to re-evaluate its BCF assumptions.

In fact it has been shown that even Columbia River salmon, species thought to be more protected from uptake because of their mobility and feeding patterns, are harboring levels of dioxin in their edible tissues (see attachment 9).

Patterns of human fish consumption in the Pacific Northwest also argue for a much stronger standard. EPA has long acknowledged that the average fish consumption rate of 6.5 grams per day per person assumed in the setting of its current standard seriously underestimates actual eating patterns, and this has been confirmed by surveys in several states. Moreover, work by EPA's Cleverly and McCormack indicates that Columbia River sports and subsistence fishers, Native Americans, and Asian Americans eat far more fish than the levels suggested by petitioners (see attachment 10). One wonders how petitioners could have arrived at the impossibly low figures they suggest.

Petitioners also make the illogical claim that only fish consumption from the Columbia River need be considered, irrespective of the rest of one's fish diet, as if to suppose that all other sources of fish (or food) are free from contamination.

THE STATE HAS A DUTY TO PROTECT US FROM OTHER HARM THAN JUST CANCER, AND FROM OTHER POLLUTANTS THAN JUST 2,3,7,8-TCDD

Petitioners make mention of Keenan, et al's re-evaluation of the Kociba rat study from which EPA's current acceptable daily intake is derived. They suggest that we should take heart from the fact that slightly more than half a team of 9 scientists funded by the industry should find that many of the liver lesions identified by Kociba as cancerous might only be pre-cancerous after all. A critique of this study is enclosed.

In any case, it is hardly reassuring to expect that one's liver be riddled with dioxin-induced lumps and bumps of any kind. We similarly find no comfort in the fact that women thoughout the industrialized world are passing dioxins and other organo-chlorines on to future generations through the placenta and via breast-feeding.

Studies on primates have shown that dioxins can cause profound behavioral and reproductive effects at very low doses. The petitioners ignore all non-cancerous effects in arguing for a weaker standard.

It must also be noted that 2,3,7,8-TCDD never occurs in

isolation. Discharges from the pulp and paper industry include other dioxins and furans and numerous other compounds which exhibit similar mechanisms of toxicity. The Sargent study mentioned above gives added weight to the likelihood that these compounds can act synergistically.

THE STATE HAS A DUTY TO PROTECT THE ENVIRONMENT AS WELL AS HUMAN HEALTH

Petitioners have offered no evidence to suggest that a weakened ambient water quality standard will be sufficiently protective of aquatic life or fish-eating birds and mammals.

Nor have petitioners demonstrated that a weakening of the current dioxin standard will not adversely effect bald eagle populations on the lower Columbia River, as required under the Endangered Species Act. Much evidence already exists to suggest that dioxins and other organochlorines are negatively impacting these birds. The pending listing of various wild salmon species will further increase the burden of proof necessary to justify any continued discharge of dioxin and other organochlorines.

A RELAXING OF THE DIOXIN STANDARD AS PROPOSED BY INDUSTRY WILL NOT RELIEVE THE INDUSTRY OF ANY FINANCIAL BURDEN FOR POLLUTION CONTROL

The same technologies that must be implemented by petitioners to meet the state's current dioxin standard will in any case be required in order to meet the technology-based standards already in their NPDES permits. Indeed, the longer the industry waits to install new bleaching technology, the greater will be their ultimate financial burden.

Capital costs for equipment will only be more expensive, and the money invested in stopgap measures such as chlorine-dioxide generators will only be money wasted. The U.S. industry can also be expected to lose market share in Europe as a result of its recalcitrance, as is already proving the case in Canada. Fletcher Challenge's failure to produce chlorine-free pulp for its foreign market has already cost them an estimated $ 5 million dollars in loss of sales.

THE ONLY ACCEPTABLE STANDARD FOR DIOXIN IS ZERO, AND THE STATE OF OREGON SHOULD TAKE IMMEDIATE STEPS TO ELIMINATE ALL KNOWN SOURCES

Dioxin is the most intensively studied compound in history, and will doubtless remain the darling of the scientific community for years to come. Even so we still do not know its precise toxicity to humans, and given the degree to which we are all already contaminated with dioxin and dioxin-like compounds, we probably never will. There is simply no such thing as a control group to serve as a baseline.

But what we do know is serious enough to make moot any further quibbling about precisely how much is too much dioxin. What we know is more than enough to justify elimination of all known sources.

We urge the Department and the Commission to deny the petition to set a weaker dioxin standard, and instead use your limited resources to moving the pulp and paper industry into chlorine-free technology. The technologies exist, and only await implementation.

Sincerely,

Shelley Stewart

Shelley Stewart
U.S. Pulp/Paper Project

***

Please note that these comments are printed on chlorine-free paper imported from Europe. No North American manufacturer has yet been willing to produce chlorine-free bleached office or printing paper.

ATTACHMENT 1

UNIVERSITY OF MARYLAND AT BALTIMORE

The University Program In Toxicology
660 West Redwood Street
Howard Hall, Room 544
Baltimore, Maryland 21201-1596
(301) 328-8196

January 29, 1991

Dr. Jan Witkowski
Director
Banbury Center
Cold Spring Harbor Laboratory
P O Box 534
Cold Spring Harbor, NY 11724

Dear Dr. Witkowski:

I was a participant in the recent Banbury Conference on "Biological Basis for Risk Assessment of Dioxins and Related Compounds" held at the Banbury Center in October 1990. I am writing you becuase I have just been informed of a very disturbing result of that conference, a press release sent out by a public relations firm along with statements by Drs Scheuplein, van der Heiden, and Gallo purporting to represent the "consensus" views of the participants at that conference with espect to regulatory conclusions related to risk assessment of dioxins. I only learned of this press release from a reporter who called me last week (Marguerite Holloway of Scientific American).

This press release, copy enclosed, was never shown to me or to most of the participants in the conference, as far as I know. Thus, in terms of process alone, it should not be represented as a "consensus" document. Morover, its contents do not accurately reflect the views of all participants, or even a consensus of those views, as best I can determine. I resent the circulation of this press release as reflecting the views of a meeting in which I was a participant, and I feel that my name attached to it somehow implies my agreement with it.

I am in fact rather astounded by such a product from a Banbury Conference. While it was rather obvious to some of us that the organizers, and some of the sponsors, of this confernece had some trans-scientific objectives in mind related to regulations concerning dioxin, I had expected that the Banbury Center would be able to keep these motives under control. The press releases and statements imply that a major focus of the conference was a discussion of the regulatory risk assessments that have been applied to the dioxins; this was not the focus of this meeting. I agreed to participate based upon my previously held high regard for Banbury and Cold Spring Harbor. I did not expect to be manipulated by industry and government spokespeople

(who are not dioxin researchers, incidentally) to be made into a supporter of their political views on dioxins and risk assessment. This is particularly annoying to me because I was invited to present the main conference paper on the topic of the scientific basis for dioxin risk assessment. In this paper, I have attempted to present the complexity of integrating the basic molecular biology of dioxins into a receptor-based model. I do not feel that the state of knowledge on this complex topic can be reduced to a simplistic press release.

The preparation and release of these documents by Drs Scheuplein, van der Heijden, Carlo, and Gallo, with the assistance of a public relations firm, discredits all of us. It challenges the precious institution of free scientific discussion, epitomized by such places as Banbury, Dahlem, and the Gordon conferences. I hope you believe that I would be just as angry if this action had been taken by an environmental group. I trust you will take aciton to dissociate Banbury from this attempt to manipulate science and scientists. Because these people have acted without consulting the rest of us, and because I have heard about this only through the press, I am with great regret also sending this letter to the persons shown under my signature, as well as to my colleagues at the conference, an action not taken by these people.

Yours sincerely,

Ellen K Silbergeld

Ellen Silbergeld, PhD
Visiting Professor of Toxicology and
Adjunct Professor of Pharmacology
and Experimental Therapeutics

cc: Leslie Roberts, Science
Marguerite Holloway, Scientific American
Cristine Russell, Washington Post
Chris Joyce, New Scientist
Judy Randall, The Economist
Betty Mushak, NIEHS
William Farland, EPA

attendees, Banbury Conference on Dioxins

History Lessons

Warfare analysts offer some disturbing—and hopeful—news

Political leaders always claim to be steering us by the lights of history toward a peaceful future. But what does a comprehensive analysis of our past actually reveal about our present course? A pessimist could conclude that our leaders are completely misreading—or misrepresenting—history. An optimist could find hope that warfare might become obsolete anyway—if the tentative spread of democracy worldwide continues.

These conclusions are both supported by the Correlates of War project, a computerized storehouse of information on 118 wars (defined as conflicts leading to at least 1,000 deaths) and more than 1,000 lesser disputes from the early 1800s to the present. Researchers at the University of Michigan created the data base in the 1970s to find statistical associations between warfare and various economic, political and social factors.

The data offer no support for the bromide "peace through strength," according to J. David Singer, a political scientist at Ann Arbor who oversees the Correlates project. A buildup of military armaments, far from deterring war, is one of the most frequent precursors of it. At the very least, Singer says, such a finding suggests that the U.S. policy of supplying arms to nations in an unstable region—such as the Middle East—is seriously flawed.

There is also no evidence that alliances help to keep the peace. In fact, a nation's participation in one or more alliances increases its risk of warfare, Singer says, particularly against its allies. History even casts doubt on the argument—used by the U.S. to justify both its current war against Iraq and its past one against Vietnam—that allowing aggression to proceed unchecked always leads to more aggression. Although Hitler's Europe certainly provides an important counterexample, Correlates of War data yielded little statistical correlation between warfare in a given region and prior unchecked aggression, Singer says.

A somewhat more hopeful finding

A Press Release on Dioxin Sets the Record Wrong

When the Chlorine Institute shopped around for a place to hold a scientific conference, they did not want just any host. "We were looking for an organization that was squeaky clean, that would not in any way, shape or form be questioned about the conference," says Robert G. Smerko, president of the Washington, D.C.–based institute, which is supported by some 170 chemical, paper and other manufacturers.

Smerko seemed to have met his requirements when he finally landed Cold Spring Harbor Laboratory. Last October the laboratory's respected Banbury Center held a conference—jointly sponsored by the Chlorine Institute and the Environmental Protection Agency—on the toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, or TCDD. That chlorinated compound achieved notoriety during the Vietnam War, when it was identified as a contaminant of the defoliant Agent Orange. It remains controversial because it is found in some commercial herbicides and is produced in other chemical processes, such as paper bleaching.

Cold Spring Harbor Laboratory may have been squeaky clean, but the conference apparently was not. And the outcome of that meeting—attended by 38 of the world's dioxin experts, few of whom say they knew it was industry sponsored—is every bit as controversial as the substance that was the topic of discussion.

The issue is a press release sent out at the conclusion of the meeting by the Chlorine Institute's public relations firm, Daniel J. Edelman, Inc. It announced that the experts had agreed on a model for the toxicity of dioxin that "allows for the presence of a substance in the environment, with no risk experienced below a certain level of exposure." The release said that the scientists had rejected a linear exposure model, in which any level of exposure would have a biological effect, in favor of a receptor-based model that implies a threshold level. (This part of the release was approved by Cold Spring Harbor Laboratory, says the Banbury Center's director, Jan A. Witkowski—although he now says Edelman made several changes after he saw it.)

Such a consensus, of course, would have implications for setting permissible levels of the substance in the environment. But those at the conference insist that no such agreement was reached. "There was no consensus in terms of risk assessment," says George W. Lucier of the National Institute of Environmental Health Sciences. In addition, none of the scientists saw the press release, although their names accompanied it. "We were being used, clearly, and that's unfortunate," declares Arnold J. Schecter, professor of preventive medicine at the State University of New York at Binghamton. "Political layering is not particularly good, especially when it is unbeknownst," Lucier adds.

Few of the participants seem to dispute that the receptor-based mechanism of dioxin is relevant to human exposure. Nor did they before the conference, observes Alan P. Poland of the University of Wisconsin at Madison, who discovered the receptor in 1976. "The basic tenets were all known since 1981 or 1982," Poland says. But Lucier notes that now "we are at the point where we can reevaluate the linear model."

Indeed, the EPA intends to explore the question of whether there is a threshold response. The agency will investigate the receptor-based model with Michael A. Gallo, one of the conference organizers and a professor of toxicology at the University of Medicine and Dentistry of New Jersey–Robert Wood Johnson Medical School. But Gallo and others agree that discussion of thresholds in a regulatory context may be premature. At the conference, "some regulators got real excited by back-of-the-envelope calculations" and thought dioxin standards could be eased, says Linda S. Birnbaum, director of the EPA's environmental toxicology division. "Clearly, we don't know that."

Although many of the Banbury attendees were the last to know about the consensus they reportedly reached, news about the conference traveled quickly in political circles. At a recent hearing on dioxin standards in Alabama, expert witness for the pulp and paper industry Russell E. Keenan invoked the Banbury results in his testimony. "There was general agreement among the attending scientists that dioxin is much less toxic to humans than originally believed," Keenan claimed. Obviously, "it is not useless to tout Banbury results if you have a political ax to grind," comments Cate Jenkins, a chemist in the EPA's hazardous waste division. —*Marguerite Holloway*

ATTACHMENT 2

To: Dioxin Nerds, et al.
From: Tom Webster, CBNS Queens College, Flushing NY 11367
Date: 3/14/91
RE: Banbury Dioxin Model, Part 1 A Critique

A recent two article series in Science[1] covered the infamous Banbury conference on dioxin toxicity. The second article addresses the scandal aspect of the story, particularly the involvement of the Chlorine Institute. The first article (attached) addresses some of the scientific aspects, but does so in what I consider a rather opaque fashion.

In particular, the article shows an S-shaped graph which appears to show why dioxin has a threshold. Science indicates, using the graph, that "responses to dioxin increase slowly at first but then shoot up after passing a critical concentration."

However, all is not as simple as it seems at first. Since there has been some confusion regarding this business, I will address the graph in this memo.

(1) Background: The Ah receptor

First, a bit of background. 2,3,7,8-TCDD and other dioxin-like compounds (PCDFs, co-planar PCBs, chlorinated naphthalenes, etc.) are generally thought to cause toxicity through a receptor mediated mechanism. This receptor also binds aromatic hydrocarbons such as 3-methylcholanthrene and other non-halogenated aromatic hydrocarbons; hence it is termed the Ah receptor.

The Ah receptor is a protein which is normally found in the fluid (cytosol) of the cell (There is some controversy here; some people think it is found solely in the nucleus). Only certain molecules ("ligands") with certain properties (size ,shape, etc.) fit it, like a key into a lock. 2,3,7,8-TCDD has the best fit of any known compound. When this occurs, the receptor-ligand complex changes shape and moves into the nucleus. The change in shape helps it to recognize and bind to certain sequences in the DNA. This in turn causes the transcription and translation of adjacent DNA into protein. (This is quite similar to the mechanism of steroid hormones.)

The most well understood effect is the production an enzyme called P450IA1 which makes aromatic hydrocarbons more water soluble--and therefore easier to excrete--by adding hydoxyl (-OH) groups. One measure of this enzyme activity is called aryl hydrocarbon hydroxylase (AHH).

Many of the types of toxicity associated with dioxin-like compounds correlate with binding to the Ah receptor or AHH activity (also with EROD, a related enzyme activity). This provides good evidence that dioxin toxicity is mediated by the Ah receptor, i.e., binding to Ah is the first (but not only) step. It also provides both a theoretical justification and a measurement technique for 2,3,7,8-TCDD equivalents. If all dioxin-like compounds act through the receptor, then the potency of a given compound can be rated against 2,3,7,8-TCDD by their relative ability to bind Ah and induce AHH or EROD activity.

Nevertheless, other experiments show that many toxic effects are probably not directly caused by enzyme induction. Hence, other genes are probably being turned on by the Ah receptor as

well. The nature of these other genes and the biochemical mechanism of many toxic responses is not so well understood. I'll discuss some of this in a future memo.

(2) Receptor Kinetics

If the toxicity of dioxin-like compounds is mediated by the Ah receptor, clearly we need to understand this first step. Receptor-ligand relationships are mathematically described by the Michaelis-Menten equation, a standard tool for describing enzymes. This is schematically described as:

$$L + R \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} LR \qquad (1)$$

where "R" is the unbound receptor, "L" is the ligand (molecule binding to the receptor) and "LR" is the receptor-ligand complex. k_1 and k_{-1} are, respectively, the association and dissociation rate constants. At equilibrium, we find

$$K_D = [L][R]/[LR] \qquad (2)$$

$$K_D = k_{-1}/k_1$$

where the items in the brackets "[ ]" are concentrations and K_D is the dissociation equilibrium constant. The constant K_D tells us, in an inverse way, about the strength of the binding between the ligand and the receptor. A small K_D means the binding is strong, and thus the receptor-ligand complex is less likely to dissociate. Conversely, a large K_D means that the receptor-ligand binding is weak.

Equation (2) can be solved in terms of the amount of occupied (bound) receptor:

$$[LR] = [L]*R0/(K_D + [L]) \qquad (3)$$

where R0 is the total amount of receptor, bound and unbound.

Equation (3) gives the relationship between the amount of 2,3,7,8-TCDD (or other ligand) and the amount of bound receptor (LR). Remember that the toxic activity of 2,3,7,8-TCDD (and other dioxin-like compounds) is thought to be associated with the concentration of dioxin-receptor complexes. We could infer a dose-response curve with two additional pieces of information: 1) the relationship between external dose (e.g., amount of exposure per day) and [L] and ii) the relationship between [LR] and toxicity.

Note that when the concentration of 2,3,7,8-TCDD is significantly less than K_D, the relationship is linear:

$$[LR] = [L]*R0/K_D \qquad \text{for } [L] \ll K_D \qquad (4)$$

Indeed, this equation indicates that even one molecule of 2,3,7,8-TCDD could bind to the receptor, indicating that there may be no theoretical threshold for activity. The slope of the curve is governed by the number of Ah receptors (R0) and the dissociation constant (K_D). Since 2,3,7,8-TCDD has a very small K_D compared to

other dioxin-like compounds, it binds tightly, and has a large slope.

For a high concentration of 2,3,7,8-TCDD, the curve saturates. One can't produce more receptor-dioxin complexes than there are receptors:

$$[LR] = R0 \qquad \text{for } [L] \gg K_D \qquad (5)$$

(We'll ignore for now so-called "supermaximal" induction as well as circumstances which alter the number of receptors).

Finally, note that when the concentration of a compound equals its K_D, the number of bound receptors is equal to one-half the total number of receptors.

$$[LR] = R0/2 \qquad \text{for } [L] = K_D \qquad (6)$$

(3) Analysis of the Science graph

When equation (3) is plotted on normal graph paper it looks like my Figure 1, linear at low levels of 2,3,7,8-TCDD--the concentration of receptor-ligand complexes directly proportional to the concentration of ligand--and plateauing--at 100% bound receptor--at high levels of 2,3,7,8-TCDD.

When the same equation is replotted using the logarithm of the concentration of 2,3,7,8-TCDD, the graph looks like Figure 2, the same S-shaped curve seen in Science. Note that the horizontal axis in the Science graph gives concentration of 2,3,7,8-TCDD increasing by a factor of ten at each step; this is equivalent to using logarithms.

Finally, 50% of the receptors are shown as occupied in the Science graph when the concentration of 2,3,7,8-TCDD equals about 10^{-9} (Although not given, the units are undoubtably the standard moles per liter). This is the old K_D value for 2,3,7,8-TCDD. Actually, recent experiments indicate that the K_D is probably even smaller, on the order of 10^{-12} to 10^{-11} moles per liter. This means that 2,3,7,8-TCDD binds Ah more tightly than previously thought.

(4) Discussion

As a result, it should be clear that the graph in Science does not by itself indicate a threshold. The S-shape of the curve is an artifact of the graphing technique. Plotted on linear axes, the equation for ligand-receptor interaction indicates that the number of occupied receptors rises linearly from zero. In other words, this response should theoretically be linear at low doses with no threshold.

What then is really going on? Clearly, there must be more to the story. I'll be writing another memo on this, but let me give a few hints.

i) There may be other compounds inside the cell which bind to Ah, albeit with less affinity, complicating the picture.

ii) Binding to the receptor is just the first step. The other steps, binding to DNA, generation of protein, action of protein, etc., might not be linear. Hence, even though the first step might be linear, the final toxic response might not be.

ii) Binding to the receptor is reversible. However, the long half-life of dioxin-like compounds and the background exposure to them diminishes the strength of this argument.

iv) The Birnbaum[2] memo makes the following assumptions: 1) all toxicity is mediated by the Ah receptor binding; 2) induction of P450IA1 (AHH activity) is the most sensitive response of this system; 3) no effect occurs until one can measure an increase in enzyme activity. This defines a "practical" threshold that one can use to determine no-effect levels, etc.

In response to this last argument (briefly), enzyme induction may be the most sensitive response, but we don't really know. Also, lack of measurable activity doesn't necessarily mean no activity. Ability to measure a response is determined by many things including the sensitivity of the assay, the statistical power of the experiment, etc. In addition, 2,3,7,8-TCDD has a very long lifetime in the human body. Finally, the already existing body-burden of dioxin-like compounds in humans and other animals needs to be taken into consideration when examining such threshold models.

References

(1) Roberts, L. (1991a). Dioxin Risks Revisited. Science 251: 624-626. February 8.

Roberts, L. (1991b). Flap Erupts Over Dioxin Meeting. Science 251: 866-867. February 22.

(2) Birnbaum, L. (1990). Memo to E. Bretthauer (EPA-ORD) regarding Consensus at Banbury Dioxin Conference. October 31.

Figure 1 : Linear Plot

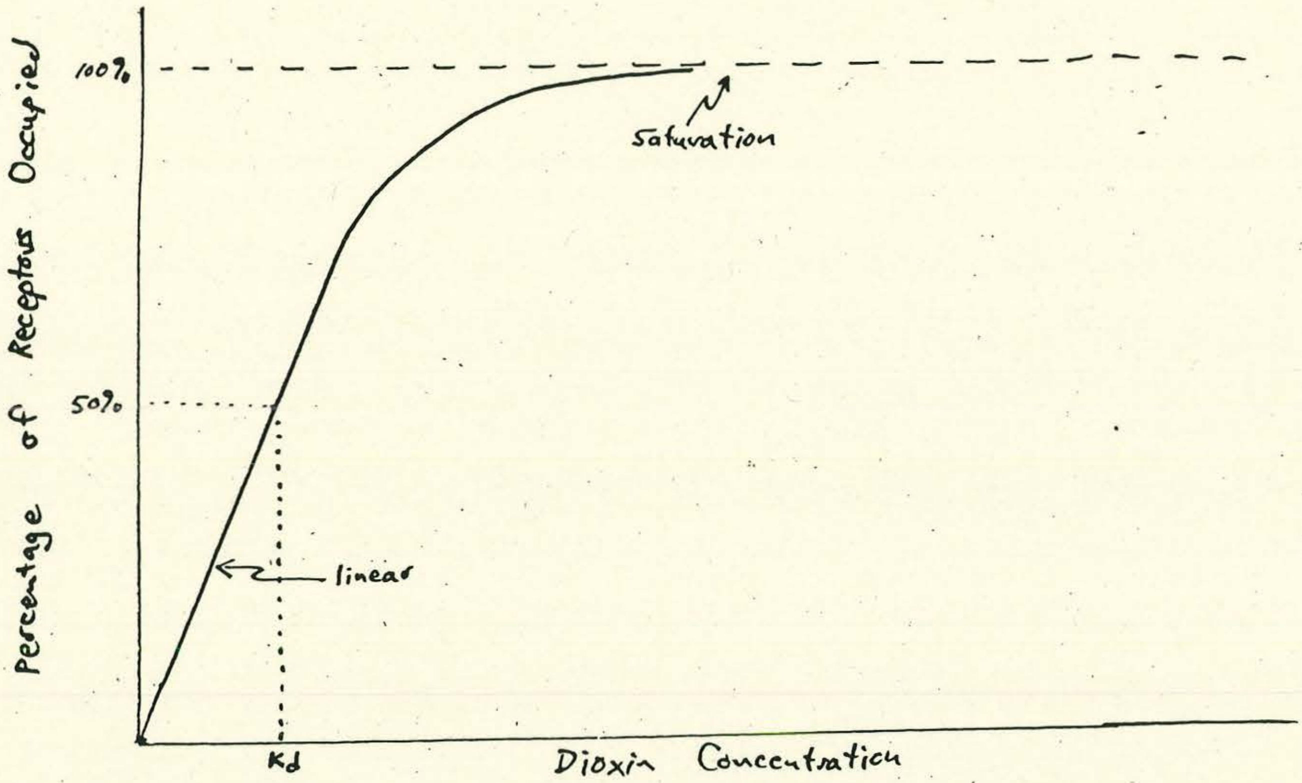
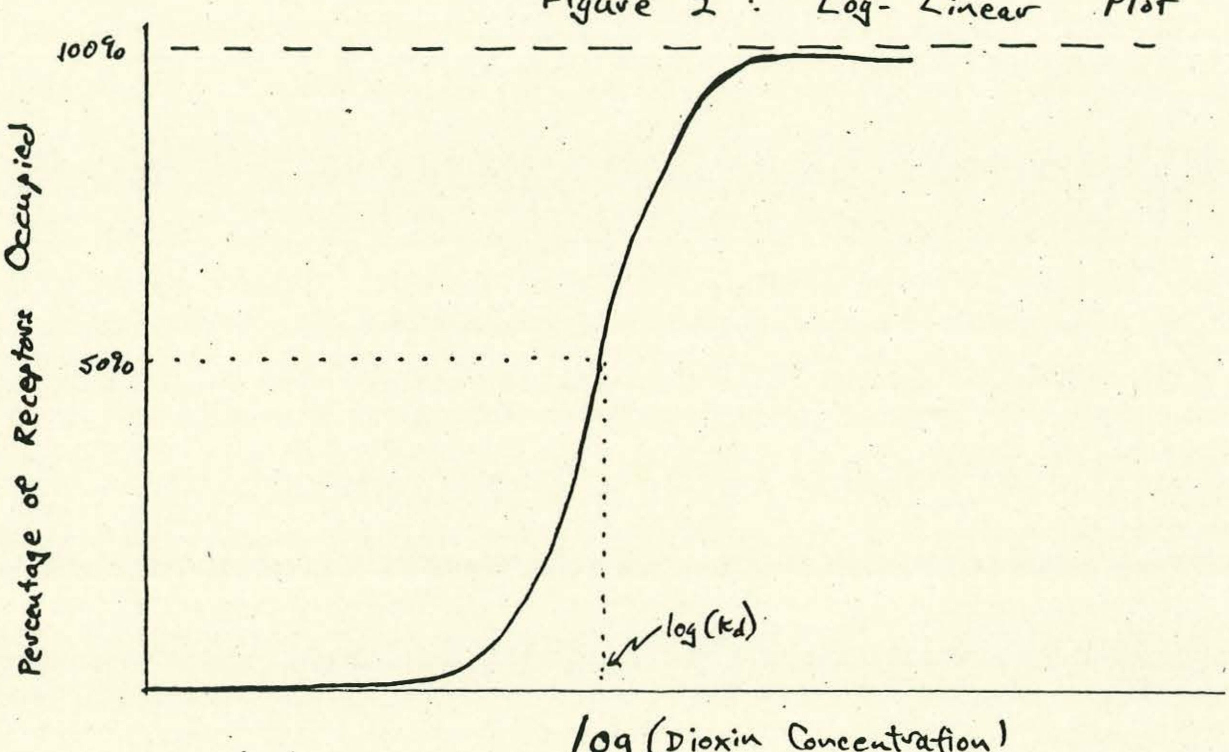


Figure 2 : Log-Linear Plot



ATTACHMENT 3

Downgrading Dioxin's Cancer Risk: Where's the Science?

By Tom Webster

Some of the concerns about the toxicity of the wood preservative pentachlorophenol have resulted because of its contamination with dioxins and furans. During manufacturing, pentachlorophenol is contaminated with several members of this family of compounds, with hexadioxins being most abundant.[1] 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD, commonly called dioxin), the most toxic dioxin, has been found in commercial pentachlorophenol formulations[1] and is often found in the soil and waste products from wood treatment plants.[2,3] This article discusses recent attempts to weaken regulatory standards for 2,3,7,8-TCDD.

-Ed.

The pulp and paper industry and certain consultants are once again attempting to relax the regulatory standards for dioxin. The consulting company ChemRisk has proposed an increase in the so-called "acceptable" dose of 2,3,7,8-TCDD by a factor as large as one thousand.[4,5] Many states are currently setting water quality standards for dioxin,[6] a regulation that depends on the "acceptable" dose.[7]

Despite assertions that the proposed change is based on new scientific evidence showing that dioxin "may be far less dangerous than previously imagined,"[8] the new information is actually a reinterpretation of the 1978 rat experiment that forms the basis for the U.S. Environmental Protection Agency's (EPA's) current estimate of dioxin's ability to cause cancer. In this reanalysis, a group of pathologists voted, according to a new set of guidelines, on the classification of tumors found in the test animals.[9]

However, if all other assumptions are left unchanged, recounting the tumors according to the revised rules [10] would result in an "acceptable" daily dioxin dose that is only two to three times larger than the current estimate. This is an insignificant change given the uncertainty in risk assessment. 2,3,7,8-TCDD is currently rated as millions of times more carcinogenic than many other compounds.

"Indeed, new scientific evidence on the amount of fish people consume, the degree to which dioxin is concentrated in fish, and the toxic equivalencies of other dioxins and furans supports stronger, not weaker, dioxin standards."

The much larger change proposed by ChemRisk was derived by altering a number of other assumptions without proper justification. Indeed, new scientific evidence on the amount of fish people consume, the degree to which dioxin is concentrated in fish, and the toxic equivalencies of other dioxins and furans (JPR 10(2):23-27) supports stronger, not weaker, dioxin standards.[7]

Human Health Effects Controversy

This episode is neither the first nor last attempt to downgrade or dismiss the toxicity of dioxin. Perhaps the best known and continuing controversy surrounds Agent Orange. 2,3,7,8-TCDD was a contaminant in the herbicide 2,4,5-T, a component of Agent Orange, which was sprayed in parts of the United States as well as in Vietnam.

Despite the claim by some that the only long-term effect of dioxin on humans is chloracne, a serious skin disorder, the compound has been hypothesized to cause a number of other health effects in humans. Several recent epidemiological studies support this position. The Agent Orange Scientific Task Force[11] linked phenoxyacetic acid herbicides (such as Agent Orange) and their dioxin contaminants to a number of diseases including certain cancers. Dioxin's close chemical relatives PCBs and dibenzofurans may cause birth defects and learning/behavioral changes in the children of exposed women.[12,13] Certain key earlier studies that found no increase in cancer in chemical workers exposed to dioxin are faulty or possibly even fraudulent,[14,15] a charge now under investigation by EPA. Recent studies of German and American chemical workers exposed to dioxin found statistically significant increases in cancer rates.[16,17]

EPA rates cancer-causing compounds qualitatively (how good is the evidence for cancer causation in humans?) and quantitatively (how much cancer is caused by a given dose?). As a result of the recent epidemiology, it is likely that EPA will upgrade the qualitative standing of 2,3,7,8-TCDD to a Class B1 probable human carcinogen (limited human data and sufficient animal data),[18] an action with important regulatory ramifications.[19]

Constructing an "Acceptable" Daily Intake of Dioxin

EPA typically assumes that cancer-causing agents have no threshold, meaning that any amount of exposure can cause damage. Some people argue that there is no acceptable exposure for dioxin, an unintentional chemical by-product with no use or benefit, and that the goal should be zero exposure to this compound. EPA, however, has stated that some level of risk is "acceptable," a decision that is a matter of policy, not science. In setting ambi-

Tom Webster is a researcher with the Center for the Biology of Natural Systems (CBNS) of Queens College. He is currently working on a project for Greenpeace concerning chlorinated compounds.

CBNS; Queens College; City University of New York; Flushing, NY 11367; (718) 670-4180.

ent water quality standards, EPA often uses an acceptable lifetime risk of cancer of one case in a million (10^{-6}).

Based on this policy, the acceptable daily dose of a chemical is established by dividing the acceptable risk level by the "potency" of the compound. EPA calls such values risk specific doses (RsD). The potency is the quantitative estimate of the strength of the carcinogen. The more potent a chemical is, the smaller the dose that is required to pose a certain level of risk.

For dioxin, as with the overwhelming majority of toxic chemicals, there are insufficient human data to establish a potency. (The new study cancer among chemical workers[17] may, however, prove sufficient.) Consequently, dioxin's potency is based on laboratory experiments with animals. The current estimate for 2,3,7,8-TCDD[1] was based on a 1978 experiment on female rats, the most sensitive sex and species tested.[20]

EPA projected from the number of tumors found in animals at experimental doses to effects at the lower doses that people might encounter using a standard mathematical technique, the linear multistage model. This model assumes that the carcinogen has no threshold and that effects at low doses are linear, i.e., directly proportional to dose.

Finally, the potency in humans is estimated by multiplying the animal value by a "scaling factor." This adjusts for differences between the experimental animal and humans. For dioxin, EPA employed the default "surface area" scaling factor, since many differences between animals and humans (e.g., metabolism) depend on relative surface area.[1,21]

The 1988 Attempt to Downgrade Dioxin

In 1988, a proposal was made by EPA's Dioxin Workgroup to decrease the carcinogenic potency of 2,3,7,8-TCDD by a factor of sixteen. The Workgroup argued that dioxin might cause cancer through several mechanisms rather than being simply a complete carcinogen (the basis of the 1985 estimate). It might, therefore, be a less potent cancer-causing agent than previously thought. The Workgroup concluded that there was "no definitive scientific basis" for determining how much less potent dioxin might be.[22]

They noted that other agencies (the Center for Disease Control, the Food and Drug Administration) as well as other countries have less stringent "acceptable" levels of dioxin. They argued that "for strictly policy purposes, there is great benefit in federal agencies adopting consistent positions in the absence of compelling scientific information" and that an order of magnitude (factor of ten) estimate conveys the uncertainty involved. Based on this somewhat arbitrary logic, the Working Group recommended increasing the "acceptable" level (RsD) from 0.006 picograms (one picogram is one trillionth of a gram) per kilogram per day (pg/kg/day) to 0.1 pg/kg/day.

In their review of this proposal, EPA's Science Advisory Panel acknowledged some criticisms of the application of the linear multistage model to dioxin. However, they rejected the Workgroup's proposal, stating that "there is no reason to necessarily believe that a new mechanism model would lead to a relaxation of the risk specific dose for 2,3,7,8-TCDD induced cancer...The Panel therefore finds no scientific basis at this time for the proposed change."[23]

Acceptable Doses of Dioxin: ChemRisk versus EPA

At about the same time that the Science Advisory Panel was rejecting the 1988 case for increasing the "acceptable" risk of dioxin by a factor of sixteen, ChemRisk's new proposal supported an increase by as much as a factor of one thousand.[4,5] Three main factors are used by ChemRisk and EPA in their respective dioxin computations (see Table 1):

"ChemRisk selects an "acceptable" risk of 10^{-5}. Since the level of acceptable risk is a question of policy, not science, ChemRisk's choice of this factor is arbitrary."

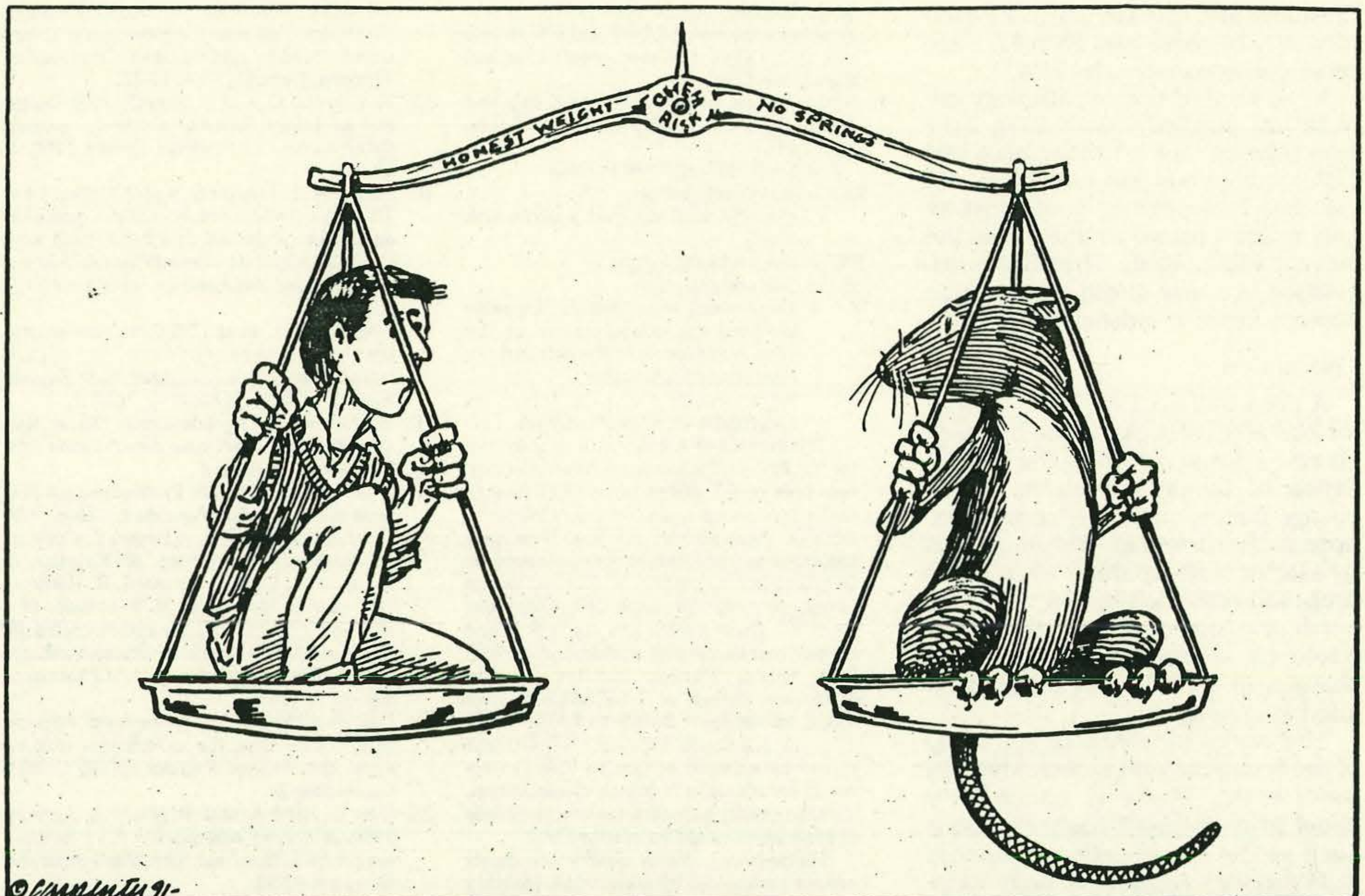
- **"Acceptable" Lifetime Cancer Risk:** For water quality standards, EPA recommends an "acceptable" lifetime cancer risk ranging from one in ten million (10^{-7}) to one in one hundred thousand (10^{-5}). However, one in one million (10^{-6}) is both the default and most commonly used value.[6,24] ChemRisk selects an "acceptable" risk of 10^{-5}. Since the level of acceptable risk is a question of policy, not science, ChemRisk's choice of this factor is arbitrary.
- **Interspecies Scaling Factor:** ChemRisk uses a body weight scaling factor to extrapolate from rats to humans. Since dose is commonly expressed as an amount per kilogram of body weight, ChemRisk's approach assumes that humans and rats are equally sensitive. EPA's surface area scaling factor assumes that humans will be more sensitive than rats per unit body weight by a

Table 1
Constructing an "Acceptable" Dose of Dioxin

	USEPA[1]	ChemRisk[4,5]	Factor[a]
1. Cancer potency in rats $(mg/kg/day)^{-1}$ (95% upper-bound estimate with linear multi-stage model)	29000	1500	19.3[b]
2. Scaling factor, rat to human (surface area)	5.38 (body weight)	1	5.38
3. "Acceptable" Lifetime Cancer Risk	10^{-6}[c]	10^{-5}	10
4. Risk-Specific Dose of 2,3,7,8-TCDD (pg/kg/day)	0.006[d]	6.74	1040

a. Factor by which ChemRisk is less stringent.
b. This factor would be 2-3 if the only change was the reclassification of tumors.
c. One in a million is a default and common value for water quality standards.[6,25]
d. An earlier draft by ChemRisk proposed an acceptable dose of 2.5 pg/kg/day.[4]

Note: RsD = (acceptable risk)/(rat potency * scaling factor)



Jim Carpenter

factor of about five.

ChemRisk argues that the use of the dose per body weight scaling factor is "more biologically relevant" because 2,3,7,8-TCDD is itself the active compound rather than any metabolite as is common with many carcinogens. EPA has disagreed with this line of reasoning in general,[25] but the case against body weight scaling is even stronger for 2,3,7,8-TCDD.

Since EPA's 1985 dioxin potency estimate, 2,3,7,8-TCDD half-life in humans has been determined to be 5-10 years, much longer than previously thought. In rats, the half-life of 2,3,7,8-TCDD is only about one month. Taking into account differences in tissue distribution, a scientist with EPA's Carcinogen Assessment Group estimated a scaling factor for the liver of as high as 37, much higher than ChemRisk's body weight scaling factor of one as well as EPA's surface area scaling factor of 5.38.[25] ChemRisk's reliance on the body weight scaling factor is not supportable.

• **Cancer Potency in Rats:** EPA's 1985 computation of dioxin potency was based on the occurrence in the 1978 rat study of carcinomas (cancerous tumors) and neoplastic nodules (lesions which may develop into cancerous tumors) in the liver, as well as tumors in other organs where the increase over control animals was statistically significant. In 1986, researchers proposed dividing neoplastic nodules into two groups: hepatocellular hyperplasia (a noncancerous proliferation of liver cells caused by toxicity) and hepatocellular adenomas (benign liver tumors).[10] This change has been questioned by some toxicologists.[26]

ChemRisk used the new classification system to argue in 1989 that the EPA's 1985 analysis was incorrect.[4]

At about the same time, Dr. Squire, a consulting pathologist involved in the original analysis of the female rat cancer data, was asked to re-examine the in conjunction with the setting of a water quality standard for Maine.[27] (Squire was involved earlier in a controversy over dioxin contaminants of pentachlorophenol: see article beginning on p. 4). After an initial review of the rat data, Dr. Squire helped convene a group of pathologists to re-examine the liver tissue slides from the experiment using the new classification system.

During this re-evaluation, in which "consensus" was defined as agreement by four out of seven pathologists (not all votes were unanimous), the group identified fewer carcinomas as well as fewer total tumors (carcinomas plus adenomas) than EPA's earlier analyses. The group concluded that because "the tumors were predominantly benign and usually associated with lesions of hepatic [liver] toxicity" the rat study demonstrated "a weak oncogenic [cancer-causing] effect of TCDD."[9] The implication of this controversial conclusion is that liver toxicity somehow caused or magnified the carcinogenic response.

ChemRisk used these results to calculate a new potency factor for 2,3,7,8-TCDD in rats, but counted only carcinomas in the liver (the primary target organ in this animal). They ignored carcinomas in other tissues as well as all adenomas, benign tumors that may progress into carcinomas. Both omissions are contrary to EPA guidelines for carcinogen risk assessment.[21]

ChemRisk also failed to adjust for early mortality of some test animals, another correction used by EPA.[1]

If the revised tumor pathology criteria are applied, eliminating liver hyperplasias, but all other standard EPA assumptions are employed, the calculated rat potency is reduced by only a factor of two to three from the current value. Again, ChemRisk's calculation of a new dioxin carcinogenic potency factor is indefensible.

Conclusion

A proposed acceptable daily dose for 2,3,7,8-TCDD is claimed to be based on new science regarding the classification of tumors. However, if this change alone is made, the "acceptable" dose of dioxin would only be altered by a factor of two to three. ChemRisk's proposed reduction by a factor of as much as a thousand is fundamentally based on scientifically indefensible changes in a number of other unrelated assumptions.

This series of events shows many of the problems with quantitative risk assessment. There is uncertainty about even the most basic questions such as the classification of tumors in laboratory animals. A large number of assumptions are required, each of which must be independently justified. Because of the uncertainty and the number of assumptions, it may be possible, in the absence of checks and balances, to construct nearly any result. ■

References and Notes

1. U.S. Environmental Protection Agency. 1985. *Health assessment document for polychlorinated dibenzo-p-dioxins.* EPA/600/8-84/014F. Washington, D.C.: Office of Health and Environmental Assessment.
2. U.S. Environmental Protection Agency. 1987. National dioxin study. EPA/530-SW-87-025. Washington, D.C.: Office of Solid Waste and Emergency Response.
3. State Water Resources Control Board. 1988. Chlorinated dibenzo-p-dioxin and dibenzofuran contamination in California from chlorophenol wood preservative use. Report 88-5WQ. Sacramento, CA: Division of Water Quality.
4. Keenan, R., R. Wenning, A. Parsons. 1989. Sensitivity analysis for dioxin risk assessment and implications for determining acceptable daily exposure: Executive summary. Portland, ME.: ChemRisk, October 20.
5. Keenan, R. Letter to Dr. R. Loehr, Chair, Executive Committee, Science Advisory Board, U.S. Environmental Protection Agency. March 20, 1990.
6. U.S. Environmental Protection Agency. 1990. *Tracking report: State water quality criteria for dioxin (2,3,7,8-TCDD).* Washington, D.C.: Office of Water Regulations and Standards. May.
7. Where people can consume both fish and water, the water quality standard is computed as:
   C = (RsD*BW)/((FC*BCF)+WC)
   RsD = risk specific dose ("acceptable" dose at a given risk level)
   BW = human body weight
   FC = fish consumption
   BCF = bioconcentration factor, the ratio between the concentration of the compound found in the fish and the concentration in water.
   WC = water consumption rate by humans (negligible when BCF is large).
   The current EPA water quality standard for 2,3,7,8-TCDD assumes a fish consumption rate of 6.5 grams per day (0.23 oz.) and a bioconcentration factor of 5000.[6,24] Both of these factors are low. New data indicate that sport fishermen can consume 30 grams per day of fish while subsistence fishermen may consume 140 grams per day.[24,28] These values are about five and twenty two times higher than the current EPA value. Recent studies of the bioconcentration of 2,3,7,8-TCDD have found values from 39,000 to 140,000.[29,30] Thus, even if the RsD for 2,3,7,8-TCDD was raised by a factor of two to three to account for changes in tumor classification, a water quality standard tens to hundreds of time lower could be constructed.
   Furthermore, water quality standards are set compound by compound, ignoring the fact that compounds closely related to 2,3,7,8-TCDD—such as 2,3,7,8-tetrachlorodibenzofuran, also emitted by pulp and paper mills that bleach with chlorine—are added together in other regulatory contexts, after adjusting for relative potency using the 2,3,7,8-TCDD equivalence methodology.
8. Gladwell, M. 1990. Scientists temper views on cancer-causing potential of dioxin. *Washington Post*, May 31, p. A3.
9. Sauer, R. and PATHCO, Inc. 1990. Pathology Working Group 2,3,7,8-tetrachlorodibenzo-p-dioxin in Sprague-Dawley Rats. 10075 Tyler Place #16, Ijamsville, MD 21754. March 13.
10. Maronpot, R., C. Montgomery, G. Boorman, and E. McConnell 1986. National Toxicology Program nomenclature for hepatoproliferative lesions of rats. *Toxicologic Pathology* 14(2): 263-273.
11. Agent Orange Scientific Task Force. 1990. *Human health effects associated with exposure to herbicides and/or their associated contaminants - chlorinated dioxins.* Washington, D.C.: National Veterans Legal Services Project.
12. Rogan, W., B. Gladen, C. Hsu, Y. Chen, and H. Ko. 1990. Yucheng: Studies in children. Presented at Dioxin '90, The Tenth International Meeting. Bayreuth, Germany.
13. Jacobson, J., S. Jacobson, and H. Humphrey. 1990. Effects of in utero exposure to polychlorinated biphenyls and related contaminants on cognitive functioning in young children. *J. Pediatrics* 116: 38-45.
14. Rohleder, F. 1989. Dioxins and cancer mortality: Reanalysis of the BASF cohort. Ninth International Symposium on Chlorinated Dioxins and Related Compounds, Toronto, Ontario, Sept. 17-22.
15. Van Strum, C. and P. Merrell. 1990. Dioxin human health damage studies: Damaged data? *Journal of Pesticide Reform* 10(1): 8-12.
16. Zober, A., P. Messerer, and P. Huber. 1990. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. *International Archives of Occupational and Environmental Health.* 62: 139-157.
17. Fingerhut, M., et al. (1991). Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324(4): 212-218.
18. "EPA likely to upgrade dioxin cancer classification to reflect new data." *Inside EPA.* February 1, 1991. p.4.
19. Jenkins, C. 1991. U.S. Environmental Protection Agency Memorandum. January 24.
20. Kociba, R., D. Keyes, J. Beyer, R. Carreon, C. Wade, D. Dittenber, R. Kalnins, L. Frauson, C. Park, S. Barnard, R. Hummel, and and C. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicology and Applied Pharmacology* 46: 279-303.
21. U.S. Environmental Protection Agency. 1986. Guidelines for carcinogen risk assessment. *Federal Register* 51(185): 33991. September 24.
22. U.S. Environmental Protection Agency. 1988. *A cancer risk-specific dose estimate for 2,3,7,8-TCDD: Draft.* EPA/600/6-88/007Aa. June. pp. 49-50.
23. Goldstein, B., N. Kim. 1989. Letter from the Chair and Co-Chair of the Ad Hoc Dioxin Panel to Dr. R. Loehr, Chair, Science Advisory Board Executive Committee, U.S. Environmental Protection Agency. November 28.
24. U.S. Environmental Protection Agency. 1990. EPA's position on Georgia's adoption of a dioxin water quality standard. Region IV. March.
25. Bayard, S. 1988. Quantitative implications of the use of different extrapolation procedures for low-dose cancer risk estimates from exposure to 2,3,7,8-TCDD. Appendix A of reference 22.
26. Alsen-Hinrichs, C, Department of Toxicology, University of Kiel School of Medicine, Kiel, Germany. Letter to the *Washington Post* (unpublished). June 21, 1990.
27. Squire, R. 1990. Letter to Dr. Robert Michaels acknowledging the request of November 28, 1989. January 8.
28. U.S. Environmental Protection Agency (1989). *Exposure factors handbook.* Versar, Inc. EPA 600/8-89-043. Washington, D.C.: EPA.
29. Mehrle, P., et al. 1988. Toxicity and bioconcentration of 2,3,7,8-tetrachlorodibenzo-p-dioxin and 2,3,7,8-tetrachlorodibenzofuran in rainbow trout. *Environ. Toxicol. Chem.* 7: 47-62.
30. Cook, P., A. Batterman, and B. Butterworth. 1990. *Laboratory study of TCDD bioaccumulation by lake trout from Lake Ontario sediments, food chain and water.* Duluth, MN: U.S. Environmental Protection Agency Environmental Research Laboratory.

ATTACHMENT 4

Eleventh International Symposium on Chlorinated Dioxins and Related Compounds

cc Steve
CR
Bt Ch
Jim N

DIOXIN '91

September 23-27, 1991

Conference Information

School of Public Health
Office of Continuing Education
The University of North Carolina at Chapel Hill
CB# 8165, Miller Hall
Chapel Hill, NC 27599-8165
Phone: 919/966-1104
Fax: 919/966-7141

Organizing Committee

Terri Damstra, Chair
National Institute of Environmental Health Sciences

Linda Birnbaum
Health Effects Research Laboratory
U.S. Environmental Protection Agency

M. Judith Charles
Department of Environmental Sciences and Engineering
The University of North Carolina at Chapel Hill

Chris Corton
Chemical Industry Institute of Toxicology

Richard Dideriksen
School of Public Health
The University of North Carolina at Chapel Hill

William Greenlee
National Institute of Environmental Health Sciences

O. Hutzinger
International Institute for Environmental Information and Communication

George Lucier
National Institute of Environmental Health Sciences

Memo

To: Conference Participants Who Plan to Submit Papers

From: Sharon Johnson Wills
Program Assistant

Date: February 10, 1991

Re: Abstract Format Instructions

The Organizing Committee of Dioxin '91 invites you to submit your abstract for the 11th International Symposium on Chlorinated Dioxins and Related Compounds. The conference will be held in Research Triangle Park, North Carolina, Sept. 23-27, 1991. Enclosed please find one instruction sheet and two forms for submitting your abstract. Also enclosed is an acknowledgment card that you should send back with your completed package. Fill in the lines marked "title" and "author" and return it with your abstract package to the Office of Continuing Education. I will return the card to you to acknowledge receipt of your abstract.

Please read the instructions carefully and take note of all mailing advisories so that we may include your abstract in this year's program. Remember that all abstracts must be received no later than April 1, 1991. Abstracts received after this date will not be considered for acceptance, published or printed.

If you have any questions or concerns, please call or write.

P.S. A complete brochure describing this program will be mailed to you in April. To register for Dioxin '91 before that time, please call me at 919/966-1104.

DOSE RESPONSE RELATIONSHIPS FOR CHRONIC EXPOSURE TO 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD) IN A RAT TUMOR PROMOTION MODEL: 2. QUANTIFICATION AND IMMUNOLOCALIZATION OF CYTOCHROMES P450c(1A1) AND P450d(1A2) IN THE LIVER. A Tritscher, G Clark, Z McCoy, C Portier, W Greenlee, J Goldstein, and G Lucier. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

TCDD and its structural analogs produce a broad spectrum of biochemical and toxic effects in animals and humans. The mechanisms responsible for these effects involve interactions with the Ah receptor but many of the steps necessary for biological response remain unknown. One of the troublesome knowledge gaps that causes uncertainty in risk assessments for TCDD is the lack of adequate dose-response relationships following chronic exposure to TCDD. One of the most sensitive responses to TCDD and its structural analogs is the induction of specific isozymes of cytochrome P450 (CYP1A1 and CYP1A2). CYP1A1 is induced in many tissues whereas CYP1A2 is induced only in liver. We have employed a two-stage model for hepatocarcinogenesis in female Sprague-Dawley rats to evaluate dose-response relationships for CYP1A1 and CYP1A2. A single dose of diethylnitrosamine was used as the initiating agent followed by biweekly gavage of TCDD at doses equivalent to 3.5, 10, 35 and 125 ng/kg/day for 30 weeks. CYP1A1 and CYP1A2 were quantified in liver microsomes from control and treated rats by immunoassay. Data revealed a maximum induction of CYP1A2 of 10-fold and induction was nearly 3-fold at the 3.5 ng/kg/day dose. The no detectable effect for 1A2 induction was estimated to be 0.1 to 0.3 TCDD ng/kg/day. A chronic dosing experiment is in progress to determine if this is an accurate estimate of the no detectable effect. Interestingly, TCDD-mediated induction of 1A2 appeared to occur at lower doses in DEN-initiated rats compared to non-initiated rats. Also, CYP1A2 induction appeared to be a slightly more sensitive marker of TCDD exposure than CYP1A1 in our rat liver tumor promotion model. We also analyzed liver TCDD concentrations by GC-MS. These data revealed a linear relationship between administered dose and TCDD liver concentrations throughout the entire dose range of our study. Therefore, induction of 1A2 does not enhance TCDD retention in liver, a hypothesis that had been proposed because 1A2 is a binding protein for TCDD. We also used immunocytochemical techniques to analyze the pattern of CYP1A1 and CYP1A2 distribution in livers of control and TCDD-treated rats. 1A2 was localized primarily in the centrolobular region with small amounts in the midzonal and periportal regions. Induction by TCDD increases the number of cells containing detectable amounts of 1A2 but not the intensity of staining of cells constitutively expressing this cytochrome. Localization patterns, in induced rats, were similar for 1A1 and 1A2. Taken together, these studies are characterizing dose response relationships for CYP1A1 and CYP1A2 that represent characteristic Ah receptor dependent responses to TCDD exposure. (Funding for TCDD analyses provided by the American Paper Institute.

DOSE RESPONSE RELATIONSHIPS FOR CHRONIC EXPOSURE TO 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD) IN A RAT LIVER TUMOR PROMOTION MODEL: 1. RELATIONSHIPS OF TCDD TISSUE CONCENTRATIONS TO SERUM CLINICAL CHEMISTRY, CELL PROLIFERATION, AND PRENEOPLASTIC FOCI. G Clark, A Tritscher, Z McCoy, C Portier, M Thompson, R Wilson, J Foley, R Maronpot, [1]T Goldsworthy, W Greenlee, and G Lucier. National Institute of Environmental Health Sciences, Research Triangle Park, NC and [1]Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

One of the important issues in a risk assessment for exposure to dioxins is the pharmacokinetic distribution of TCDD in a long term chronic exposure regimen and the biological responses associated with a potential carcinogenic outcome. A specific cytoplasmic binding protein, the Ah receptor, is generally thought to mediate most of the biological responses to TCDD including its action as a tumor promoter. We have used a rat liver tumor promotion model to investigate biochemical responses that may be associated with promotion of carcinogenesis. In previous studies we have found that alterations of hepatic cell proliferation and the appearance of enzyme altered foci (γ-glutamyl transpeptidase and glutathione S-transferase-positive foci) correlate with liver tumor formation but that the ovaries are necessary for the expression of these effects. In the current study we are investigating dose response relationships in female Sprague-Dawley rats with an initiating dose of 175 mg/kg DEN and biweekly exposure to TCDD for 30 weeks to give doses equivalent to 3.5, 10.7, 35.7, and 125 ng/kg/day TCDD. A linear distribution of TCDD in livers of exposed animals was found. The mean liver concentration of TCDD was 19.9 ppb at 125 ng/kg/day and the mean liver concentration was 0.5 ppb at 3.5 ng/kg/day. In serum samples from the rats exposed to 125 ng/kg/day the TCDD concentration was 23.9 ppt while the concentration at the lowest dose was 8 ppt. Several serum clinical chemistry parameters were measured including alkaline phosphatase, glucose, alanine transaminase, total cholesterol, triglycerides, sorbitol dehydrogenase, 5' nucleotidase, and total bile acids. A significant dose effect for TCDD exposure was determined for serum alkaline phosphatase, 5' nucleotidase activities and on the levels of serum cholesterol. We are in the process of analyzing cell proliferation in livers from these animals by incorporation of bromodeoxyuridine into newly-formed cells and immunohistochemical analysis. We are also quantifying γ-glutamyl transpeptidase and placental glutathione S-transferase-positive foci as indicators of preneoplastic lesions. These parameters will be correlated with the applied dose, the tissue specific dose, and the levels of occupied Ah receptors. We hope to determine a) what is the most sensitive biochemical response to TCDD exposure and b) which parameter correlates with carcinogenicity. These data will be useful in the development of mechanistic models for dioxin risk assessment. (Funding for TCDD analyses provided by the American Paper Institute).

Carcinogenesis vol.12 no.5 pp.793–800, 1991

ATTACHMENT 5

Study of the separate and combined effects of the non-planar 2,5,2′,5′- and the planar 3,4,3′,4′-tetrachlorobiphenyl in liver and lymphocytes *in vivo*

Linda Sargent[1], Yvonne P.Dragan, Chris Erickson, Chris J.Laufer and Henry C.Pitot[2]

McArdle Laboratory for Cancer Research, Department of Oncology and the Center for Environmental Toxicology, The Medical School, University of Wisconsin, Madison, WI 53706, USA

[1]Present address: Chemical Industry Institute of Toxicology, 6 Davis Drive, Research Triangle Park, NC 27709, USA
[2]To whom reprint requests should be sent

Polychlorinated biphenyls (PCBs) are a group of industrial chemicals that are widely distributed in the environment. Because these compounds occur as mixtures, studies of their possible interactive effects are essential for an understanding of the mechanism of the toxicity of these mixtures. For the determination of a possible interaction of the effects *in vivo* of 2,5,2′,5′-tetrachlorobiphenyl (TCB) and 3,4,3′,4′-TCB, rats were exposed to a single dose of diethylnitrosamine (DEN) and subsequently to 0.1 p.p.m. 3,4,3′,4′-TCB and/or 10 p.p.m. 2,5,2′,5′-TCB in the feed for 1 year. The two major targets of PCB toxicity, the liver and the peripheral blood, were examined after these treatments. TCB treatment after DEN exposure caused a predominance of increased placental glutathione S-transferase (PGST) and deficiencies of ATPase as preneoplastic markers in focal hepatic lesions. When 0.05% phenobarbital (PB) was administered after DEN exposure, the distribution of markers in altered hepatic foci (AHF) was essentially equal for increased PGST and γ-glutamyltranspeptidase (GGT) and for ATPase deficiency. Many of these AHF also exhibited increased P450 b/e expression. Our results demonstrated that the two PCB congeners interacted *in vivo* to produce an increase in AHF that were PGST positive and ATPase negative. PGST-positive and ATPase-negative AHF correlated best with focal areas of P450 b/e expression. The combination of the two PCBs caused a greater than additive decrease in the total number of lymphocytes and antibody-producing B-cells. Also the thymocyte-dependent T-helper cells isolated from the animals receiving the combination of TCBs demonstrated a morphologically abnormal subpopulation. The results indicate that the interaction of 2,5,2′,5′-TCB and 3,4,3′,4′-TCB *in vivo* induced much greater toxicity and mutagenicity in peripheral lympyhocytes and hepatocytes than treatment with either congener alone.

Introduction

Polychlorinated biphenyls (PCBs*) are a group of industrial chemicals that, in the past, had diverse uses owing to their chemical stability and their miscibility in organic solvents. These properties resulted in the use of PCBs as hydraulic fluids, plasticizers, adhesives, heat transfer fluids, wax extenders, dedusting agents, organic diluents, lubricants, flame retardants and as dielectric fluids in capacitors and transformers (1). The advantages that made PCBs such a versatile industrial chemical proved to be the source of their problem in the environment. Traces of PCBs have been found in environmental samples world-wide (2,3). Analyses of human breast milk, blood and adipose tissue have demonstrated that most individuals have been exposed to PCBs (2,3). The primary route of human exposure is through oral ingestion of contaminated products.

Technical mixtures of PCBs contain a combination of planar and non-planar congeners. The planar congeners bind to the Ah receptor, induce cytochrome P450 c and P450 d (4–7), and cause a cascade of events primarily in the liver and immune cells, including weight loss, thymic atrophy, decreased spleen weights (8), reduction of circulating lymphocytes of both the bursae and thymic cell populations (9–11), hepatomegaly, and subcapsular and midzonal hepatic necrosis. They are also potent promoters of the growth of preneoplastic hepatic foci (12). The non-planar congeners are less toxic, have a low affinity for the Ah receptor, and induce P450 b/e. The non-planar congeners cause hepatic enlargement and are relatively weak promoting agents in hepatocarcinogenesis (12,13). They do not cause thymic atrophy or reduction in immune function (5,6,14).

Planar and non-planar congeners occur as mixtures, yet there are few studies which have examined the potency of specific combinations of PCB congeners. The planar 3,4,3′,4′-tetrachlorobiphenyl (TCB) and the non-planar 2,5,2′,5′-TCB are found in the Aroclor mixtures 1254, 1248 and 1242. The ratio of the concentration of these two congeners in the major Aroclors was used to determine the concentration ratio for this study. In addition, we chose to use low-level, environmentally relevant doses of these TCBs in order to assess the potency of the combination for the determination of doses in this experiment. The sample of Aroclor that was used as a standard contained 0.002 μg of 3,4,3′,4′-TCB/ml and 0.2 μg of 2,5,2′,5′-TCB/ml. Hepatocytes and lymphocytes were chosen as target cells to study a possible superadditive toxicity and promotion potency of the combination of the planar and the non-planar TCBs, since these two target cell types are among the most sensitive to PCB toxicity.

Materials and methods

Chemicals

The Pariza purified diet was purchased from Teklad (Madison, WI). Diethylnitrosamine (DEN) was obtained from the Eastman Kodak Co. (Rochester, NY). 3,4,3′,4′-TCB was purchased from Ultra Scientific (Hope, RI) and 2,5,2′,5′-TCB was a gift from Dr James Miller (McArdle Laboratory, Madison, WI). All of the antibodies used for immunohistochemistry were obtained from Bioproducts for Science Inc. (Indianapolis, IN).

Animals and treatment protocol

Female Sprague–Dawley rats (Harlan Sprague Dawley, Madison, WI) weighing an average of 90 g were housed in wire mesh cages and fed the Pariza diet (30% casein, 5% corn oil, 10% partially hydrogenated corn oil, 40% sucrose, 15% cornstarch) and water *ad libitum*. A 70% partial hepatectomy was performed under ether anesthesia and 24 h later 50% of the animals were intubated with

*Abbreviations: PCBs, polychlorinated biphenyls; TCB, tetrachlorobiphenyl; DEN, diethylnitrosamine; PB, phenobarbital; AHF, altered hepatic foci; GGT, γ-glutamyl transpeptidase; PGST, placental form of glutathione S-transferase; ATP, canalicular ATPase; G6P, glucose-6-phosphatase; HCC, hepatocellular carcinoma; TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin; HCB, hexachlorobiphenyl.

10 mg DEN in trioctanoin/kg. After 1 week, the animals were randomly assigned to the treatment groups outlined in Figure 1. TCBs were dissolved in methylene chloride, added to the powdered chow, and mixed thoroughly in plastic bags. The solvent was evaporated in the hood for 24 h. Randomly selected rats were then placed on a control diet or control diet with one of the following additions: 0.1 p.p.m. 3,4,3′,4′-TCB only, 10 p.p.m. 2,5,2′,5′-TCB only, 0.1 p.p.m. 3,4,3′,4′-TCB and 10 p.p.m. 2,5,2′,5′-TCB, or 100 p.p.m. 2,5,2′,5′-TCB. Another group was fed phenobarbital (PB) at a level of 0.05% in the diet as a positive control (15,16).

Analysis of lymphocytes

Rats were treated with 100 mg cyclophosphamide/kg and anesthetized with ether; blood was drawn by cardiac puncture 48 h later. The red blood cells were lysed with 2 ml hypotonic buffer (1000 ml of deionized water, 8.29 g NH_4Cl, 1.0 g KH_2CO_3, 0.372 g disodium EDTA, pH 7.4) and washed with phosphate-buffered saline. Washed lymphocytes were then mixed with fluorescein-conjugated antibodies generated against the CD-4 protein, the CD-8 protein, the 1.1 Thy protein and a general B-cell protein (17). The stained cells were then analyzed on the flow cytometer by standard methods (18). Lymphocytes of abnormal morphology were examined by scanning electron microscopy according to standard methods. Sections of the spleen were frozen on solid CO_2 and fixed in 10% buffered formalin.

Analysis of preneoplastic foci (altered hepatic foci, AHF)

The liver was removed, weighed, and sections from each liver lobe were immediately frozen on solid CO_2. Five 10-μ-thick serial sections were stained for γ-glutamyl transpeptidase (GGT), the placental form of glutathione S-transferase (PGST), canalicular ATPase (ATP), cytochrome P450 b/e, P450 c/d and glucose-6-phosphatase (G6P), according to the methods for staining outlined by Xu *et al.* (19). AHF were then quantitated by the procedure of Campbell *et al.* (20). Additional slices of tissue were stored in 10% formalin for histopathological analysis.

Statistics

Non-parametric Wilcoxon statistics were used to compare groups. For the determination of additivity, Steel and Torrie's χ-square test for additivity (21) was used.

Results

Lymphocyte analysis

The total number of circulating antibody-producing cells (B-cells) was reduced in the peripheral blood prepared from animals treated with 3,4,3′,4′-TCB, but not from those treated with 2,5,2′,5′-TCB (groups 3 and 5, Figure 2) when compared with untreated controls. The number of circulating B-cells isolated from animals treated with both TCBs was reduced by a greater than additive level ($P < 0.001$, group 7) when analyzed by flow cytometry. When DEN was included in the treatment protocol (Figure 3), the level of circulating B-cells was reduced in the 2,5,2′,5′-TCB group as well as the 3,4,3′,4′-TCB group ($P < 0.05$, groups 4 and 6). The level of B-cells in the group with DEN plus both TCBs (group 8) was reduced to 1%. A reduction to this level was greater than would be expected by an additive model when analyzed by the χ-square test for additivity.

There was no statistical reduction in the number of CD-4, CD-8 or Thy 1.1 cells. Although the total number of cells was the same, a population of light-staining CD-4 cells was observed by flow cytometry (Figure 4). Of the CD-4 cells, 50 ± 8% from group 7 (both TCBs) and 95 ± 5% of the samples from group 8 (DEN + both TCBs) had an abnormal population of light-staining CD-4 cells. The forward scatter of these cells was the same as that of the normal CD-4 cells, but the side scatter was different (Figure 4). A difference in the side scatter would indicate a difference in size or morphology. When these light-staining CD-4 cells were separated and examined by scanning electron microscopy, the surface morphology of all of the cells examined was distinctly different from the normal population (Figure 5). By standard methods (17), these abnormal cells were further examined for esterase activity and were determined to be negative and therefore not monocytes.

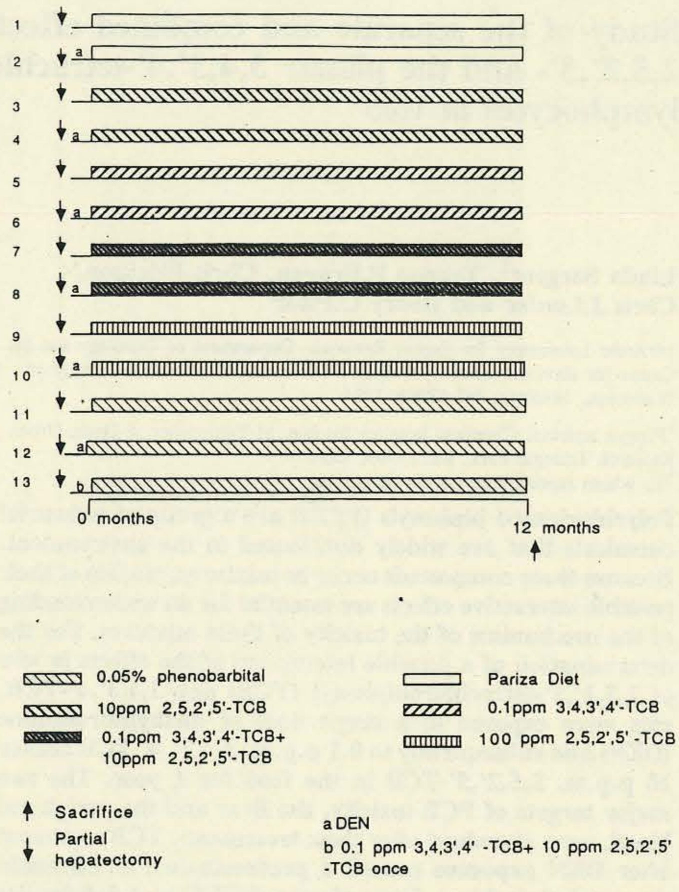


Fig. 1. Format of the protocol used for the initiation and promotion of AHF in female Sprague–Dawley rats.

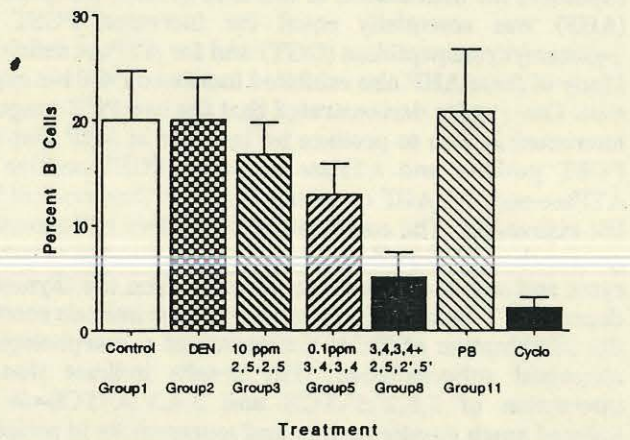


Fig. 2. Percentage of B-cells in the peripheral blood after chronic exposure to DEN alone or followed by 0.05% PB, 3,4,3′,4′-TCB, 2,5,2′,5′-TCB, or a combination of 3,4,3′,4′-TCB + 2,5,2′,5′-TCB or to cyclophosphamide. See text for details. Steel and Torrie's χ-square test for additivity (21) was used to examine an additive or greater than additive result. The conclusions of this test are given in the text. The bars above the columns indicate the standard error of the mean for analysis (1/rat in duplicate). The numbers of rats/group may be obtained from Table I.

Liver analysis

Number of preneoplastic foci. There was no statistical increase in the ratio of residual liver wt to body wt with any of the TCB treatments, but there was a significant increase in the PB and DEN + PB groups (Figure 6). A single dose of 0.1 p.p.m. 3,4,3′,4′-TCB and 10 p.p.m. 2,5,2′,5′-TCB did not increase the

Table I. Histopathologic changes in livers of rats on protocols depicted in Figure 1[a]

Group no.	Treatment	Portal damage[b]	Bile duct proliferation	Neoplastic nodules/rat	Cellular atypia/ neoplastic nodule/rat[c]	HCC/rat
1	Control	–	2/8	–	–	1/8
2	DEN	0/8	2/8	1/8	1/8	1/8
3	2,5,2′,5′-TCB (10 p.p.m.)	0/14	2/14	2/14	0/14	0/14
4	DEN + 10 p.p.m. 2,5,2′,5′-TCB	2/12	1/12	4/12	1/12	1/12
5	3,4,3′,4′-TCB (0.1 p.p.m.)	0/14	5/14	3/14	0/14	0/14
6	DEN + 0.1 p.p.m. 3,4,3′,4′-TCB	0/12	4/12	4/12	0/12	0/12
7	3,4,3′,4′-TCB + 2,5,2′,5′-TCB	9/12	9/12	1/12	1/12	0/12
8	DEN + 3,4,3′,4′-TCB + 2,5,2′,5′-TCB	9/11	11/11	11/11	9/11	2/11
10	DEN + 100 p.p.m. 2,5,2′,5′-TCB	3/5	2/5			
12	DEN + PB	2/11	11/11	11/11	11/11	9/11

[a]Data are presented as the number of rats exhibiting the pathologic process/total number of rats examined.
[b]Includes fibrosis, chronic inflammation and/or hydopic change of periportal hepatocytes. Control animals receiving control diets showed only occasional minimal portal damage and bile duct proliferation. The histopathology of livers of rats in groups 9, 11 and 13 (Figure 1) was no different from that seen in groups 1, 3 and 5.
[c]Cellular atypia is defined as morphological and cytological changes, usually focal, seen in neoplastic nodules, such changes being histologically compatible with one or more patterns of well-differentiated hepatocellular carcinomas (43–45).

total number of AHF or the volume fraction of the regenerated liver occupied by AHF.

Treatment with TCBs caused a predominance of AHF that were scored by the presence of PGST ($PGST^+$) and ATP deficiency as preneoplastic markers (Figure 7), whereas $PGST^+$, ATP deficiency and GGT^+ markers were equally distributed in AHF after DEN + PB (Figure 8). TCB treatment alone did not elevate the number of AHF when compared with the control livers; however, treatment with both TCBs increased the number of AHF to a level that was greater than that of the untreated control and statistically the same as the DEN control (groups 2, 3 and 5 in Figure 1; see also Figure 9). The numbers of preneoplastic foci per liver in the DEN + 10 p.p.m. 2,5,2′,5′-TCB group (group 4) or the DEN + 0.1 p.p.m. 3,4,3′,4′-TCB group (group 6 in Figure 1) were not significantly different from the DEN group (group 2, Figure 1). When rats were treated with DEN followed by both TCBs, the number of AHF was dramatically greater than additive (Figure 9) ($P < 0.001$). Treatment with DEN + 100 p.p.m. 2,5,2′,5′-TCB (group 10) did not cause a significant increase in the number of AHF when compared with DEN (Figure 9). Rats treated with the standard DEN + PB protocol had a significant increase in the number of AHF ($P < 0.001$, Figure 9).

Volume fraction of preneoplastic foci. When the volume fraction of AHF was analyzed, rats inititated with DEN and fed 10 p.p.m. 2,5,2′,5′-TCB (group 4) exhibited statistically the same volume percentage AHF as the DEN group (group 2 in Figure 10); however, the volume of AHF in the DEN + 3,4,3′,4′-TCB group (group 6) was slightly increased over that in the regenerated livers of animals receiving DEN only (group 2, Figure 10). The combination of DEN + both TCBs (group 8 in Figure 1) greatly increased the volume of the residual liver occupied by preneoplastic foci to a level that was much greater than would be expected by an additive model ($P < 0.001$; Figure 10). The group given a 10-fold greater level of 2,5,2′,5′-TCB (group 10) exhibited a significant increase in the volume of the regenerated liver occupied by AHF to 7% of the liver (Figure 10). This level was statistically greater than that of rats given DEN alone but not as great as the DEN plus both TCBs group. When the livers of rats given DEN followed by 0.05% PB in the diet were examined, there was a significant increase in the volume fraction of preneoplastic foci to 20% of the total regenerated liver (group 12 in Figure 1; see Figure 10).

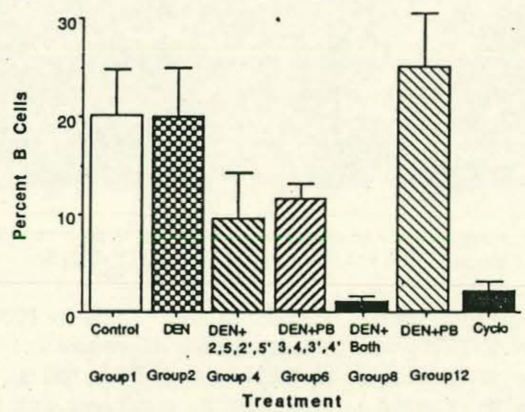


Fig. 3. Percentage of B-cells in the peripheral blood after 10 mg DEN/kg and 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB, 10 p.p.m. 2,5,2′,5′-TCB, or a combination of 3,4,3′,4′-TCB + 2,5,2′,5′-TCB or to cyclophosphamide. See text and legend to Figure 2 for details and statistical conclusions. Steel and Torrie's χ-square test for additivity was used to assess significance. $P < 0.05$.

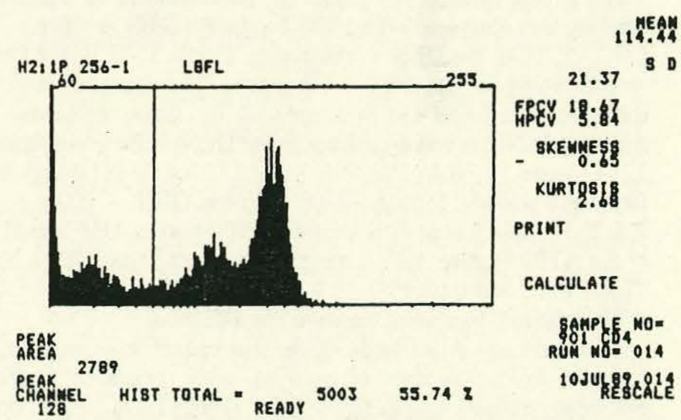


Fig. 4. Histogram of the fluorescence of T-helper cells following 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB. Antibodies conjugated with fluorescence and generated to the CD-4 protein were used to identify the T-helper cells. See text for experimental details.

Cytochrome P450 b/e was found in 10 ± 7% of the preneoplastic foci marked by PGST or ATP of the DEN + 10 p.p.m. 2,5,2′,5′-TCB, but 68 ± 10% of the AHF expressed the

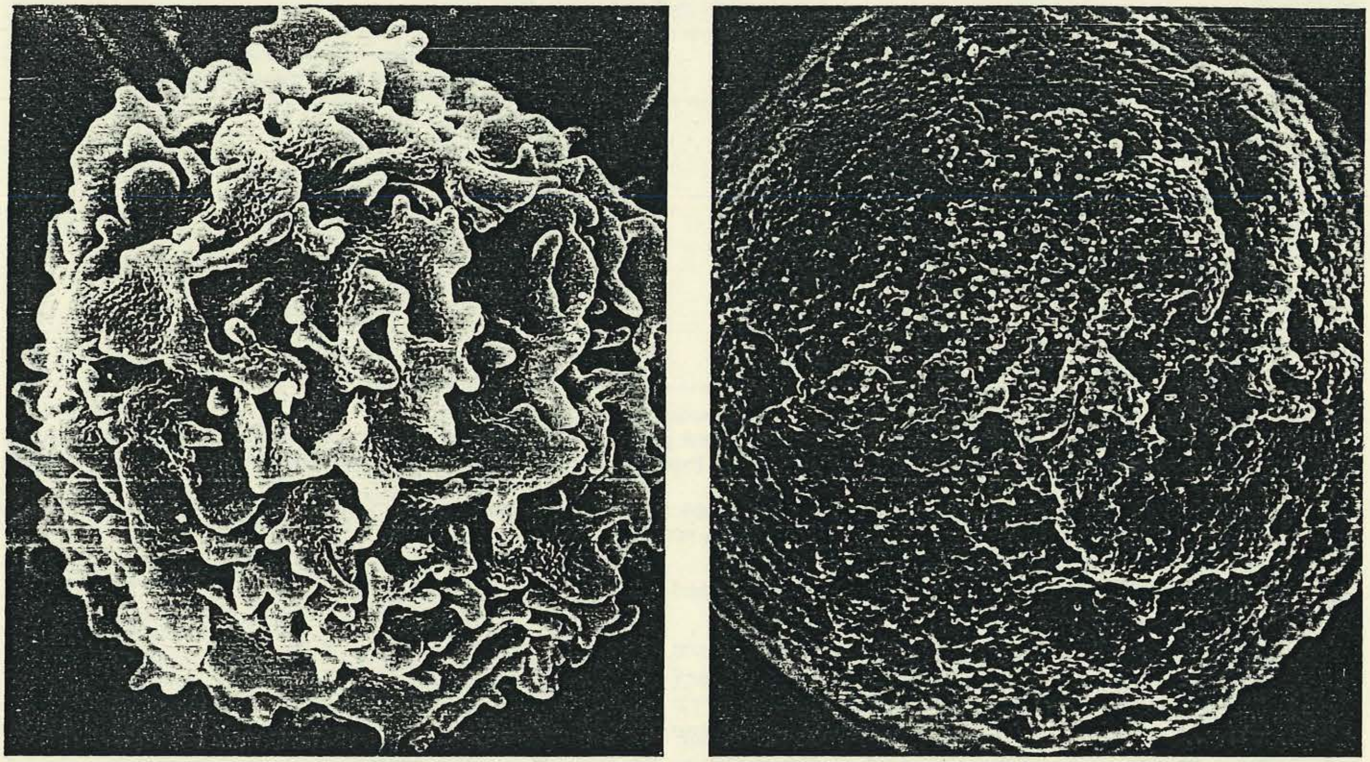


Fig. 5. Scanning electron micrograph of a normal T-helper cell (**left**) and an abnormal T-helper cell (**right**) isolated from the peripheral blood of an animal fed 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB for 1 year (×5000). See text for details.

cytochrome P450 marker in the DEN + 100 p.p.m. 2,5,2′.5′-TCB group. A larger number of positive foci was found in the group treated with DEN + both TCBs (60 ± 5%) than would be expected on the basis of the result seen with 10 p.p.m. 2,5,2′,5′-TCB alone. The number of P450 b/e positive foci found in the DEN + PB group was as large as that of the group given DEN + both TCBs (65 ± 5%) (Table II).

The expression of P450 c/d was localized to the centrolobular and midzonal region of the regenerated liver in the DEN + 3,4,3′,4′-TCB group, the DEN + both TCBs group, and the TCBs group (groups 6, 8 and 9). Centrilobular to midzonal staining was also seen with P450 b/e in the DEN + 10 p.p.m. 2,5,2′,5′-TCB, the DEN + 100 p.p.m. 2,5,2′,5′-TCB, the DEN + both TCBs and the DEN + PB groups. This degree of staining indicates that P450 c/d was induced by these regimens. In addition, P450 b/e was examined; in the DEN + PB group (group 12 in Figure 1), 76% of the PGST and 32% of the ATP-deficient foci were positive for this enzyme. In the DEN + 100 p.p.m. 2,5,2′,5′-TCB group, 22% of the PGST-positive AHF and 41% of the ATP-negative AHF were positive for P450 b/e. When both TCBs were administered, 40% of the PGST and 40% of the ATP-deficient foci were positive for P450 b/e.

The combination of both TCBs also caused a superadditive increase in the number of animals with neoplastic nodules exhibiting cellular atypia ($P < 0.05$, Table I); however, only two of the animals treated with DEN + both TCBs developed hepatocellular carcinoma (HCC). Treatment with DEN + PB for 1 year caused 80% of the animals to develop HCC.

Discussion

The planar congener, 3,4,3′,4′-TCB, and its non-planar isomer, 2,5,2′,5′-TCB, which are found in the major Aroclor mixtures 1254, 1242 and 1248, induced a greater than additive toxicity

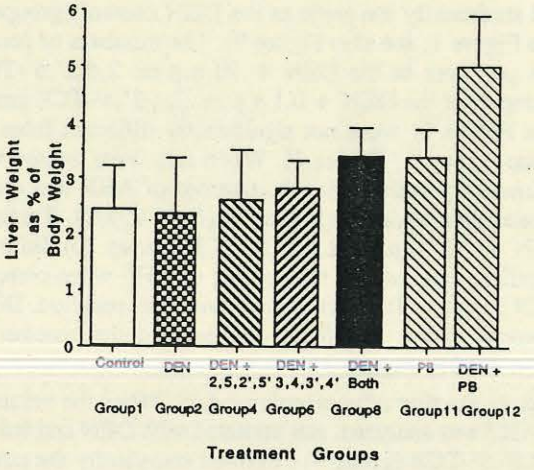


Fig. 6. Histogram of the ratio of the regenerated liver to body wt following 10 mg DEN/kg and 1 year of exposure to TCBs or to PB. The group numbers below each bar refer to the groups listed in Figure 1. The group designated PB is group 11 of Figure 1. Groups seen in Figure 1 not shown in this figure exhibited no significant change from the group 1 control.

in the two major target cell types of PCB toxicity, hepatocytes and lymphocytes, in the studies described here. Our results demonstrated that low doses of the planar 3,4,3′,4′-TCB were more toxic to lymphocytes than a 100-fold higher dose of the non-planar 2,5,2′,5′-TCB congener. The 3,4,3′,4′-TCB congener caused a reduction in the number of B-cells. A similar reduction of B-cells has been noted after acute exposure to 3,4,3′,4′-TCB (10). The combination of the two TCBs caused a greater than additive decrease in the number of circulating B-cells as well as the appearance of an abnormal subpopulation of T-helper cells. The esterase test verified that this abnormal population of

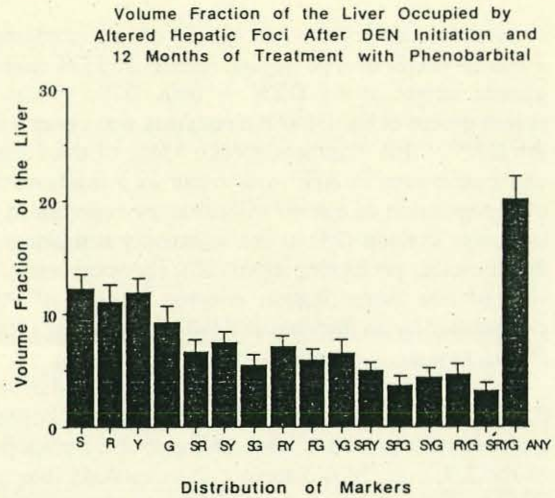


Fig. 7. Distribution of the volume fraction of AHF scored by multiple markers for AHF following initiation with 10 mg DEN/kg and 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB and 10 p.p.m. 2,5,2′,5′-TCB (group 8, Figure 1). Abbreviations: S, glutathione S-transferase-positive volume fraction; R, GGT-positive volume. Y, ATPase-negative volume; G, G6Pase-negative volume; SR, S and R combined; SY, S and Y combined. SG, S and G combined; RY, R and Y combined; RG, R and G combined; YG, Y and G combined; SYG, S and Y and G combined; SRY, S and R and Y combined. See ref. 19 for further details.

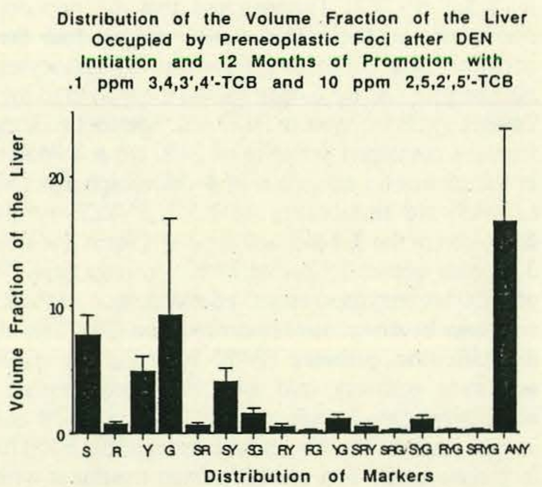


Fig. 8. Histogram of the distribution of the volume fraction of AHF scored by multiple markers for AHF following initiation with 10 mg DEN/kg and 1 year of exposure to 0.05% PB (group 12, Figure 1). See legend to Figure 7 for marker designation.

light-staining CD-4 cells was not a monocyte population, but was a new population of CD-4 cells exhibiting an abnormal surface membrane configuration.

The results from this research also demonstrated that the planar congener had more potent effects in liver cells than the non-planar TCB. The low dose of 3,4,3′,4′-TCB chosen for this study produced a moderate increase in the volume of preneoplastic foci as well as an increase in chromosome damage (L.Sargent and H.C.Pitot, unpublished observations). The relative potency of promoting agents has been expressed by the following relationship:

$$\text{promotion index} = V_f/V_c \times 1/\text{mmol per week}$$

where V_f is the total volume fraction (%) occupied by AHF in the livers of rats treated with the promoting agent, V_c is the total

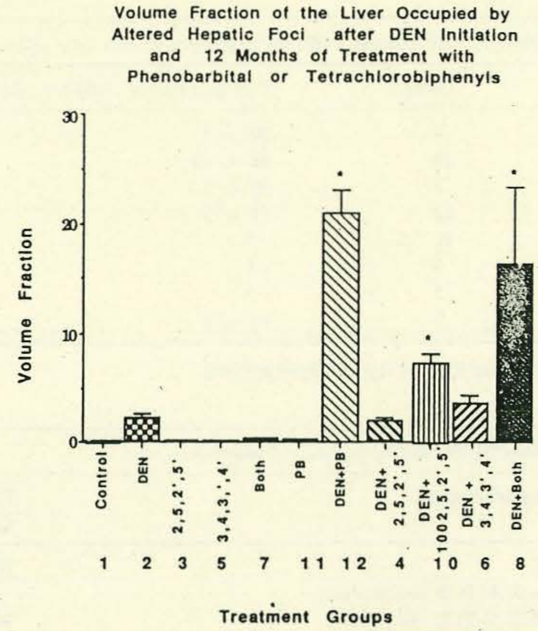


Fig. 9. Number of AHF per liver after initiation with 10 mg DEN/kg and/or 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB (groups 6 and 5), 10 p.p.m. 2,5,2′,5′-TCB (groups 4 and 3), 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB (groups 8 and 7) or to 0.05% PB in the diet for 1 year (groups 12 and 11). Eleven animals per group were killed after each treatment. The bars above the columns indicate the standard error of the mean from 11 animals. See Figure 1 for details of each group designated by number under the columns. *$P < 0.001$ by Student's *t*-test.

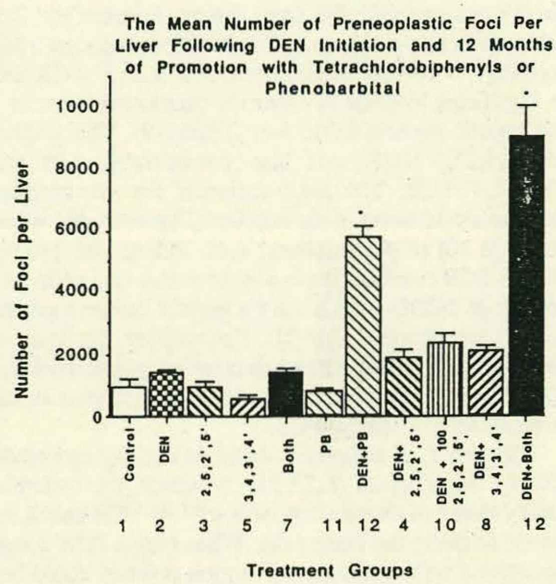


Fig. 10. Volume fraction (%) of AHF following initiation with 10 mg DEN/kg and/or 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB (groups 6 and 5), 10 p.p.m. 2,5,2′,5′-TCB (groups 4 and 3), 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB (groups 8 and 7) or to 0.05% PB (groups 12 and 11) in the diet for 1 year. Each group had 11 animals. See legend to Figure 9 for further details.

volume of AHF in control animals that have only been initiated and not treated with the promoting agent, and mmol is the number of millimoles of the promoting agent.

The promotion index (22) is based on the total number of altered cells within all AHF, thus giving a measure of tumor promotion. Table III shows the relative promotion indices of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB as well as their combination

Table II. AHF-positive P450 b/e expression after 1 year of treatment (%)

Groups	Foci positive for P450 b/e (%)
4	10 ± 7
10	68 ± 10
8	60 ± 5
12	65 ± 5
11	–[a]
3	–[a]
5	–[a]
9	40 ± 6

[a]Too few AHF to report significant data.

Table III. Promoting agents and promotion index

Promoting agents	Promotion index[a]
PB	100
3,4,3′,4′-TCB (0.1 p.p.m.)	1.5×10^4
2,5,2′,5′-TCB (10 p.p.m.)	200
2,5,2′,5′-TCB (100 p.p.m.)	250
2,5,2′,5′-TCB (10 p.p.m.) and 3,4,3′,4′-TCB (0.1 p.p.m.)	8×10^5
2,3,7,8-TCDD[b]	2.8×10^7

[a]See text for details of calculations. Promotion indices were determined in animals that had been initiated with DEN (10 mg/kg) following a 70% partial hepatectomy (see text for details).
[b]Ref. 22.

in comparison with PB from this experiment and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) from an earlier study (22). By contrast, a 10-fold higher dose of 2,5,2′,5′-TCB did not cause a significant increase in either the promotion index or the number of hepatic preneoplastic foci (Figure 9). The promotion index of 2,5,2′,5′-TCB was also considerably less than that of 3,4,3′,4′-TCB. The combination of the two congeners caused a dramatic increase in the number (Figure 9) and volume fraction (Figure 10) of preneoplastic foci. Indeed, the promotion index of the TCB combination is almost within one order of magnitude of that of TCDD, which has the highest known promotion potency of any compound (Table III). The number of animals treated with both TCBs that had numerous large neoplastic nodules exhibiting cellular atypia was also greater than that seen in either group treated with a single TCB.

The two TCB congeners differ in toxicity and binding affinity for the Ah receptor (8,23,24); however, the systemic clearance and volume of distribution of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB are essentially the same (15). When single PCB congeners were examined by others, the promotion potency could be correlated with the affinity for the Ah receptor (23). Our results also demonstrated that the strong Ah receptor ligand, 3,4,3′,4′-TCB, was a strong promoter of AHF, but the non-planar congener was a weak promoter relative to 3,4,3′,4′-TCB and TCDD. Furthermore, previous results have shown that TCDD, which has a 500-fold greater affinity for the Ah receptor than TCBs, was a stronger promoter than 3,4,3′,4′-TCB (24). The non-planar congeners, 2,4,5,2′,4′,5′-TCB (23), 2,4,2′,4′-TCB and 2,5,2′,5′-TCB, have been reported to exhibit promoting activity for hepatic preneoplastic foci (14). The presence of chlorine substitution in the *para* position correlated with an enhancement of promoting potency, but all the non-planar congeners were less potent than the planar 3,4,3′,4′-TCB.

An enhancement of the amount of P450 b/e enzymes was seen in preneoplastic hepatic foci (AHF) of rats receiving 10 p.p.m. 2,5,2′,5′-TCB or 100 p.p.m. 2,5,2′,5′-TCB and to an even greater extent in the DEN + both TCBs group. This same enhancement of the P450 b/e enzymes was observed in AHF of the DEN + PB treatment group. Many of the changes in gene expression seen in AHF may occur as a result of the selection of a population of altered cells that are resistant to the specific treatment utilized (25) or are selectively stimulated to grow by the particular promoting agent (26). Enhancement of the expression of this detoxification enzyme in cells of AHF is also exemplified by an increase of P450 b/e following promotion with PB as well as hexachlorocyclohexane (27,28).

The greater than additive toxicity of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB that was seen *in vivo* in hepatocytes and lymphocytes may have been owing to the metabolic activation of the 2,5,2′,5′-TCB congener to an epoxide intermediate (14, 29,30). This epoxide intermediate is more toxic and more chromosome damaging than the parent compound (31) and has been shown to bind to DNA (29,32). PCB congeners that have both the *meta* and *para* sites available for oxidation can be metabolized through an epoxide intermediate. These intermediates can bind to DNA and have been found to be mutagenic (25,31). Examination of the dose–response curves of previous *in vitro* studies of chromosome damage in human lymphocytes (33) caused by 3,4,3′,4′-TCB and a combination of 3,4,3′,4′-TCB + 2,5,2′,5′-TCB demonstrated that the two dose–response curves are parallel. This would suggest that the two events occurred by a common mechanism. Lymphocytes express the Ah receptor and have been shown to respond to the Ah receptor ligands by an increase in P450 c/d. Metabolic changes resulting from the combined induction of P450 c/d and P450 b/e can result in the metabolic activation of 4-chlorobiphenyl (34). Inhibition of P450 c/d metabolism of 2,5,2′,5′-TCB results in greater formation of the 3,4-diol and the 4-OH form, indicating that more 3,4-oxide occurs following P450 c/d induction. The induction of P450 b/e enzymes results in detoxification of the 2,5,2′,5′-TCB congener by direct *meta*-hydroxylation (32). The absence of the detoxification pathway (P450 b/e) and the presence of the activation pathway (c/d induction) may explain the greater sensitivity of the lymphocytes to 2,5,2′,5′-TCB observed in the *in vivo* studies (35). The enhancement of the P450 b/e expression in preneoplastic foci resulting from treatment with both TCBs and with DEN + 2,5,2′,5′-TCB as well as with DEN + PB may result in a selective reduced toxicity to 2,5,2′,5′-TCB conferred to these cells by this gene expression.

Although centrilobular to midzonal staining for P450 b/e was observed by Buchman *et al.* (36) after DEN initiation and promotion with 3,4,5,3′,4′,5′-hexachlorobiphenyl (HCB) or with 2,4,5,2′,4′,5′-HCB, no increased staining for the P450 b/e isozyme occurred in AHF with this protocol. The 2,4,5,2′,4′,5′-HCB congener is an inducer of the P450 b/e isozyme; however, this congener is not known to be metabolized by this form or any other form of P450. Increased expression of a detoxification enzyme in cells of AHF has been observed as an increase of P450 b/e after promotion with PB as well as with hexachlorocyclohexane (36). Cells of AHF resulting from *N*-hydroxy ethylnitrosamine treatment exhibit reduced levels of P450 b/e and P450 c/d forms and an increase in glutathione S-transferase and expoxide hydrolase (23). Chronic treatment of rats with 2-acetylaminofluorene, which is metabolized by multiple forms of P450 (36), causes the proliferation of focal areas of preneoplastic hepatocytes; this may significantly lower the expression of many P450 genes as well as increase the conjugating enzymes that

detoxify the reactive intermediate (37). When PB administration followed AAF treatment, however, the level of P450 b/e was induced in AHF that had previously been negative for the enzyme (38). Thus, as a result of the alteration of drug-metabolizing enzymes, cells of AHF may have a selective advantage in a toxic environment. Since the growth of normal cells is suppressed by the cytotoxic effects of these treatments, the preneoplastic cells have an additional proliferative advantage.

The centrilobular to midzonal staining for P450 b/e that was evident in the livers of rats treated with DEN + PB or DEN + both TCBs indicates that enzyme induction occurred in response to these compounds in hepatocytes in these zones. Centrilobular staining with P450 c/d after treatment with DEN + 3,4,3',4'-TCB or DEN + both TCBs indicates that induction of this isozyme also occurred. The dose of 3,4,3',4'-TCB was 0.3% of the 6-day chronic dose used for maximal induction by Clevenger (14), and 0.003% of the acute dose used by Parkinson (6). The dose of 2,5,2',5'-TCB utilized in our studies was 33% of the maximal chronic dose and 3% of the maximal acute dose used in other studies (13,23,24).

The greater than additive effect of the mixture of 3,4,3',4'-TCB and 2,5,2',5'-TCB reported in this study may be the result of one or more of three possible mechanisms: (i) Ah receptor gene expression (1,4,5); (ii) the PB-type of cytochrome P450 response (24,39); (iii) the metabolic activation of PCBs to epoxides (29,30). Glutathione conjugation is the major phase II detoxification pathway for the 3,4-oxide of 2,5,2'-TCB. Several different mechanisms can contribute to the toxic effects of 2,5,2',5'-TCB. Although the mechanism of glutathione depletion may be different in hepatocytes and lymphocytes, continuous exposure to the TCB combination may have resulted in depletion of the glutathione levels in both cell types. Depletion of glutathione would prevent a major part of the detoxification of the 3,4-oxide of 2,5,2',5'-TCB (32).

Our results demonstrate an interaction of low doses of two PCBs *in vivo* in the two major target organs of PCB toxicity, the liver and the immune system, at doses that are relevant to human exposure levels (40). The observation of immune depression and promotion of AHF with very low PCB concentrations suggests that the biological effects of a complex Aroclor mixture in two different target cell populations of PCB toxicity may not be owing simply to the summed effects of each of the constituent chemicals or to the individual concentrations of the most toxic congeners, but rather largely to the effects of only a few constituents interacting at low concentrations.

This study also represents the first report of the appearance of an abnormal population of CD-4 lymphocytes in the peripheral blood after PCB exposure. This may be an important finding not only for rodent exposure, but also for human exposure, because this same PCB combination was very genotoxic to cultured human lymphocytes. The abnormal population of CD-4 cells in the peripheral blood may be the result of a genetic change that occurred in these cells. The aneuploidy of many hepatocytes (L.M.Sargent, G.Sattler, C.A.Sattler, B.Roloff, Y.Xu and H.C.Pitot, in preparation) and numerous large neoplastic nodules exhibiting cellular atypia in the liver are indications that the combination of 3,4,3',4'-TCB and 2,5,2',5'-TCB induces the stage of progression of hepatocarcinogenesis (41,42). Confirmation of this hypothesis will require further testing because the percentage of animals with hepatocellular carcinoma was not elevated after 1 year of treatment in this experiment. The numerous large neoplastic nodules with cellular atypia probably represent rapidly growing populations of abnormal cells. If this protocol had been allowed to continue further, it is possible that there would have been an increase in the frequency of hepatocellular carcinoma in the livers of rats receiving the combination compared with those administered each TCB alone.

Acknowledgements

We would like to thank Dr Colin Jefcoate for supplying the P450 antibodies. We would like to extend our gratitude to Dr James A.Miller for the gift of 2,5,2',5'-TCB. We also thank Dr David Auerbach and the State Laboratory of Hygiene for their help in performing the flow cytometry. The expert histotechnology of Ms Jane Weeks and Mrs Jennifer Potter is also gratefully acknowledged, as well as the expert technical typing of Mrs Mary Jo Markham. The authors are grateful to Dr Ilse Riegel for technical editing and comments on the manuscript. The experiments described in this document were funded in part by grants from the National Cancer Institute (CA-07175, CA-2284 and CA-45700) and by a training grant from the National Institute of Environmental Health Sciences (ES-07015).

References

1. Safe,S. (1989) Polychlorinated biphenyls (PCBs): mutagenicity and carcinogenicity. *Mutat. Res.*, **220**, 31–47.
2. Passivirta,J. and Linko,R. (1980) Environmental toxins in Finnish wildlife. A study of trends of residue contents in fish during 1973–1978. *Chemosphere*, **9**, 643.
3. Jacobs,L.W., Chou,S.F. and Tiedje,J.M. (1978) Field concentrations and persistence of polybrominated biphenyls in soils and solubility of polybrominated biphenyls in natural waters. *Environ. Health Perspect.*, **23**, 1.
4. Safe,S., Bandiera,S., Sawyer,T., Robertson,L.W., Safe,L., Parkinson,A., Thomas,P.E., Ryan,D.E., Reik,L.M., Levin,W., Denomme,M.A. and Fujita,T. (1985) PCBs: structure–function relationships and mechanisms of action. *Environ. Health Perspect.*, **60**, 47–56.
5. Poland,A. and Knutson,J.C. (1982) 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin and related halogenated aromatic hydrocarbons: examination of the mechanism of toxicity. *Annu. Rev. Pharmacol. Toxicol.*, **22**, 517–554.
6. Parkinson,A., Robertson,L., Safe,L. and Safe,S. (1981) Polychlorinated biphenyls as inducers of hepatic microsomal enzymes: structure–activity rules. *Chem.-Biol. Interactions*, **35**, 1–2.
7. McKinney,J.D. and Singh,P. (1981) Structure–activity relationships in halogenated biphenyls: unifying hypothesis for structural specificity. *Chem.-Biol. Interactions*, **333**, 271–283.
8. Yoshimura,H., Yoshihara,S., Ozawa,N. and Miki,M. (1979) Possible correlation between induction modes of hepatic enzymes by PCBs and their toxicity in rats. *Ann. NY Acad. Sci.*, **320**, 179–192.
9. Silkworth,J.B. and Grabstein,E.M. (1982) Polychlorinated biphenyl immunotoxicity: dependence on isomer planarity and the *Ah* gene complex. *Toxicol. Appl. Pharmacol.*, **65**, 109–119.
10. Greenlee,W.F. and Irons,R.E. (1981) Modulation of benzene-induced lymphocytopenia in the rat by 2,4,5,2',4',5'-hexachlorobiphenyl and 3,4,4',5'-tetrachlorobiphenyl. *Chem.-Biol. Interactions*, **33**, 345–360.
11. Wölfle,D., Münzel,P., Fischer,G. and Bock,K.-W. (1988) Altered growth control of rat hepatocytes after treatment with 3,4,3',4'-tetrachlorobiphenyl *in vivo* and *in vitro*. *Carcinogenesis*, **9**, 919–924.
12. Osterele,D. and Deml,E. (1981) Promotion effect of various PCBs and DDT on enzyme altered islands in rat liver. *Nauyn-Schmiedberg's Arch. Pharmacol. Suppl. R*, **16**, 316.
13. Preston,B.D., Miller,E.C. and Miller,J.A. (1985) The activities of 2,2',5,5'-tetrachlorobiphenyl, its 3,4-oxide metabolite and 2,2',5,5'-tetrachlorobiphenyl in tumor induction and promotion assays. *Carcinogenesis*, **6**, 451–453.
14. Clevenger,M.A., Roberts,S.M., Sattin,D.L., Harbison,R.D. and James,R.C. (1989) The pharmacokinetics of 2,2',5,5'-tetrachlorobiphenyl and 3,3',4,4'-tetrachlorobiphenyl and its relationship to toxicity. *Toxicol. Appl. Pharmacol.*, **100**, 315–327.
15. Pitot,H.C., Campbell,H.A., Maronpot,R., Nimrat,B., Rizvi,T.A., Xu,Y.-H., Sargent,L.M., Dragan,Y. and Pyron,M. (1989) Critical parameters in the quantitation of the stages of initiation, promotion, and progression in one model of hepatocarcinogenesis in the rat. *Toxicol. Pathol.*, **17**, 594–612.
16. Pitot,H.C., Barsness,L., Goldsworthy,T. and Kitagawa,T. (1978) Biochemical characterization of stages of hepatocarcinogenesis after a single dose of diethylnitrosamine. *Nature*, **271**, 456–458.
17. Yam,L.T., Li,C. and CrosbyW.H. (1971) Cytochemical identification of monocytes and granulocytes. *Am. J. Clin. Pathol.*, **55**, 283–290.
18. Braylan,R.C. (1983) Attributes and applications of flow cytometry. *Ann. Clin. Lab. Sci.*, **13**, 379–384.

19. Xu,Y.-H., Campbell,H.A., Sattler,G.L., Hendrich,S., Maronpot,R., Sato,K. and Pitot,H.C. (1990) Quantitative stereological analysis of the effects of age and sex on multistage hepatocarcinogenesis in the rat by use of four cytochemical markers. *Cancer Res.*, **50**, 472–479.
20. Campbell,H.A., Xu,Y.-H., Hanigan,M.H. and Pitot,H.C. (1986) Application of quantitative stereology to the evaluation of phenotypically heterogeneous enzyme-altered foci in the rat liver. *J. Natl. Cancer Inst.*, **76**, 751–767.
21. Steel,R.G.D. and Torrie,J.H. (1980) Enumeration data II: contingency tables, some uses of χ-square. In *Principles and Procedures of Statistics, a Biometrical Approach.* McGraw-Hill Book Company, New York, pp. 469–520.
22. Pitot,H.C., Goldsworthy,T.L., Moran,S., Kennan,W., Glauert,H.P., Maronpot,R.R. and Campbell,H.A. (1987) A method to quantitate the relative initiating and promoting potencies of hepatocarcinogenic agents in their dose–response relationships to altered hepatic foci. *Carcinogenesis*, **8**, 1491–1499.
23. Safe,S. (1983) Polychlorinated biphenyls (PCBs) and polybrominated biphenyls: biochemistry, toxicology and mechanisms. *CRC Rev. Toxicol.*, **13**, 319–325.
24. Silberhorn,E.M., Glauert,H.P. and Robertson,L.W. (1990) Carcinogenicity of polyhalogenated biphenyls: PCBs and PBBs. *Crit. Rev. Toxicol.*, **20**, 439–496.
25. Eriksson,L., Ahluwalia,M., Spiewak,J., Lee,G., Sarma,D.S.R., Roomi,M.J. and Farber,E. (1983) Distinctive biochemical pattern associated with resistance to hepatocytes in hepatocyte nodules during liver carcinogenesis. *Environ. Health Perspect.*, **49**, 171–174.
26. Dragan,Y.P., Xu,Y.-H., Hully,J.R., Bawa,N., Rizvi,T., Campbell,H.A., Maronpot,R.R. and Pitot,H.C. (19??) An initiation-promotion assay in rat liver as a potential complement to the two-year carcinogenesis bioassay. *Fund. Appl. Toxicol.*, in press.
27. Schulte-Hermann,R., Roome,N., Timmermann-Trosiener,I. and Schuppler,J. (1984) Immunocytochemical demonstration of a phenobarbital-induced cytochrome P450 in putative preneoplastic foci of rat liver. *Carcinogenesis*, **5**, 149–153.
28. Schwarz,M., Peres,G., Buchmann,A., Friedberg,T., Waxman,D.J. and Kunz,W. (1987) Phenobarbital induction of cytochrome P450 in normal and preneoplastic rat liver: comparison of enzyme and mRNA expression as detected by immunohistochemistry and *in situ* hybridization. *Carcinogenesis*, **8**, 1355–1357.
29. Forgue,S.T., Preston,B.D., Hargraves,W.A., Reich,I.L. and Allen,J.R. (1979) Direct evidence that an aerene oxide is a metabolic intermediate of 2,5,2′,5′-tetrachlorobiphenyl. *Biochem. Biophys. Res. Commun.*, **91**, 475–483.
30. Forgue,S.T. and Allen,J.R. (1982) Identification of an aerene oxide metabolite of 2,5,2′,5′-tetrachlorobiphenyl by gas chromatography–mass spectroscopy. *Chem.-Biol. Interactions*, **40**, 233–245.
31. Stadnicki,S.S., Francis,S.D.L. and Allen,J.R. (1979) DNA strand breaks caused by 2,5,2′,5′-tetrachlorobiphenyl and its metabolites. *Res. Commun. Chem. Pathol. Pharmacol.*, **24**, 313–325.
32. Preston,B.D., Miller,J.A. and Miller,E.C. (1984) Reactions of 2,2′,5,5′-tetrachlorobiphenyl 3,4-oxide with methionine, cysteine and glutathione in relation to the formation of methylthio-metabolites of 2,2′,5,5′-tetrachlorobiphenyl in the rat and mouse. *Chem.-Biol. Interactions*, **50**, 289–312.
33. Sargent,L.M., Roloff,B.D. and Meisner,L.F. (1989) *In vitro* chromosome damage due to PCB interactions. *Mutat. Res.*, **224**, 79–88.
34. Wyndhman,C., Devenish,J. and Safe,S. (1978) The *in vitro* metabolism, macromolecular binding and bacterial mutagenicity of 4-chlorobiphenyl, a model PCB substrate. *Res. Commun. Chem. Pathol. Pharmacol.*, **15**, 563–570.
35. Kawabata,T.T. and White,K.L., Jr (1989) Benzo[*a*]pyrene metabolism by murine spleen microsomes. *Cancer Res.*, **49**, 5816–5822.
36. Buchmann,A., Kunz,W., Wolf,C.R., Oesch,F. and Robertson,L.W. (1986) Polychlorinated biphenyls, classified as either phenobarbital- or 3-methylcholanthrene-type inducers of cytochrome P450, are both hepatic tumor promoters in diethylnitrosamine-initiated rats. *Cancer Lett.*, **32**, 243–253.
37. Roomi,M.W., Ho,R.K., Sarma,D.S.R. and Farber,E. (1985) A common biochemical pattern in preneoplastic hepatocyte nodules generated in four different models in the rat. *Cancer Res.*, **45**, 564–571.
38. Ghoshal,A., Gurtoo,H.L., Faletto,M.B., Koo,P., Nagi,M. and Farber,E. (1990) Molecular basis for the constitutive decrease in cytochromes P450 in putative preneoplastic hepatocytes. *Proc. Am. Assoc. Cancer Res.*, **31**, 136.
39. Goldstein,J.A., Hickman,P., Bergman,H., McKinney,J.D. and Walker, M.P.(1977) Separation of pure polychlorinated biphenyl isomers into two types of inducers on the basis of induction of P450 or P448. *Chem.-Biol. Interactions*, **17**, 69–87.
40. Cordle,F., Corneliussen,P., Jelinek,C., Hackley,B., Lehman,R., McLaughlin,J., Rhoden,R. and Shapiro,R. (1978) Human exposure to polychlorinated biphenyls and polybrominated biphenyls. *Environ. Health Perspect.*, **24**, 157–172.
41. Sherer,E., Feringa,A.W. and Emmelot,P.(1984) Initiation–promotion–initiation induction of neoplastic foci within islands of precancerous liver cells in the rat. In Börzxönyi,M., Lapi,K., Day,N. and Yamasaki,H. (eds), *Models, Mechanisms and Etiology of Tumour Promotion.* IARC Scient. Pub. 56, Lyon, pp. 57–66.
42. Pitot,H.C. (1989) Progression: the terminal stages in carcinogenesis. *Jpn. J. Cancer Res.*, **80**, 599–607.
43. Schauer,A. and Kunze,E. (1976) Tumours of the liver. In Turusov,V.S. (ed.), *Pathology of Tumours in Laboratory Animals. Vol. 1. Tumours of the Rat, Part* 2. IARC, Lyon, pp. 41–72.
44. Squire,R.A. and Levitt,M.H. (1975) Report of a workshop on classification of specific hepatocellular lesions in rats. *Cancer Res.*, **35**, 3214–3223.
45. National Research Council (1980) Histologic typing of liver tumors in the rat. *J. Natl. Cancer Inst.*, **64**, 179–206.

Received on August 20, 1990; revised on January 17, 1991; accepted on January 25, 1991

ATTACHMENT 6

CANCER MORTALITY IN WORKERS EXPOSED TO 2,3,7,8-TETRACHLORODIBENZO-*p*-DIOXIN

Marilyn A. Fingerhut, Ph.D., William E. Halperin, M.D., David A. Marlow, B.S., Laurie A. Piacitelli, M.S., Patricia A. Honchar, Ph.D., Marie H. Sweeney, Ph.D., Alice L. Greife, Ph.D., Patricia A. Dill, A.B., Kyle Steenland, Ph.D., and Anthony J. Suruda, M.D.

Abstract *Background.* In both animal and epidemiologic studies, exposure to dioxin (2,3,7,8-tetrachlorodibenzo-*p*-dioxin, or TCDD) has been associated with an increased risk of cancer.

Methods. We conducted a retrospective cohort study of mortality among the 5172 workers at 12 plants in the United States that produced chemicals contaminated with TCDD. Occupational exposure was documented by reviewing job descriptions and by measuring TCDD in serum from a sample of 253 workers. Causes of death were taken from death certificates.

Results: Mortality from several cancers previously associated with TCDD (stomach, liver, and nasal cancers, Hodgkin's disease, and non-Hodgkin's lymphoma) was not significantly elevated in this cohort. Mortality from soft-tissue sarcoma was increased, but not significantly (4 deaths; standardized mortality ratio [SMR], 338; 95 percent confidence interval, 92 to 865). In the subcohort of 1520 workers with ≥1 year of exposure and ≥20 years of latency, however, mortality was significantly increased for soft-tissue sarcoma (3 deaths; SMR, 922; 95 percent confidence interval, 190 to 2695) and for cancers of the respiratory system (SMR, 142; 95 percent confidence interval, 103 to 192). Mortality from all cancers combined was slightly but significantly elevated in the overall cohort (SMR, 115; 95 percent confidence interval, 102 to 130) and was higher in the subcohort with ≥1 year of exposure and ≥20 years of latency (SMR, 146; 95 percent confidence interval, 121 to 176).

Conclusions. This study of mortality among workers with occupational exposure to TCDD does not confirm the high relative risks reported for many cancers in previous studies. Conclusions about an increase in the risk of soft-tissue sarcoma are limited by small numbers and misclassification on death certificates. Excess mortality from all cancers combined, cancers of the respiratory tract, and soft-tissue sarcoma may result from exposure to TCDD, although we cannot exclude the possible contribution of factors such as smoking and occupational exposure to other chemicals. (N Engl J Med 1991; 324:212-8.)

Several epidemiologic and toxicologic studies have suggested an association between 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), or the chemicals it contaminates, and soft-tissue sarcoma,[1-4] Hodgkin's disease,[5] non-Hodgkin's lymphoma,[6-8] stomach cancer,[9,10] nasal cancer,[11] and cancer of the liver.[12,13] In other studies of these cancers, no significant associations with TCDD exposure were found.[14-19] The carcinogenicity of TCDD has been demonstrated in studies of rats, mice, and hamsters; histiocytic lymphomas, fibrosarcomas, and tumors of liver, skin, lung, thyroid, tongue, hard palate, and nasal turbinates have been found.[12,13,20] TCDD acts as a promoter[21,22] and may also initiate carcinogenesis.[12,13,20] To evaluate the effect of occupational exposure to TCDD, particularly with respect to the cancers listed above, we conducted a retrospective cohort study of mortality among U.S. chemical workers assigned to the production of substances contaminated with TCDD.

Methods

Identification of Companies

In 1978 the National Institute for Occupational Safety and Health began an effort that would eventually identify the exposed workers at all U.S. chemical companies that had made TCDD-contaminated products between 1942 and 1984. TCDD was generated as a contaminant in the production of 2,4,5-trichlorophenol and was carried into subsequent production processes.[23] One derivative, 2,4,5-trichlorophenoxyacetic acid, was widely used in the United States to kill brush and was a constituent of defoliants such as Agent Orange. Other derivatives included the herbicides 2-(2,4,5-trichlorophenoxy)propionic acid (Silvex) and 2-(2,4,5-trichlorophenoxy)-ethyl 2,2-dichloropropionate (Erbon), the insecticide *O,O*-dimethyl *O*-(2,4,5-trichlorophenyl)phosphorothioate (Ronnel), and the bactericide 2,2′-methylene-bis[3,4,6-trichlorophenol] (hexachlorophene).

Identification of Exposed Workers

Workers from 12 companies were included in the study cohort if a personnel or payroll record documented that they had been assigned to a production or maintenance job in a process involving TCDD contamination (n = 5000), or if they had been identified in a previously published study on the basis of exposure to TCDD (n = 172).[24] Personnel records for 202 workers did not reveal the duration of their assignment to processes involving TCDD contamination; they were therefore included in the analysis of overall mortality but excluded from analyses according to duration of exposure. Sixty-seven women are not included in this report; there were 10 deaths among them, including a single death from cancer (lung cancer).

At each plant, we made a thorough review of operating conditions, job duties, and records of TCDD levels in industrial-hygiene samples, intermediate reactants, products, and wastes. This review provided clear evidence of potential daily exposure to TCDD. The production of TCDD-contaminated substances at the various plants involved similar raw materials, processes, and job duties.[25] However, there were differences between jobs and between plants in the extent of TCDD exposures. Occupational exposure to substances contaminated with TCDD was confirmed by measuring serum TCDD levels, as adjusted for lipids, in 253 surviving members of the study cohort from two plants who were also participants in a related cross-sectional medical study.[26]

Life-Table Analysis

Vital status was determined as of December 31, 1987, from records of the Social Security Administration or Internal Revenue Service, or from the National Death Index. All death certificates

From the Industrywide Studies Branch, Division of Surveillance, Hazard Evaluations, and Field Studies, National Institute for Occupational Safety and Health, Centers for Disease Control, 4676 Columbia Pky., Cincinnati, OH 45226, where reprint requests should be addressed to Dr. Fingerhut.

Supported in part by the Agency for Toxic Substances and Disease Registry.

were independently classified by two nosologists according to the rules of the revision of the *International Classification of Diseases* (ICD) in effect at the date of death.[27]

Life-table analysis was used to evaluate mortality in the cohort.[28] At each plant, the number of person-years at risk was calculated as the interval between the first systematically documented assignment to a process involving TCDD contamination and the date of death or December 31, 1987, whichever occurred first. Those whose vital status was unknown were assumed to be alive at the end of the study. Standardized mortality ratios (SMRs) were computed by dividing the observed number of deaths by the expected number and multiplying by 100, after stratification to adjust for the confounding effects of age, race, and year of death. Two-sided 95 percent confidence intervals were computed for each cause-specific SMR, with use of the Byar approximation for eight deaths or more and Fisher's exact method for fewer than eight deaths.[29] The U.S. population was used as the reference group, because the 12 plants were located in 11 states throughout the country.

Analyses According to Duration of Exposure and Employment

Duration of exposure was defined as the number of years the worker was employed in processes involving TCDD contamination and was calculated with data from personnel records. We used duration of exposure as a surrogate for cumulative exposure to TCDD on the basis of the high correlation of the logarithm of serum TCDD levels with the logarithm of the number of years assigned to processes involving TCDD contamination in our sample of 253 workers (Pearson's product-moment coefficient $r = 0.72$) (Fig. 1), and on the assumption that the production processes were similar in the 12 plants.[25]

Because of the concentration of person-years in the short-duration categories, duration of exposure was stratified before analysis into categories of <1, 1 to <5, 5 to <15, and ≥15 years (Table 1). Mortality was also examined according to time since first exposure (latency) in periods of 0 to <10, 10 to <20, and ≥20 years since first exposure. To examine mortality in a subgroup with substantial exposure and adequate time for cancer to develop, we identified a group of workers who had 1 year or more of exposure to processes involving TCDD contamination and at least 20 years of latency. One year was chosen as a cutoff point for this high-exposure subcohort because in the sample of workers whose serum TCDD levels were measured, 100 percent of those exposed for more than one year had serum TCDD levels higher than the mean level in the unexposed reference group (7 pg per gram of lipid). For this subcohort, the number of person-years at risk was calculated from the date the person attained both 20 years of latency and 1 year of exposure.

Most of the 12 plants were large U.S. chemical manufacturing sites that produced thousands of chemicals. Complete documentation of each worker's exposures was impossible. A separate measure called "duration of employment," defined as the total time that each worker was employed at a study plant, was therefore used. Because of the long total employment at the plants, analyses according to duration of employment were stratified into periods of <5, 5 to <10, 10 to <15, 15 to <20, 20 to <25, 25 to <30, and ≥30 years (Table 1). For these analyses, latency was defined as time since first employment.

When the SMRs showed an apparent trend associated with duration of exposure or employment and when the observed numbers of deaths were sufficiently large, we conducted internal comparisons using directly standardized rate ratios and tests for trend.[30] For the standardized rate ratios, the cause-specific mortality rate in each of the categories of longer duration was compared with the rate in the category of shortest duration, after stratification of the rates for the potential confounding effects of age, race, and calendar time.

Results

The cohort of 5172 male workers from 12 plants had 116,748 person-years of observation. Table 1 describes the vital status, race, latency, and duration of exposure and employment of the workers. Overall mortality for all causes of death was similar to national rates in the United States (1052 deaths; SMR, 99; 95 percent confidence interval, 93 to 105). Mortality from heart disease was also similar to national rates

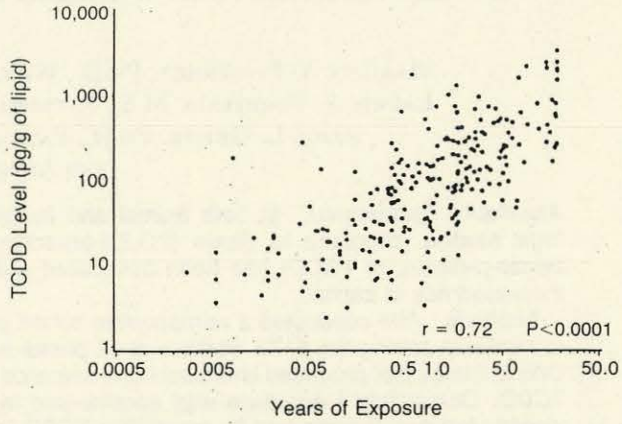


Figure 1. Serum Levels of TCDD, as Adjusted for Lipids, in 253 Workers, According to Years of Exposure.

Table 1. Vital Status and Demographic and Employment Characteristics of the Study Cohort.

Variable	Number (Percent)
Vital status*	
Alive	4043 (78)
Dead	1052 (20)
Unknown	77 (2)
Total	5172 (100)
Deaths*	
White men	985 (94)
Nonwhite men	67 (6)
Total	1052 (100)
Death certificates obtained	1037 (99)
Race	
White	4590 (89)
Nonwhite	385 (7)
Unknown	197 (4)
Total	5172 (100)
Duration of exposure (yr)†	
<1	2697 (54)
1 to <5	1427 (29)
5 to <15	639 (13)
≥15	207 (4)
Total	4970 (100)
Duration of employment (yr)†	
<5	2125 (43)
5 to <10	501 (10)
10 to <15	605 (12)
15 to <20	403 (8)
20 to <25	391 (8)
25 to <30	415 (8)
≥30	530 (11)
Total	4970 (100)
Years since first exposure (latency)†	
<10	271 (5)
10 to <20	1663 (33)
≥20	3036 (61)
Total	4970 (100)
Years since last exposure†	
<10	453 (9)
10 to <20	1789 (36)
≥20	2728 (55)
Total	4970 (100)

*As of December 31, 1987.

†Excludes 202 workers for whom duration of assignment to processes involving TCDD contamination was not available from work records.

(393 deaths; SMR, 96; 95 percent confidence interval, 87 to 106). There were significant reductions in the mortality rates for diseases of the circulatory system (67 deaths; SMR, 77; 95 percent confidence interval, 60 to 98), primarily because of fewer deaths from stroke, and for diseases of the digestive system (38 deaths; SMR, 70; 95 percent confidence interval, 49 to 96), primarily because of fewer deaths from cirrhosis. There were also significantly fewer deaths from alcoholism and personality disorders (2 deaths; SMR, 23; 95 percent confidence interval, 3 to 87). The low mortality from circulatory disease may be a reflection of the "healthy worker" effect — cohorts of workers die at lower rates than the general population, particularly of causes other than cancer.[31] The reduced number of deaths from cirrhosis and alcoholism implies that this cohort consumed less alcohol than the general population. Reduction may also have occurred simply by chance, since numerous comparisons were made between the cohort and the U.S. population. Fatal injuries were significantly more frequent in the cohort (106 deaths; SMR, 128; 95 percent confidence interval, 104 to 154), but they did not appear to be associated particularly with exposure to TCDD. Mortality from all cancers combined (265 deaths; SMR, 115; 95 percent confidence interval, 102 to 130) was significantly elevated in the cohort.

Cancers of a Priori Interest

The term "soft-tissue sarcoma" describes the group of rare malignant neoplasms arising from supporting tissue other than bone.[32] We restricted our analysis of mortality due to soft-tissue sarcoma to cases of soft-tissue sarcoma listed as the underlying cause of death

Table 2. Cancer Mortality in the Entire Cohort and in Workers with More Than 20 Years of Latency.

Site of Cancer	ICD Code*	Entire Cohort (N = 5172)†			Subcohort with ≥20 Yr of Latency (N = 3036)‡					
					<1 yr of exposure (N = 1516)§			≥1 yr of exposure (N = 1520)¶		
		deaths observed	deaths expected	SMR‖	deaths observed	deaths expected	SMR‖	deaths observed	deaths expected	SMR‖
All cancers	140–208	265	229.9	115 (102–130)**	48	46.8	102 (76–136)	114	78.0	146 (121–176)**
Buccal and pharynx	140–149	5	7.0	70 (23–166)	2	1.4	145 (18–524)	2	2.2	90 (11–325)
Pharynx	146–149	3	3.4	88 (18–259)	2	0.7	298 (36–1080)	0	1.2	0 (—)
Other parts	142–145	2	1.9	105 (13–379)	0	0.4	0 (—)	2	0.6	329 (40–1190)
Digestive organs	150–159	67	59.7	112 (87–143)	13	11.8	111 (59–189)	28	20.1	140 (93–202)
Esophagus	150	9	5.9	152 (70–290)	2	1.2	165 (20–602)	4	2.0	200 (55–513)
Stomach	151	10	9.7	103 (50–190)	3	1.7	178 (37–521)	4	2.9	138 (38–353)
Small intestine and colon	152–153	25	20.4	122 (79–181)	5	4.3	117 (38–274)	13	7.3	178 (95–304)
Rectum	154	5	5.6	89 (29–209)	1	1.0	100 (3–557)	2	1.7	115 (14–415)
Liver and biliary	155, 156	6	5.2	116 (42–252)	1	1.0	100 (3–557)	1	1.7	59 (1–327)
Pancreas	157	10	11.9	84 (40–155)	1	2.4	41 (1–232)	4	4.0	100 (27–253)
Peritoneum and unspecified	158, 159	2	1.1	184 (22–666)	0	0.2	0 (—)	0	0.4	0 (—)
Respiratory system	160–165	96	84.5	113 (92–139)	19	18.4	103 (62–161)	43	30.2	142 (103–192)
Larynx	161	7	3.3	211 (84–434)	2	0.7	297 (36–1074)	3	1.1	268 (55–783)
Trachea, bronchus, and lung	162	89	80.1	111 (89–137)	17	17.5	96 (56–155)	40	28.8	139 (99–189)
Male genital organs	185–187	17	15.3	111 (65–177)	2	3.2	63 (8–229)	9	6.0	149 (68–283)
Prostate	185	17	13.9	122 (71–195)	2	3.0	67 (8–237)	9	5.9	152 (70–290)
Urinary organs	188–189	17	11.4	148 (86–238)	3	2.4	128 (26–373)	6	4.0	149 (55–324)
Kidney	189.0–189.2	8	5.7	140 (60–275)	3	1.2	253 (52–742)	2	1.9	106 (13–384)
Bladder and other	188, 189.3–189.9	9	5.7	157 (72–298)	0	1.2	0 (—)	4	2.2	186 (51–476)
Lymphatic and hematopoietic tissue	200–208	24	22.1	109 (70–162)	4	3.9	102 (28–260)	8	6.4	125 (54–247)
Hodgkin's disease	201	3	2.5	119 (25–349)	0	0.2	0 (—)	1	0.4	276 (7–1534)
Non-Hodgkin's lymphoma††	200, 202	10	7.3	137 (66–254)	2	1.5	135 (16–488)	2	2.1	93 (11–337)
Lymphosarcoma and reticulosarcoma††	200	5	3.5	142 (46–332)	0	0.6	0 (—)	1	0.9	107 (3–594)
Other lymphatic††	202	5	3.7	133 (43–313)	2	0.9	215 (26–779)	1	1.4	71 (2–385)
Multiple myeloma††	203	5	3.0	164 (53–385)	0	0.6	0 (—)	3	1.1	262 (54–766)
Leukemia and aleukemia	204–208	6	8.9	67 (24–146)	2	1.6	126 (15–457)	2	2.6	77 (9–277)
Other sites	170–173, 190–199	39	29.6	131 (94–180)	5	5.8	87 (28–202)	18	9.0	201 (118–316)**
Skin	172, 173	4	4.9	82 (22–211)	0	0.9	0 (—)	2	1.3	155 (19–559)
Brain and nervous system	191, 192	5	7.3	68 (22–160)	0	1.3	0 (—)	2	1.9	106 (13–384)
Bone	170	2	0.9	227 (27–819)	0	0.1	0 (—)	1	0.2	521 (13–2903)
Connective tissue and soft tissue	171	4	1.2	338 (92–865)	0	0.2	0 (—)	3	0.3	922 (190–2695)**
Other and unspecified	194–199	24	14.8	162 (104–241)**	5	3.1	159 (52–372)	10	5.1	196 (94–361)

*From the *International Classification of Diseases*, 9th revision.

†Mean number of years exposed, 2.7; mean number of years employed, 12.6.

‡Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records.

§Mean number of years exposed, 0.3; mean number of years employed, 10.7; 12,299 person-years at risk.

¶Mean number of years exposed, 6.8; mean number of years employed, 19.2; 15,136 person-years at risk.

‖SMR equals deaths observed divided by deaths expected and multiplied by 100. Slight differences are due to rounding. Values in parentheses are 95 percent confidence intervals.

**P<0.05.

††Person-years at risk and observed deaths are computed from 1960; no deaths occurred before that year.

on death certificates and assigned to the ICD category "malignant neoplasms of connective and other soft tissue." In the cohort, mortality from soft-tissue sarcoma was nonsignificantly higher than in the reference population (four deaths; SMR, 338; 95 percent confidence interval, 92 to 865) (Table 2). The deaths occurred at 2 of the 12 plants, with a significant increase at 1 plant (two deaths; SMR, 1512; 95 percent confidence interval, 183 to 5462). A review of tissue specimens from the four men whose deaths were attributed to soft-tissue sarcoma showed that only two were in fact soft-tissue sarcomas (Cases 1 and 4, Table 3).[33] Mortality from soft-tissue sarcomas was increased significantly in the subcohort of 1520 workers with 1 year or more of exposure and at least 20 years of latency (the high-exposure subcohort) (three deaths; SMR, 922; 95 percent confidence interval, 190 to 2695). Two other deaths in the cohort (Cases 5 and 6) were attributed to soft-tissue sarcoma according to hospital records, and one of them (Case 5) was confirmed by review of a tissue specimen. These two deaths did not contribute to mortality due to soft-tissue sarcoma in our life-table analysis, because the deaths were assigned other ICD codes. We are aware of a seventh death from soft-tissue sarcoma, which occurred in a group of 139 workers with chloracne who were excluded from the cohort because they did not meet the entry criteria.

In the cohort, the SMRs for the other cancers of a priori interest were nonsignificantly increased (Table 2). There were no deaths from nasal cancer, although approximately one was expected. In the high-exposure subcohort, the SMRs were nonsignificantly higher for Hodgkin's disease and stomach cancer and lower for non-Hodgkin's lymphoma and cancer of the liver, biliary passages, and gallbladder (Table 2).

A Posteriori Findings

A small but significant increase in mortality due to all cancers combined was observed in the entire cohort (SMR, 115; 95 percent confidence interval, 102 to 130). In the high-exposure subcohort the SMR was 146 (95 percent confidence interval, 121 to 176) (Table 2). At 9 of the 12 plants, mortality from all cancers combined was increased; at one of these plants the increase was statistically significant. Mortality was significantly higher than expected in the category of cancers of unspecified sites, which included those of rare sites not included in a category of the life-table analysis and those for which no primary site was listed on the death certificate. Hospital records, which were obtained for 96 percent of these cancers, revealed no particular clustering according to site.

The cohort had a nonsignificant increase in mortality from cancers of the trachea, bronchus, and lung (ICD code 162; SMR, 111; 95 percent confidence interval, 89 to 137). Mortality from cancers of the respiratory system (ICD codes 160 to 165) was significantly higher than expected in the high-exposure subcohort (SMR, 142; 95 percent confidence interval, 103 to 192) (Table 2). To estimate the effect of smoking on the increase in lung cancer, the expected number of lung cancers was adjusted according to the smoking prevalence found in lifetime histories obtained in 1987 by interviewing 223 workers from two plants.[25] This adjustment increased the expected number of lung cancers in the overall cohort by 5 percent and in the high-exposure subcohort by 1 percent, which reduced the SMR in the full cohort to 105 (95 percent confidence interval, 85 to 130) and in the high-exposure subcohort to 137 (95 percent confidence interval, 98 to 187).

Analyses According to Duration of Exposure and Employment

The study cohort worked a mean of 2.7 years in processes involving TCDD contamination and 12.6 years at the plants. The high-exposure subcohort worked a mean of 6.8 years in processes involving TCDD contamination and a mean of 19.2 years in total employment at the plants.

The numbers of deaths due to the rare cancers of

Table 3. Deaths from Soft-Tissue Sarcoma among Workers in the Cohort.*

Case No.	Years Employed	Type of Exposure	Year First Exposed	Years Exposed	Year of Death	Latency (yr)†	Cause of Death: Death Certificate	Cause of Death: Hospital Records	Cause of Death: Tissue Review‡
1	1946–1978	TCP and 2,4,5-T	1950	8.8	1978	28	MFH	MFH	MFH
2	1946–1972	TCP and 2,4,5-T	1948	7.1	1972	24	Liposarcoma	Liposarcoma	Carcinoma, poorly differentiated§
3	1950–1975	TCP	1963	1.2	1975	12	Fibrosarcoma	Fibrosarcoma	Renal carcinoma§
4	1951–1982	TCP	1951	14.9	1983	32	MFH	MFH	MFH
5¶	1943–1975	TCP or 2,4,5-T	Intermittent	Unknown	1980	Unknown	Carcinomatosis§	Myxoid neurogenic sarcoma	Leiomyosarcoma
6¶	1941–1964	TCP	1949	Unknown	1965	16	Metastatic osteosarcoma§	Fibrosarcoma	Not available

*Cases 1 through 5 have been previously described.[33] For other previously described cases, records of exposure to TCDD were not available, and the cases were not included in this cohort study. Some information differs slightly from that reported earlier, since additional records were reviewed. Few details about exposure were available for Cases 5 and 6. TCP denotes 2,4,5-trichlorophenol; 2,4,5-T, 2,4,5-trichlorophenoxyacetic acid; and MFH, malignant fibrous histiocytoma.

†Time from first exposure to death.

‡Conducted at the Armed Forces Institute of Pathology.

§Not a soft-tissue sarcoma.

¶Death was not attributed to soft-tissue sarcoma in the life-table analysis.

Table 4. Mortality from All Cancers and from Cancers of the Trachea, Bronchus, and Lung, According to Latency Period and Duration of Exposure to Processes Involving TCDD Contamination.*

Cause/Latency Period	Duration of Exposure (yr)										Test for Trend
	<1		1 to <5		5 to <15		≥15		Overall		
	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	
All cancers											
<10 Yr	10	68	8	71	3	71	0	0	21	70	
10 to <20 Yr	28	109	16	87	18	122	7	340†	69	113	
≥20 Yr	48	102	59	165‡	37	138	18	115	162	129‡	
Total	86	98	83	127†	58	126	25	141	252	116†	
SRR		100		127		123		129			0.3
Trachea, bronchus, and lung											
<10 Yr	3	77	3	95	1	79	0	0	7	84	
10 to <20 Yr	6	69	5	79	9	180	1	137	21	101	
≥20 Yr	17	96	17	126	14	146	9	156	57	123	
Total	26	86	25	109	24	151	10	154	85	112	
SRR		100		109		166		136			0.2

*Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records. The number of observed deaths and the SMRs therefore differ slightly from those in Table 2. SRR denotes standardized rate ratio.

†P<0.05. ‡P<0.01.

a priori interest were too small to permit meaningful analyses according to duration. For all cancers combined and for cancers of the trachea, bronchus, and lung, Table 4 shows the distribution of mortality with increasing duration of exposure to products contaminated with TCDD. The standardized rate ratios were increased in the strata of longer duration for both these categories, but significant linear trends were not found. Mortality increased with increasing latency for both these categories of cancer. Table 5 shows the distribution of mortality for the same categories with increasing duration of employment. Significant linear trends were not observed for either category with increasing length of employment, although standardized rate ratios were higher than expected in several strata of employment ≥20 years. Mortality increased with increasing latency for both categories of cancer.

Serum Levels of TCDD

The mean serum TCDD level, as adjusted for lipids, in the sample of 253 workers from two plants was 233 pg per gram of lipid (range, 2 to 3400) (Fig. 1). A mean level of 7 pg per gram was found in the comparison group of 79 unexposed persons, all of whose levels were under 20, a range found in other unexposed populations.[34] The mean for 119 workers with one year or more of exposure was 418 pg per gram. All the workers had received their last occupational exposures 15 to 37 years earlier.

Discussion

TCDD, widely known as dioxin, has acquired the reputation of a potent carcinogen. Our study, although limited in its ability to detect increased numbers of rare cancers, found little increase in mortality from the cancers associated with TCDD in previous studies in humans. The exception was an increase in soft-tissue sarcoma. The difficulties of evaluating soft-tissue sarcomas in a cohort study of mortality have been described.[33] These include variability in pathological diagnosis and misclassification on death certificates. Consequently, the interpretation of the increased mortality from soft-tissue sarcoma in our study is limited by the small number of cases and the fact that the cause of death was sometimes misclassified on the death certificates of the workers (Table 3) and in the U.S. comparison population.[35]

Several case–control studies have found significant fourfold increases in non-Hodgkin's lymphoma in persons reporting exposure to phenoxy herbicides or chlorophenols, some of which contained TCDD.[6,8] The magnitude of the increase in mortality in the cohort described here (SMR, 137; 95 percent confidence interval, 66 to 254) suggests a smaller increase in this risk, or no increase at all. Mortality was not significantly higher than expected for other cancers of a priori interest — liver and stomach cancers and Hodgkin's disease. No deaths from nasal cancer were observed. The inconsistency between the results reported here and those of earlier epidemiologic studies is accentuated by the longer and probably greater exposure of this cohort to phenoxy herbicides and chlorophenols contaminated with TCDD.

Mortality from cancers of the trachea, bronchus, and lung was nonsignificantly higher in the cohort. Among the workers with 20 years or more of latency, mortality from respiratory cancer was significantly increased in the high-exposure subcohort, which had 1 year or more of exposure (SMR, 142; 95 percent confidence interval, 103 to 192) but not in the subcohort with less than 1 year of exposure (SMR, 103; 95 percent confidence interval, 62 to 161) (Table 2). SMRs for lung cancer are known to be somewhat higher in blue-collar groups than in the general U.S. population because of more cigarette smoking in the blue-collar groups.[36] However, the increased number of lung cancers in the high-exposure subcohort was probably not due to confounding by smoking, for several reasons. First, other diseases related to smoking were not more common than expected in this subco-

Table 5. Mortality from All Cancers and from Cancers of the Trachea, Bronchus, and Lung, According to Latency Period and Duration of Employment at the Study Plants.*

CAUSE/LATENCY PERIOD	DURATION OF EMPLOYMENT (YR)																TEST FOR TREND
	<5		5 TO <10		10 TO <15		15 TO <20		20 TO <25		25 TO <30		≥30		OVERALL		
	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	
All cancers																	
<10 Yr	10	85	1	18	0	0	0	0	0	0	0	0	0	0	11	64	
10 to <20 Yr	21	114	5	126	12	103	8	80	0	0	0	0	0	0	46	105	
≥20 Yr	40	138	15	140	6	70	15	98	34	134	31	116	54	135†	195	125‡	
Total	71	120	21	104	18	89	23	91	34	134	31	116	54	135†	252	116	
SRR		100		99		61		76		128		84		115			0.9
Trachea, bronchus, and lung																	
<10 Yr	3	103	1	74	0	0	0	0	0	0	0	0	0	0	4	94	
10 to <20 Yr	5	82	0	0	5	139	4	122	0	0	0	0	0	0	14	98	
≥20 Yr	11	102	2	51	2	65	3	55	12	133	18	180†	19	126	67	117	
Total	19	96	3	46	7	105	7	81	12	133	18	180†	19	126	85	112	
SRR		100		65		91		89		171		147		98			0.6

*Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records. SRR denotes standardized rate ratio.
†P<0.05. ‡P<0.01.

hort; mortality from nonmalignant respiratory disease (ICD codes 470 to 478 and 490 to 519), which is often associated with smoking, was lower than expected (15 deaths; SMR, 96; 95 percent confidence interval, 54 to 158). Second, in the exposed population with 20 years of latency, whose members presumably shared similar smoking habits, the increase was confined to the high-exposure subcohort. Third, on the basis of empirical evidence from other studies, Siemiatycki et al.[36] have shown that between a blue-collar population and the general U.S. population, confounding by smoking is unlikely to account for an excess risk of more than 10 to 20 percent. Finally, a limited adjustment in the risk of lung cancer,[37,38] based on the smoking prevalence of surviving workers at only two plants, did not substantially change our results.[25] Although confounding by smoking is unlikely to explain the higher rate of respiratory cancer in the high-exposure subcohort, it remains possible that the increase was due to confounding by occupational exposures other than TCDD. For example, asbestos may have contributed to mortality from lung cancer in the cohort, since two deaths were due to mesotheliomas.

An unexpected finding was the small but significant increase in mortality from all cancers combined. The observed increase is consistent with a carcinogenic effect of TCDD. For all cancers combined, mortality was significantly higher than expected in the entire cohort, more pronounced in the high-exposure subcohort, and increased at 9 of 12 plants. With mortality from cancers of the trachea, bronchus, and lung excluded, mortality from all remaining cancers combined was still higher than expected in the overall cohort (SMR, 117; 95 percent confidence interval, 100 to 136) and in the high-exposure subcohort (SMR, 150; 95 percent confidence interval, 118 to 189). Consequently, the increased risk for all cancers combined is not explained by smoking or by increased mortality due to cancer of the trachea, bronchus, and lung. The generation of tumors in a number of organs in animals exposed to TCDD[12,13] and the demonstration that TCDD promoted tumors in two organs[21,22] make it biologically plausible that TCDD may produce tumors in more than one organ in humans. Moreover, a significantly increased SMR for all cancers combined is unusual in occupational studies of chemical workers. Results similar to ours were observed in a study of German workers exposed to TCDD after a 2,4,5-trichlorophenol reactor accident in 1953. A subgroup of workers with chloracne (used as a surrogate for exposure) and at least 20 years of latency had an SMR of 201 (90 percent confidence interval, 122 to 315) for all cancers combined, based on 14 deaths.[39] This is the only other industrial cohort with both substantial exposure to TCDD and a long period of latency during which mortality was examined. Workers from U.S. production cohorts described in previous studies were included in the current study if they met our entry criteria.[40-42]

Two observations argue against a carcinogenic effect of TCDD. First, there was not a significant linear trend of increasing mortality with increasing duration of exposure to products contaminated with TCDD (Table 4). However, our use of duration of exposure may have misclassified the cumulative dose of some workers. In addition, a dose–response relation is generally viewed as strong evidence for an association when it is present, but as fairly weak evidence against an association when it is absent.[43] Second, our study did not directly assess the effect of exposure to TCDD alone. The workers were exposed concurrently to the chlorophenols and phenoxy herbicides that were contaminated with TCDD. In addition, they may have been exposed to numerous other chemicals while employed at the plants.

Because the exposure of our cohort was substantially higher than that of most nonoccupational populations, the estimates of effect in this study may provide an upper level of risk to be anticipated in humans. For several types of cancer previously associated with

TCDD, we found no increases above expected levels. Soft-tissue sarcoma was an exception; a ninefold increase was found among workers who were exposed for 1 year or more and who had at least 20 years of latency. Interpretation of the increased SMR is limited, however, by the small number of cases and because this cause of death was sometimes misclassified on the death certificates of the workers and in the national comparison population. Continued surveillance of the cohort may provide a firmer estimate of risk.

Mortality from all cancers combined was 15 percent higher than expected in the overall cohort. The subcohort with 1 year or more of exposure and 20 years or more of latency had a 46 percent increase in all cancers combined and a 42 percent increase in cancers of the respiratory tract. Although the study could not completely exclude the possible contribution of other occupational carcinogens or smoking, the increased mortality, especially in the subcohort with one year or more of exposure, is consistent with the status of TCDD as a carcinogen.

We are indebted to the National Institute for Occupational Safety and Health statistical clerks, Steve Green, Joyce Godfrey, and others, for their technical contributions; to representatives of the companies and unions for assistance in gathering the data for the study; to our colleagues at the Center for Environmental Health and Injury Control, Centers for Disease Control, for analysis of the serum samples; and to Lawrence Fine, David Brown, and the members of our blue-ribbon review panel for their helpful advice.

References

1. Hardell L, Sandstrom A. Case-control study: soft-tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. Br J Cancer 1979; 39:711-7.
2. Eriksson M, Hardell L, Adami HO. Exposure to dioxins as a risk factor for soft tissue sarcoma: a population-based case-control study. J Natl Cancer Inst 1990; 82:486-90.
3. Eriksson M, Hardell L, Berg N, Moller T, Axelson O. Soft-tissue sarcomas and exposure to chemical substances: a case-referent study. Br J Ind Med 1981; 38:27-33.
4. Hardell L, Eriksson M. The association between soft tissue sarcomas and exposure to phenoxyacetic acids: a new case-referent study. Cancer 1988; 62:652-6.
5. Hardell L, Bengtsson NO. Epidemiologic study of socioeconomic factors and clinical findings in Hodgkin's disease, and reanalysis of previous data regarding chemical exposure. Br J Cancer 1983; 48:217-25.
6. Hardell L, Eriksson M, Lenner P, Lundgren E. Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols and phenoxy acids: a case-control study. Br J Cancer 1981; 43:169-76.
7. Woods JS, Polissar L, Severson RK, Heuser LS, Kulander BG. Soft tissue sarcoma and non-Hodgkin's lymphoma in relation to phenoxyherbicide and chlorinated phenol exposure in western Washington. J Natl Cancer Inst 1987; 78:899-910.
8. Persson B, Dahlander A, Fredriksson M, Brage HN, Ohlson CG, Axelson O. Malignant lymphomas and occupational exposures. Br J Ind Med 1989; 46:516-20.
9. Axelson O, Sundell L, Andersson K, Edling C, Hogstedt C, Kling H. Herbicide exposure and tumor mortality: an updated epidemiologic investigation on Swedish railroad car workers. Scand J Work Environ Health 1980; 6:73-9.
10. Thiess AM, Frentzel-Beyme R, Link R. Mortality study of persons exposed to dioxin in a trichlorophenol-process accident that occurred in the BASF AG on November 17, 1953. Am J Ind Med 1982; 3:179-89.
11. Hardell L, Johansson B, Axelson O. Epidemiological study of nasal and nasopharyngeal cancer and their relation to phenoxy acid or chlorophenol exposure. Am J Ind Med 1982; 3:247-57.
12. Kociba R, Keyes D, Beyer J, et al. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. Toxicol Appl Pharmacol 1978; 46:279-303.
13. National Toxicology Program (NTP). Carcinogenesis bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin (CAS No. 1746-01-6) in Osborne-Mendel rats and B6C3F1 mice (gavage study) 1982. Washington, D.C.: Government Printing Office, 1982. (DHHS publication no. (NIH) 82-1765.)
14. Smith AH, Pearce NE, Fisher DO, Giles HJ, Teague CA, Howard JK. Soft tissue sarcoma and exposure to phenoxyherbicides and chlorophenols in New Zealand. J Natl Cancer Inst 1984; 73:1111-7.
15. Wiklund K, Holm L. Soft tissue sarcoma risk in Swedish agricultural and forestry workers. J Natl Cancer Inst 1986; 76:229-34.
16. Pearce NE, Sheppard RA, Smith AH, Teague CA. Non-Hodgkin's lymphoma and farming: an expanded case-control study. Int J Cancer 1987; 39:155-61.
17. Wiklund K, Dich J, Holm LE. Risk of malignant lymphoma in Swedish pesticide appliers. Br J Cancer 1987; 56:505-8.
18. Olsen JH, Jensen OM. Nasal cancer and chlorophenols. Lancet 1984; 2:47-8.
19. Hardell L, Bengtsson N, Jonsson V, Ericksson S, Larsson L. Aetiological aspects on primary liver cancer with special regard to alcohol, organic solvents and acute intermittent porphyria — an epidemiological investigation. Br J Cancer 1984; 50:389-97.
20. Rao MS, Subbarao V, Prasad JD, Scarpelli DG. Carcinogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the Syrian golden hamster. Carcinogenesis 1988; 9:1677-9.
21. Poland A, Palen D, Glover E. Tumour promotion by TCDD in skin of HRS/J hairless mice. Nature 1982; 300:271-3.
22. Pitot HC, Goldsworthy T, Campbell HA, Poland A. Quantitative evaluation of the promotion by 2,3,7,8-tetrachlorodibenzo-p-dioxin of hepatocarcinogenesis from diethylnitrosamine. Cancer Res 1980; 40:3616-20.
23. Esposito M, Tiernan T, Dryden F. Dioxins. 1980. Cincinnati: Industrial Environmental Research Laboratory, 1980. (EPA publication 600/2-80-197.)
24. Suskind RR, Hertzberg VS. Human health effects of 2,4,5-T and its toxic contaminants. JAMA 1984; 251:2372-80.
25. Fingerhut M, Halperin W, Marlow D, et al. Mortality among U.S. workers employed in the production of chemicals contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). NIOSH Final Report PB91125971. Springfield, Va.: National Technical Information Service, 1990.
26. Sweeney MH, Fingerhut MA, Connally LB, et al. Progress of the NIOSH cross-sectional medical study of workers occupationally exposed to chemicals contaminated with 2,3,7,8-TCDD. Chemosphere 1989; 19:973-7.
27. World Health Organization. International classification of diseases: manual of the international statistical classification of diseases, injuries, and causes of death. Geneva: World Health Organization, 1977.
28. Steenland K, Beaumont J, Spaeth S, et al. New developments in the NIOSH lifetable analysis system. J Occup Med 1990; 32:1091-8.
29. Rothman K, Boice J. Epidemiologic analysis with a programmable calculator. Washington, D.C.: Government Printing Office, 1979:30-1. (DHEW publication no. (NIH) 79-1649.)
30. Rothman KJ. Modern epidemiology. Boston: Little, Brown, 1986:229, 338-9.
31. Fox AJ, Collier PF. Low mortality rates in industrial cohort studies due to selection for work and survival in the industry. Br J Prev Soc Med 1976; 30:225-30.
32. Suit HD. Sarcoma of soft tissue. CA 1978; 28:284-95.
33. Fingerhut MA, Halperin WE, Honchar PA, Smith AB, Groth DH, Russell WO. An evaluation of reports of dioxin exposure and soft tissue sarcoma pathology among chemical workers in the United States. Scand J Work Environ Health 1984; 10:299-303.
34. Patterson DG Jr, Fingerhut MA, Roberts DR, et al. Levels of polychlorinated dibenzo-p-dioxins and dibenzofurans in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Am J Ind Med 1989; 16:135-46.
35. Percy C, Stanek E III, Gloekler L. Accuracy of cancer death certificates and its effect on cancer mortality statistics. Am J Public Health 1981; 71:242-50.
36. Siemiatycki J, Wacholder S, Dewar R, Cardis E, Greenwood C, Richardson L. Degree of confounding bias related to smoking, ethnic group, and socioeconomic status in estimates of the association between occupation and cancer. J Occup Med 1988; 30:617-25.
37. Axelson O. Aspects on confounding in occupational health epidemiology. Scand J Work Environ Health 1978; 4:98-102.
38. Steenland K, Beaumont J, Halperin W. Methods of control for smoking in occupational cohort mortality studies. Scand J Work Environ Health 1984; 10:143-9.
39. Zober A, Messerer P, Huber P. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. Int Arch Occup Environ Health 1990; 62:139-57.
40. Zack JA, Suskind R. The mortality experience of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident. J Occup Med 1980; 22:11-4.
41. Zack JA, Gaffey WR. A mortality study of workers employed at the Monsanto Company plant in Nitro, West Virginia. Environ Sci Res 1983; 26:575-91.
42. Ott MG, Olson RA, Cook RR, Bond GG. Cohort mortality study of chemical workers with potential exposure to the higher chlorinated dioxins. J Occup Med 1987; 29:422-9.
43. Monson RA. Occupational epidemiology. Boca Raton, Fla.: CRC Press, 1990:100.

750 Attachment 7

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE 4 February 1987

SUBJECT 2,3,7,8-TCDD in Aquatic Environments

FROM Philip M. Cook, Ph.D. PMC
Chief, Hazardous Waste Research Branch, ERL-Duluth

TO Jim Cummings
Office of the Assistant Administrator
for Solid Waste and Emergency Response

This memorandum is provided in response to your request for an update on the state of knowledge concerning 2,3,7,8-TCDD in aquatic environments. A considerable amount of new information is being generated and much will be reported during 1987. Most of the information I can provide results from our own research. I believe you have already received reprints for research results already published.

I reported bioconcentration factor (BCF) determinations for 2,3,7,8-TCDD, 1,2,3,4-TCDD, 1,3,6,8-TCDD and 1,3,7,9-TCDD at the Society for Environmental Toxicology and Chemistry meeting last November. A journal publication is in preparation. The EPA Water Quality Criteria Document presently uses a value of 5000 for the 2,3,7,8-TCDD BCF. We determined a value of 66,000 for carp and 97,000 and 159,000 for fathead minnows at two different exposure concentrations. Our BCF data for the four TCDD isomers is summarized in the attached table. We concluded from this study that ---

1. BCFs for different TCDD isomers vary greatly as expected from field monitoring data.

2. TCDD isomers other than 2,3,7,8-TCDD have lower BCFs than predicted on the basis of structure or log Kow due to more rapid rates of elimination.

3. Differences in rates of metabolism probably explain differences in TCDD rates of elimination and thus BCFs.

4. The gill uptake efficiencies for the four TCDD isomers studied appear to be similar despite structural differences and different uptake rate measurements attributed to large differences in elimination rates.

5. Approximately 90% of the TCDD in the fish exposure water was associated with particulate and dissolved organic matter. Thus, BCFs calculated on the basis of organic carbon free TCDD in the water would be ten times greater.

EPA Form 1320-6 (Rev. 3-76)

6. The Water Quality Criteria Document BCF value for 2,3,7,8-TCDD is very low because previously reported BCF determinations were made on the basis of very short exposure periods, inadequate depuration data, static exposure conditions, overestimates of water exposure concentrations, and other factors which lower the estimate of equilibrium fish concentrations with respect to actual water concentrations.

7. 2,3,7,8-TCDD is so toxic to fish that BCF determinations have not yet been made over long exposure periods without toxic effects and mortality occurring. No-effect levels are likely to be less than 10 ppq total 2,3,7,8-TCDD in water and possibly less than 1 ppq if only "dissolved" 2,3,7,8-TCDD is considered in the bioaccumulatable and toxic component.

8. 2,3,7,8-TCDD was lethal to carp at an accumulated dose of 2 ug/Kg. Rainbow trout appear to be a little more sensitive. This toxicity is comparable to the 1 ug/Kg LD50 found for the guinea pig, the most sensitive mammalian species known. Fathead minnows appear to be at least five times less sensitive than carp or rainbow trout.

It is likely that fish bioaccumulation of PCDDs and PCDFs is greatly influenced by food chain links to contaminated sediments and contact time of fish with sediment. Field monitoring data generally supports this premise. For example, fish collected from field surveys when analyzed for all TCDD isomers generally only have detectable amounts of 2,3,7,8-TCDD despite the presence of greater amounts of other TCDD isomers in contaminated sediments. Many of the TCDD isomers have relatively low bioaccumulation potential as seen from our BCF measurements for 1,2,3,4-TCDD and 1,3,7,9-TCDD and thus are not likely to be detected. 1,3,6,8-TCDD, however, would be expected in the fish in detectable levels if uptake from water was the major route for bioaccumulation. The lack of 1,3,6,8-TCDD in the fish is consistent with a kinetic effect involving decreasing amounts of 1,3,6,8-TCDD with respect to 2,3,7,8-TCDD in each step along the food chain to a fish and the absence of significant uptake from water.

For higher chlorinated PCDD and PCDF congeners, differences in elimination rates from fish and their food chain organisms create similar preferential bioaccumulation of 2,3,7,8-substituted planar molecules which are likely to be metabolized at a slower rate. In addition, as molecular weight and size increase with increasing degree of chlorination, it is apparent that the rate uptake from water across the gills decreases. Absorption efficiency from ingested material is also probably less for higher chlorinated congeners.

The net result of the above considerations is that many PCDDs and PCDFs found in sediments are not detectable in fish. The attached table on "Congener Dependent Bioavailability of PCDDs and PCDFs"

demonstrates how this same effect occurs for laboratory exposure of fish to municipal incinerator fly ash. The effect is more extreme when the "food chain chromatography" effect is present and longer exposure times are involved (much longer time required to reach steady state) as with the fish exposed to sediment in a reservoir. The compounds included in the table are all members of the "biosignificant fraction of PCDDs and PCDFs in that they do appear to bioaccumulate, are all 2,3,7,8-substituted and thus all have significant toxic potential. We developed a simple expression called the "bioavailability index" (BI) for comparing relative bioaccumulation tendencies for different chemicals associated with different solid wastes on sediments. The BI is simply the ratio of chemicals accumulated per gram of fish lipid to the amount present per gram of organic carbon in the solid material the fish are exposed to. The BI can be normalized to a value of 1.0 for 2,3,7,8-TCDD in order to make comparison of the other PCDD and PCDF congener's BIs easier. Although the magnitudes of the fly ash and sediment BIs cannot be directly compared due to great differences in the fish exposures, the normalized BIs for both fly ash and sediment show the same trends. For both PCDDs and PCDFs the normalized BIs decrease as the degree of chlorination increases. There also appears to be a tendency for 2,3,7,8-TCDF to be less bioaccumulable than 2,3,7,8-TCDD. The penta-CDD and -CDF results for the sediment seem divergent and will be rechecked before this data is published in this form. We will soon have much more of this kind of data when results are obtained for Lake Ontario sediments and paper mill sludges.

EPA is frequently faced with the question of what fish TCDD contamination levels will result from known or projected environmental contamination levels. The use of a BCF value, no matter how accurate, for predicting fish residues has a major limitation in that environmental TCDD water concentrations can never be detected even with the most sensitive techniques. Even if water measurements could be made, it would be difficult to determine what fraction of TCDD in water is not associated with dissolved or particulate organic carbon so that a laboratory derived BCF could be applied. An alternative approach is to use expected equilibrium partitioning relationships for sediment and fish to predict maximum levels of fish contamination and rely on site-specific sediment to fish TCDD ratios to determine more realistic "approach to steady-state" relationships likely to exist between sediments and fish. This should be done on the basis of partitioning between organic carbon in sediment and lipid in fish. In theory there should be a simple 1:1 equilibrium relationship between sediment organic carbon and lipid concentrations for very hydrophobic organic compounds such as 2,3,7,8-TCDD which are very slowly metabolized and eliminated from the organism. There are data for compounds such as PCBs which indicate approximately a four-fold preference of these compounds for lipids over organic carbon in sediment. Our 2,3,7,8-TCDD BI value of .27 for sediment is 4X less than the theoretical partitioning value of 1.0 and 16 ~~8X~~ less than the lipid preference value of 4.0 at least in part because steady-state conditions were not reached when the fish were exposed to the sediment.

In many environmental situations expected steady-state relationships between fish bioaccumulation levels and sediment contamination levels will

not be reached. Kinetic models and appropriate rate constants are needed to accurately predict fish bioaccumulation levels. When an aquatic ecosystem has a constant input of TCDD so that surface sediment concentrations are relatively constant, fish concentrations will approach a steady-state level dependent on rates of uptake from water, food and contact with sediment. For Lake Ontario we are investigating sediment to fish TCDD ratios under present conditions so that remedial actions for Superfund sites and other sources of TCDD can be evaluated with respect to changes in fish residues which will result in the future. That is, if sediment TCDD levels are decreased or increased in the future through man's activities, we should be able to predict eventual changes in fish contamination levels when a new "approach to steady-state" system results. In Lake Ontario our preliminary data indicates that fish lipids have only about 5% of the TCDD concentration found in the organic carbon fraction of the surface sediments. An extensive survey of sediment and fish TCDD levels throughout Lake Ontario is scheduled for this summer.

CONGENER DEPENDENT BIOAVAILABILITY OF PCDDs AND PCDFs IN FLY ASH AND SEDIMENT

Compound	Fly Ash PG/G Carbon	Fish PG/G Lipid	BI	Normalized BI	Sediment PG/G Carbon	Fish PG/G Lipid	BI	Normalized BI
2,3,7,8-TCDD	1.3×10^5	93	7.4×10^{-4}	1.00	5450	1500	.27	1.00
2,3,4,8-TCDF	1.7×10^5	95	5.7×10^{-4}	.77	5870	300	.06	.22
1,2,3,7,8-PeCDD	1.2×10^6	540	4.3×10^{-4}	.58	1000	60	.06	.22
2,3,4,7,8-PeCDF	7.3×10^5	180	2.5×10^{-4}	.34	190	55	.28	1.04
1,2,3,6,7,8-; 1,2,3,4,7,8-H_xCDD	5.0×10^6	1300	2.6×10^{-4}	.35	5800	200	.04	.15
1,2,3,6,7,8-H_xCDF	8.2×10^5	290	3.5×10^{-4}	.47	560	~~200~~ 12	.04	.14
1,2,3,4,6,7,8-H_pCDD	1.6×10^7	1300	7.8×10^{-5}	.11	71000	540	.005	.018
1,2,3,4,6,7,8-H_pCDF	3.7×10^6	340	9.2×10^{-5}	.12	9400	31	.003	.012

Attachment 8

Environmental Toxicology and Chemistry, Vol. 7, pp. 47-62, 1988
Printed in the USA. Pergamon Journals Ltd.

555

TOXICITY AND BIOCONCENTRATION OF 2,3,7,8-TETRACHLORODIBENZODIOXIN AND 2,3,7,8-TETRACHLORODIBENZOFURAN IN RAINBOW TROUT

PAUL M. MEHRLE,* DENNY R. BUCKLER, EDWARD E. LITTLE, LARRY M. SMITH, JIM D. PETTY, PAUL H. PETERMAN and DAVID L. STALLING
National Fisheries Contaminant Research Center, U.S. Fish and Wildlife Service, Columbia, Missouri 65201

G. M. DE GRAEVE and JAMES J. COYLE
Battelle Laboratories—Columbus, Columbus, Ohio 43201

WILLIAM J. ADAMS
Monsanto, St. Louis, Missouri 63167

(*Received* 25 *March* 1987; *Accepted* 14 *July* 1987)

Abstract—Among the most toxic isomers of polychlorinated dibenzodioxins and polychlorinated dibenzofurans, two groups of toxic aromatic compounds, are 2,3,7,8-tetrachlorodibenzodioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF). We examined the chronic toxicity of these compounds to rainbow trout (*Salmo gairdneri*). The fish (0.38 ± 0.09 g) were continuously exposed in an intermittent-flow proportional diluter for 28 d to 0, 38, 79, 176, 382, and 789 pg TCDD/L (parts per quadrillion) or to 0, 0.41, 0.90, 1.79, 3.93, and 8.78 ng TCDF/L (parts per trillion); exposures to each chemical were followed by a 28-d depuration phase. TCDD had significant effects on survival, growth, and behavior during the exposure and depuration phases. The no observed effect concentration was lower than the lowest exposure concentration of 38 pg/L. The average measured BCF at 28 days was 26,707. The estimated bioconcentration factor at steady-state equilibrium was 39,000 in the lowest exposure concentration where fish were least affected. TCDF, like TCDD, induced similar effects on survival, growth and behavior. The no observed effect concentration, based on survival, was 1.79 ng/L; that based on growth was 0.41 ng/L. The measured bioconcentration factor was 6,049 in fish exposed to 0.41 ng/L, and 2,455 in fish exposed to 3.93 ng/L for 28 d.

Keywords—Dioxin Furan 2,3,7,8-tetrachlorodibenzodioxin (TCDD) Rainbow trout 2,3,7,8-tetrachlorodibenzofuran (TCDF)

INTRODUCTION

Polychlorinated dibenzofurans (PCDFs) and polychlorinated dibenzo-*p*-dioxins (PCDDs) are two groups of toxic compounds composed of 135 and 75 individual isomers, respectively. Certain of these isomers are extremely toxic, particularly those with chlorine substituents in the 2,3,7,8-positions of the aromatic rings. PCDFs occur as trace contaminants in polychlorinated biphenyls (PCBs) and are sometimes formed in significant quantities from pyrolysis or incomplete combustion of PCBs [1]. Isomer specific PCDFs and PCDDs also occur as contaminants in the manufacture and pyrolysis of certain chlorinated phenols [2]. During combustion of these formulations, PCDDs are formed primarily from thermal dimerization and conversion of chlorinated phenoxyphenols, whereas PCDFs are formed from chlorinated diphenyl ethers. PCDDs and PCDFs have also been found in fly ash of municipal waste incinerators [3].

The isomers 2,3,7,8-tetrachlorodibenzodioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF) have been reported as contaminants in fish and sediment. Both have been detected in fish from the Great Lakes [4–6], and residues have been found in resident and migratory fish, crustaceans and sediment in the Chesapeake Bay area [7] and in industrialized and heavily populated areas of the northeastern United States [8]. The concentrations of these compounds in fish vary widely from low pg/g to ng/g quantities, and those of

*To whom correspondence may be addressed.

TCDF are usually higher than those of TCDD. In certain areas of the Great Lakes and the northeastern United States (Newark Bay, Passaic River), TCDD residues in fish and crustaceans exceed the U.S. Food and Drug Administration (FDA) "levels of concern" of 25 pg/g and 50 pg/g, respectively [8,9].

The chronic toxicity and bioconcentration of TCDD and TCDF in aquatic species have not been elucidated. Helder [10,11] reported that exposing fertilized eggs of rainbow trout (*Salmo gairdneri*) for 96 h to TCDD concentrations of 0.1 ng/L significantly decreased the growth of the resulting fry, and that exposing rainbow trout fry for 96 h to 10 and 100 ng/L TCDD retarded growth, caused histological changes in tissues and delayed mortality. Miller et al. [12] reported the toxicity and pathologic changes induced by short-term exposures of guppies (*Poecilia reticulata*) and coho salmon (*Oncorhyncus kisutch*) to TCDD. Coho salmon exposed to 56 pg/L and 1,000 ng/L for 24 h exhibited delayed mortality. Cooper et al. [13] observed delayed development and decreased survival in Japanese medaka (*Oryzias latipes*) exposed to TCDD concentrations of 6 to 500 ng/L. The oral toxicity and metabolism of TCDD in rainbow trout and yellow perch (*Perca flavescens*) were recently reported by Kleeman et al. [14,15]. In rainbow trout exposed for 6 h to 107 ng/L TCDD, followed by a 139-d depuration period, Branson et al. [16] estimated the bioconcentration factor (BCF) to be 9,270 and the elimination half-life to be 58 d. Significant delayed effects were similar to those reported by Miller et al. [12]. No similar studies have been conducted to characterize the toxicity and bioconcentration of TCDF in aquatic species.

Because of the lack of chronic toxicity data involving continuous low-level exposures of fish to TCDD and TCDF, we attempted to measure the chronic toxicity of these two compounds to rainbow trout. Their effects on survival, growth, and behavior were evaluated during a 28-d continuous exposure followed by a 28-d depuration phase. Uptake and depuration kinetics and BCFs for TCDD and TCDF were also evaluated.

METHODS

Test organisms

Eyed eggs of rainbow trout obtained from the Erwin (Tennessee) National Fish Hatchery came from two-year-old spawners of the "Fish Lake" strain; they were transferred to the National Fisheries Contaminant Research Center (NFCRC), Columbia, Missouri, where they hatched on 11 April 1985. About 2,000 swim-up fry produced from the eggs were shipped by air to Battelle Laboratories, Columbus, Ohio, on 2 May 1985. Mortality associated with shipping was less than 5%.

The fish were maintained in reconstituted water in 1,200-liter fiberglass tanks until the study was begun. The fish were held at a temperature of 11°C (±1°C), and were fed Tetramin floating flake food ad libitum. Analysis of the food showed no detectable quantities of TCDD (detection limit, less than 0.06 ng/g), TCDF (detection limit, less than 0.04 ng/g) or other organochlorine compounds.

Experimental approach

A flow-through diluter was used to continuously expose rainbow trout for 28 d to five duplicated concentrations each of [^{3}H]TCDD and TCDF plus duplicated controls. After the exposure period, toxicant input to the exposure chambers was terminated and the fish were held in laboratory water under flow-through conditions in the same test chambers during the 28-d depuration period. The fish were fed Tetramin floating flake food ad libitum throughout the study.

Fifty fish (0.38 ± 0.09 g each) were stocked in each aquarium. Samples of fish for residue analyses were taken on days 7, 14, 21, and 28 of the exposure phase and on day 28 of the depuration phase. To determine initial background concentrations of TCDD and TCDF, 30 fry with no previous TCDD and TCDF exposure history were weighed, measured, frozen, and analyzed for TCDD and TCDF. Fish collected for residue analyses were frozen until the time of analysis.

Daily survival records were maintained throughout the study. In addition, we recorded daily observations of swimming behavior, feeding behavior, location and position in the exposure tank, external lesions, and deformities.

Diluter and toxicant exposure system

The diluter system used in the study was constructed at NFCRC and installed in the West Jefferson Environmental Research Laboratory, Battelle Laboratories, Columbus, Ohio. The system consisted of two separate proportional flow-through diluters in a temperature-controlled waterbath. Both the diluter and waterbath were enclosed in a vented Plexiglas structure to reduce environmental exposures resulting from volatilization of the compounds. Each diluter delivered five concentrations (50% dilutions) of each compound (plus water for controls) into duplicate tanks containing

15 liters of water. Over the course of the study the diluter cycle rate varied between 2.4 and 3.0 cycles per hour; the replacement volume was 500 ml per replicate tank per cycle. The approximate water turnover rate in the exposure tanks was 2.4 times per day. The maximum fish loading in each test tank throughout the study was about 1.3 g/L and the maximum fish loading was 0.5 g/L of water passing through the tank in 24 h. Excess food and fecal matter were removed daily. Daily records of diluter operations were maintained throughout the studies. Nominal exposure concentrations (ng/L) were 0 (control), 0.115, 0.231, 0.463, 0.925, and 1.85 for TCDD; and 0 (control), 1.3, 2.7, 5.3, 10.6, and 21.3 for TCDF. Water temperature in the exposure tanks was maintained at 12 ± 1°C.

The combined effluents from the diluter system were recycled through two columns containing activated charcoal to remove TCDD and TCDF from solution. GC-MS and radiometric analyses were used to monitor the effluent for TCDD and TCDF.

Toxicants

Monsanto Company (St. Louis, MO) supplied the TCDD and TCDF used in the studies. The [^{3}H]TCDD (99+% pure; 22% unlabeled, 42% monotritiated and 36% ditritiated) used had a specific activity of 2.81×10^5 dpm/ng (0.128 μCi/ng) as determined by radiometric and GC-MS analyses. The TCDF provided by Monsanto was originally obtained from KOR, Inc. (Cambridge, MA), and was 98+% pure as determined by GC-MS.

Preparation of stock solutions

All glassware used to prepare stock solutions was rinsed several times with reagent-grade solvents. Carrier solvent for the compounds was acetone (Baker-analyzed). The [^{3}H]TCDD was diluted with acetone to a concentration of 36 ng/L. The stock solution was analyzed by GC-MS and by liquid scintillation radiometric analysis. Toxicants were delivered by an automatic pipetting system (Micromedic) that provided 0.05 ml/L or less of acetone to each exposure concentration. The TCDF was diluted with acetone to a measured concentration of 407 ng/L. This stock solution was used throughout the study and was delivered to exposure tanks by Micromedic pipetting systems. The acetone concentration delivered to each tank was 0.05 ml/L or less.

Water chemistry

In an effort to reduce the number of instruments coming in contact with the toxicants, we performed routine water chemistry only on the control chambers of both compounds, and only once during the exposure phase and once during the depuration phase. Alkalinity was measured by potentiometric titration with 0.02 N H_2SO_4 to pH 4.5, and hardness was titrated with EDTA according to standard methods [17]. We used an Orion

Table 1. Concentration of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in exposure water as measured by radiometric and GC-MS analyses

		TCDD nominal concentration (pg/L)					
Day	Measurement	0	115	231	463	925	1,850
1	pg/L (^{3}H)[a]	1.2	31	62	130	280	527
	pg/L (GC-MS)	—[b]					—[b]
7	pg/L (^{3}H)[a]	1.4	41	78	169	359	705
	pg/L (GC-MS)	<25[c]					840
14	pg/L (^{3}H)[a]	1.1	34	69	146	298	606
	pg/L (GC-MS)	<15[c]					730
21	dpg/L (^{3}H)[a]	0.7	41	87	200	466	970
	pg/L (GC-MS)	<15[c]					1,220
28	pg/L (^{3}H)[a]	1.3	44	99	234	507	1,135
	pg/L (GC-MS)	<20[c]					1,400
$\bar{x}$ pg/L (^{3}H) ± SD		1.1	38 ± 5	79 ± 15	176 ± 42	382 ± 101	789 ± 256
$\bar{x}$ pg/L (GC-MS) ± SD		<15[c]					1,048 ± 315

[a]Measured by radiometric analyses for [^{3}H]TCDD. Conversion of dpm/L to pg/L (^{3}H) based on specific activity of 2.81×10^5 dpm ^{3}H/ng TCDD.

[b]Not determined.

[c]None detected (less than minimal detectable limits).

digital pH meter to measure pH, a Sybron/Barnstead Model pM-70CB conductivity bridge to measure conductivity and a Varian Model 3700 gas chromatograph to measure ammonia. Water chemistry determinations were as follows: hardness, 153 ppm; alkalinity, 88 ppm; pH, 7.7; conductivity, 215 μohms; un-ionized ammonia, 0.0013 mg/L; and dissolved oxygen, 65 to 85% saturation.

Analyses of exposure water

During the exposure phase of the study, samples for GC-MS analysis were extracted from the TCDD control and highest exposure concentrations and from all TCDF exposure concentrations on days 0, 7, 14, 21, and 28. On each day immediately following the date of sample collection for GC-MS, we took samples for radiometric TCDD analyses from all exposure chambers. Radiometric analyses of all water extracts were conducted at Battelle Laboratories. Water from replicate *A* was sampled on days 0, 7 and 21, and water from replicate *B* on days 1, 14, and 28. On day 7 of the depuration period, the TCDD control and highest concentrations were measured radiometrically, and the TCDF control and highest concentrations were sampled for GC-MS analysis. On day 7 of the depuration phase, only 92 pg/L TCDD was measured in water from the highest TCDD exposure chamber, and 0.56 ng/L TCDF in the highest TCDF exposure chamber. The TCDD and TCDF exposure concentrations measured throughout the exposures are shown in Tables 1 and 2.

Water samples of a volume necessary to provide an adequate amount of analyte were collected from the diluter tanks with solvent-washed glassware and transferred directly to a glass separatory funnel. The water sample was then spiked with the appropriate internal standard solution containing $[^{13}C_{12}]$2,3,7,8-TCDD and $[^{13}C_{12}]$2,3,7,8-TCDF at 4.0 pg/μl in acetonitrile. The water sample was extracted three times with 50-ml portions of methylene chloride (CH_2Cl_2) and the extracts were passed through a column (about 2 × 6 cm) of anhydrous, granular sodium sulfate to break emulsions and remove suspended water. The extract was then rotary-evaporated to a low volume and transferred with three or four portions of CH_2Cl_2 to a glass ampoule, blown to dryness with nitrogen and flame-sealed.

The sample was removed from the opened ampoule with four 1.5-ml portions of 20% CH_2Cl_2 in hexane onto a dual column arrangement of 2 × 0.5 cm 40% H_2SO_4 on silica gel (SA-SG) in the first column and 15 mg Amoco PX-21 activated carbon dispersed in 150-mg glass fibers (CGF) [18]. The efficiency of transfer of $[^3H]$TCDD from these ampoules in the presence of solid residues was determined to exceed 99%. The SA-SG column was then discarded and the CGF column slightly pressurized to move the sample entirely onto the carbon adsorbent. We applied 15 ml CH_2Cl_2 to the CGF column at about 2 ml/min under pressure, and discarded the eluate.

The analyte, either $[^3H]$TCDD or TCDF, was recovered from the CGF by back-flushing with 15 ml toluene. The toluene was removed by rotary evaporation in a waterbath at 65 to 70°C under a 9.8-cm vacuum (sample taken just to dryness).

At this point, we added 2-(4-biphenyl)-6-phenylbenzoxazole (PBBO) to perform radiometric analyses on each sample or aliquots thereof containing $[^3H]$TCDD. The quench curve for counting efficiency was determined by the sealed tritium standard (HAV3612), corrected for decay, as the reference point, and replicate analyses of samples of $[^3H]$TCDD at various quench values. We used the equation, dpm = cpm/0.85 × *S*, where dpm is disintegrations per minute, cpm is counts per minute and *S* is the quench value.

Table 2. Concentration (ng/L) of 2,3,7,8-tetrachlorodibenzofuran (TCDF) as measured by GC-MS in exposure water during a 28-d chronic toxicity study with rainbow trout

	TCDF nominal concentration (ng/L)					
Day	0	1.3	2.7	5.3	10.6	21.3
1	0.02	0.38	0.70	1.40	3.20	6.60
7	<0.06	0.33	0.91	1.98	3.84	9.04
14	<0.029	0.44	0.86	1.56	3.82	7.97
21	<0.025	0.37	0.93	1.93	4.19	10.4
28	0.017	0.52	1.10	2.10	4.60	9.9
$\bar{x}$ ± SD	<0.02	0.41 ± 0.07	0.90 ± 0.14	1.79 ± 0.30	3.93 ± 0.52	8.78 ± 1.53

We applied the sample to alumina (Bio-Rad AG4 acid alumina, 3.5 ml = 3.65 g activated at 190°C) packed in a 5-ml graduated pipet with solvent reservoir using multiple washings of hexane totaling 5.0 ml. The column was then washed with 10 ml 5% CH_2Cl_2 in hexane (discarded) and the analyte recovered with 10 ml 20% CH_2Cl_2/hexane. The sample was evaporated just to dryness by rotary evaporation and transferred with three 1-ml portions of CH_2Cl_2 to a conical vial. The solvent was gently removed under a stream of nitrogen. The sample was then dissolved in a minimum of 5 μl *o*-xylene in preparation for GC-MS analysis.

We carried out the GC-MS analysis on a Finnigan 4023 quadrupole mass spectrometer (EI mode at 35 eV), using a 30 m × 0.25 mm DB-5 (0.25 μm) column (J&W Scientific, Inc., Rancho Cordova, CA) and helium carrier gas at about 35 cm/s. The temperature program was 120°C, hold 1 min, increase 20°C/min to 210°C, 5°C/min to 270°C and 4.5°C/min to 300°C. Selected ions monitored were m/z 304, 306, and 308 summed for 2,3,7,8-TCDF; m/z 316, 318 and 320 summed for $[^{13}C_{12}]$2,3,7,8-TCDF; m/z 320, 322, 324 and 326 summed for $[^3H]$2,3,7,8-TCDD; and m/z 332, 334, and 336 summed for $[^{13}C_{12}]$2,3,7,8-TCDD. We calibrated the internal standard solutions by preparing calibration mixtures of these standards with quantitative standards of native 2,3,7,8-TCDD and 2,3,7,8-TCDF prepared at the NFCRC and 2,3,7,8-TCDD solution as a U.S. Environmental Protection Agency (EPA) quality assurance material (Ref. No. 20603; EPA, Las Vegas, NV). We assumed equal integrated GC-MS responses for the molecular ions of native and $[^3H]$2,3,7,8-TCDD. The level of tritiation of the $[^3H]$2,3,7,8-TCDD computed from the molecular ion abundances measured by GC-MS gave a mole fraction of tritium of 27.3% and a specific activity of 2.15×10^5 dpm/ng. We calculated the specific activity, using the GC-MS–determined concentration and measured activity, to be $2.81 \pm 0.07 \times 10^5$ dpm/ng (triplicate analyses).

Collection of fish for residue analyses

Fish for whole-body TCDD and TCDF residue analyses were collected during the exposure period on days 0 (prior to exposure), 7, 14, 21, and 28, and on day 56 (after 28 d of depuration). When we removed fish from the exposure tanks for residue analyses on day 7, we removed unequal numbers from different tanks to reduce the number of fish remaining in all tanks to 42, and thus reduce the biomass and avoid potential overloading in the exposure tanks.

Fish for residue analyses were collected randomly from the exposure tanks for each toxicant. Individual weights and lengths were measured for fish collected on day 7 of the exposure and on day 28 of the depuration phase. Fish collected on other sampling days were weighed but not measured for length. All fish were blotted dry before they were weighed and were then wrapped in hexane-rinsed aluminum foil, placed in labeled screw-topped glass vials and stored at −10°C until residue analyses were begun.

GC-MS determinations of TCDD and TCDF in fish

Analyses of fish samples were performed by the method of Smith et al. [19]. The GC-MS conditions and spiking procedures were as described above for the analysis of the water samples.

Sample extracts that required radiometric analysis for $[^3H]$TCDD were rotary-evaporated and brought to 10.0-ml volumes; an appropriate aliquot (usually 1.00 ml) was then taken for scintillation counting. The quench values for the aliquots of the fish extracts were uniformly near the minimum (*S* values of 0.65), as observed for analytical standards. Negative and positive control samples were routinely included in the radiometric determinations of $[^3H]$TCDD and established so that there was no procedural background contribution in these determinations.

The internal standard procedure for GC-MS determinations of both $[^3H]$TCDD and TCDF provided internal quality control for overall accuracy of quantitation. In all reported determinations of these analytes, the criteria attained were relative GC retention time (±1 scan number in 1,160 or ±0.001 relative retention units) and correct ion abundances of the three or four molecular ion cluster members (±10% of theoretical value). The limit of quantitation was five times the signal-to-noise ratio and the limit of detection was three times the signal-to-noise ratio. The molecular ion cluster for $[^3H]$TCDD was significantly distorted from that produced by the native populations of ^{35}Cl and ^{37}Cl. Relative ion abundances of m/z 320, 324, and 326 were 24, 75, 100 and 70%, respectively. This pattern remained constant throughout the study, indicating no significant exchange of hydrogen for tritium in TCDD during the exposure. This observation also demonstrated no significant background of native 2,3,7,8-TCDD in any of the samples, because the presence of

native dioxin would have had an easily discernible effect on this pattern. Procedural background controls showed no 2,3,7,8-TCDD (limit of quantitation, less than 0.006 ng/g) by radiometric analysis and no TCDF (limit of quantitation, less than 0.06 ng/g) by GC-MS. The limit of quantitation for [^{3}H]TCDD was also less than 0.06 ng/g by GC-MS.

Analyses of fish food were carried out by the same procedure used for fish samples, and analyses of [^{3}H]TCDD and TCDF stock solutions were performed by direct dilution before analysis.

We computed percent recoveries of [^{13}C]TCDD and [^{13}C]TCDF internal standards by the less precise external standard technique, using the responses of the [^{13}C]TCDD and [^{13}C]TCDF internal standards; the recoveries of [^{13}C]TCDF and [^{13}C]TCDD, respectively, are listed here according to the various matrices: stock solutions, 71 ± 30% and 71 ± 33%; exposure water, 134 ± 55% and 109 ± 52%; fish, 101 ± 37% and 117 ± 46%; all matrices combined, 112 ± 51% and 105 ± 47%.

Determination of total concentration of [^{3}H]TCDD species in fish by biological material oxidation procedure

Determinations of total body burden of [^{3}H]TCDD residues in fish, as opposed to extractable residue, were made on homogenate aliquots of individual fish by the method of total burn, followed by liquid scintillation radiometric analysis of the combustion products. A Harvey Biological Materials Oxidizer (Model OX-100, R. J. Harvey Instrument Corp., Hillsdale, NJ) and a Harvey tritium cocktail (lot No. DC02) were used in the procedure. The combustion/trapping efficiency was 84% with triplicate analyses of a [^{14}C]PCB standard. Cryogenic traps and dry ice and methanol were used to trap the tritiated water produced in the combustion. The combustion/trapping efficiency observed for a standard of [^{3}H]TCDD was 89 ± 3% for spiked fish tissue. The scintillation counting efficiency when the tritium cocktail was used was 37%, and radioactivity was calculated from scintillation analysis using the equation, $dpm = cpm/0.64 \times S$, after subtraction of 50 cpm background.

Samples that had previously been weighed, wrapped in filter paper and aluminum foil and stored in the freezer were transferred along with the approximately 1-cm^2 pieces of filter paper to the quartz combustion boats. Before combustion of samples, we ran a series of blanks and spikes to ensure that performance was satisfactory. Each sample was combusted twice into the cryogenic trap, which contained about 0.5 ml residual methanol. The glass elbow connecting the trap and oxidation chamber was heated with a hot air gun during the procedure to prevent loss by condensation. The condensed residue was transferred from the trap to a scintillation vial with three 5-ml portions of the cocktail. We then washed the trap thoroughly three times with methanol, leaving about 0.5 ml to aid in the next trapping. Because previous tests had indicated that carryover between sample combustions was a potential problem, blank combustions were performed after each sample and control. Scintillation analysis of the blanks showed that carryover was negligible.

Observation of fish for behavioral responses

The behavioral responses of rainbow trout were assessed daily during the TCDD and TCDF exposures. A checklist of behavioral reactions modified from Drummond et al. [20] was used to systematically document and characterize abnormal responses. The responses included coloration, activity (hyperactive, lethargic), excitability by external stimuli (hyperactive, unresponsive), location in aquaria, mode of swimming (head-up, frequent sinking and rising, swimming on side, swimming on back, free swimming), feeding, and morphological observations (bent spine, fin erosion). Observations were made each day by the same observer at the time of feeding.

An aberrant behavioral reaction was recorded when at least one fish in a given treatment responded in a manner that obviously differed from that of controls. Although no attempt was made to quantify the number of fish responding abnormally, an overall measure of the onset, duration and sequence of behavioral changes was made from the systematic daily observations.

Statistical analyses

Daily mortality was analyzed by one-way analysis of variance on the arc-sin transformed values. Differences among means were determined using Fisher's least significant difference (LSD) procedure [21].

Growth as measured by weight or length was analyzed by analysis of variance, including the effects of treatment, replicate within treatment, day, treatment × day, and replicate (treatment × day). Since the replicates, not the individual fish, were the experimental unit, replicate within treatments was used as the error term for testing the effect of treatment, and replicate (treatment × day) was used as the error term for testing the effects of day and treatment × day. We deter-

mined differences among means by calculating a *t* statistic, using the standard error of the difference for a split-plot design. For growth of TCDD-exposed fish during the depuration phase, we tested the control and lowest exposure concentration groups for equal population means, using a two-sample *t* test adjusted for unequal variance where appropriate [21].

The cumulative number of days on which fish showed abnormal behavior, from the time of induction to the day of depuration, was analyzed by simple regression against concentration, to provide an estimate of the behavioral responses to chemical exposure.

The BIOFAC computer program [22] was used to estimate the bioconcentration kinetics for TCDD and TCDF. Data from only the exposure phase in each study were used to estimate the kinetics because the number of fish residue samples available during the depuration phase was not adequate. In addition, the fish were held in their original exposure test tanks during the depuration phase, which resulted in the presence of the toxicants in the water because they desorbed from the glass aquaria. Because water concentration measurements and sufficient fish to sample during the depuration phase were not available, we were unable to use data from the depuration phase to estimate rate constants for the toxicants.

To estimate the 56-d LC50 value for TCDD, we computed a multiple-regression model to determine the relationship between percent mortality (arc-sin transformation) to concentration and time of exposure. The linear statistical model contained the effects of linear concentration (CL), days of exposure linear (DL), concentration quadratic (CQ), and day of exposure quadratic (DQ): CL * DL, CL * DQ, CQ * DL and CQ * DQ [21]. We used a quadratic function relationship to estimate the concentration of TCDD at a constant mortality (50%) and period of exposure (56 d).

RESULTS AND DISCUSSION

Mortality

TCDD induced significant mortality in rainbow trout within 14 d of exposure in the highest exposure concentration (789 pg/L), and there was a trend toward increased mortality in fish exposed to 176 and 382 pg/L (Table 3). After 28 d of exposure, significant mortality was evident in the three highest exposure concentrations; the no observed effect concentration (NOEC) was 79 pg/L. Although no mortality was observed, fish in the 38 and 79 pg/L exposure groups were obviously stressed, as judged by reduced growth and behavioral responses. Only rainbow trout in the control group and the three lowest exposure concentrations were observed during the 28-d depuration phase of the study; fish in the two highest exposure concentrations were excluded because the survivors were few and obviously stressed. Significant mortality continued to occur throughout the depuration period in fish previously exposed to 38, 79, and 176 pg/L. There was no apparent recovery in the fish during the 28-d depuration period in clean

Table 3. Cumulative mortality (%) in rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzodioxin (TCDD) for 28 d followed by a 28-d depuration period

	Mean TCDD exposure concentration (pg/L)						
Phase and day	0	38	79	176	382	789	*F* value
Exposure							
7	5	0	1	4	6	10	1.79
14	5	1	1	13	17	33[a]	5.48[b]
21	5	3	9	36[a]	46[a]	74[a]	28.02[b]
28	5	6	18	50[a]	73[a]	85[a]	27.51[b]
Depuration							
7	5	12	64[a]	85[a]	—[c]	—[c]	9.33[b]
14	5	22	78[a]	95[a]	—	—	30.49[b]
21	7	33	83[a]	95[a]	—	—	28.63[b]
28	7	45[a]	83[a]	95	—	—	27.72[b]

[a]Significantly different from controls by least-significant-difference multiple means comparison test ($p < 0.05$).

[b]Significant treatment effect (one-way analysis of variance: $p < 0.05$).

[c]Exposure groups not part of depuration phase.

water. The NOEC of TCDD, based on mortality throughout the exposure and depuration phases, was less than the lowest exposure concentration of 38 pg/L (parts per quadrillion).

Further insight into the NOEC was inferred from the background concentration of 1.1 pg/L of TCDD detected by radiometric analyses in the control group throughout the study. This low background was probably due to volatilization of TCDD and translocation within the diluter system. Mortality in the control group was 5% during the exposure phase and most of the depuration phase. We suggest from these observations that the NOEC was between 1.1 and 38 pg/L. However, the minimal detectable limits for TCDD in water by GC-MS were not adequate to confirm the 1.1 pg/L detected by radiometric analyses.

A 56-d LC50 of 46 pg/L was calculated from the combined mortality data for the exposure and depuration phases. The surface response curve describing the relation among daily mortality, time and exposure concentrations is shown in Figure 1. The quadratic equation describing this relation was used to derive the 56-d LC50.

Significant mortality was induced by TCDF in rainbow trout within 14 d at exposure concentrations of 3.93 and 8.78 ng/L (Table 4). No additional significant mortality occurred throughout the 28-d exposure phase. During the depuration phase, additional mortality occurred only in fish exposed to 8.78 ng/L. The NOEC throughout the exposure and depuration phases was 1.79 ng/L.

Growth

Growth as measured by the weight of the fish was significantly decreased by all TCDD concentrations after 28 d of exposure (Table 5). There were trends of decreased growth within 14 d of exposure, but significant effects in all concentrations were not observed until 28 d of exposure. During the 28-d depuration phase, growth was measured in fish from only the control and the lowest exposure concentration because of the excessive mortality in the higher TCDD exposure concentrations. There was a significant decrease in growth in the fish exposed to 38 pg/L after the 28-d depuration phase. Fish exposed to 38 pg/L TCDD did not grow during the depuration phase, whereas the weight of fish in the control group exhibited an 80% increase. The NOEC of TCDD on growth during the exposure and depuration phases was less than the lowest exposure concentration of 38 pg/L.

TCDF exposure concentrations of 1.79, 3.93 and 8.78 ng/L significantly decreased the growth of rainbow trout within 28 d of exposure (Table 6). There were trends toward decreased growth

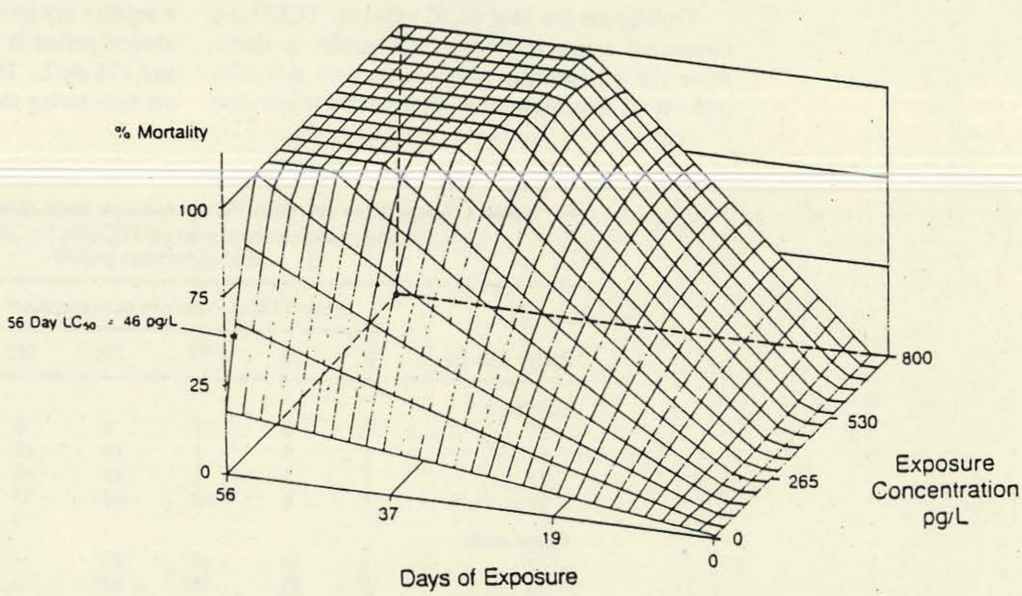


Fig. 1. Surface response describing the relation among daily mortality, time of exposure during the 28-d exposure and 28-d depuration phases, and TCDD exposure concentrations. The quadratic relation was used to derive a 56-d LC50 value of 46 pg/L TCDD for rainbow trout.

Table 4. Cumulative mortality (%) in rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d followed by a 28-d depuration period

Phase and day	Mean TCDF exposure concentration (ng/L) 0	0.41	0.90	1.79	3.93	8.78	F value
Exposure							
7	0	1	1	2	2	12	2.54
14	0	1	3	3	16[a]	22[a]	4.51[b]
21	0	2	5	3	18[a]	23[a]	3.73[b]
28	0	2	6	3	18[a]	28[a]	4.49[b]
Depuration							
7	0	2	6	3	20[a]	37[a]	6.53[b]
14	0	2	6	3	22[a]	46[a]	8.56[b]
21	0	2	6	3	22[a]	46[a]	8.56[b]
28	0	2	6	3	22[a]	46[a]	8.56[b]

[a]Significantly different from controls by least-significant-difference multiple means comparison test ($p < 0.05$).
[b]Significant treatment effect (one-way analysis of variance; $p < 0.05$).

Table 5. Weight (g) of rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzodioxin (TCDD) for 28 d followed by a 28-d depuration period

Phase and day	Mean TCDD exposure concentration (pg/L) 0	38	79	176	382	789
Exposure[a]						
7	0.37	0.36	0.38	0.33	0.36	0.33
14	0.41	0.39	0.42	0.33	0.35	0.40
21	0.48	0.35[b]	0.40	0.39	0.39	0.44
28	0.61	0.53[b]	0.47[b]	0.49[b]	0.45[b]	0.42[b]
Depuration[c]						
28	1.1	0.54[b]	—[d]	—[d]	—[d]	—[d]

Weights are expressed as the mean of 7 to 22 observations.
[a]Analysis of variance used for testing the effects of exposure concentration and time; $F = 2.43$ (time × exposure), $p < 0.03$.
[b]Significantly different from control group (t test; $p < 0.05$).
[c]Fish weight in depuration phase analyzed by t test adjusted for unequal variances.
[d]No measurements made.

after 21 d of exposure but the decrease observed was significant only in the group exposed to 3.93 ng/L. Decreased growth was evident in fish exposed to 0.90 ng/L or more after the 28-d depuration phase. The NOEC for TCDF based on growth during the exposure and depuration phases was 0.41 ng/L. This was the most sensitive response to TCDF.

Behavioral responses

Exposure to TCDD and TCDF induced behavioral impairments that became progressively worse over time and with increasing concentration. The two highest concentrations of TCDD caused behavioral changes within two weeks of exposure that included lethargic swimming, feeding inhibition, and lack of response to external stimuli, for example, waving of hand above aquaria (Fig. 2). Similar changes were evident in all groups exposed to TCDD by the end of the 28-d exposure, whereas the behavior of the controls remained normal. Although significant mortality did not occur in the two lowest exposure concentrations during 28 d of exposure, the fish were seriously stressed, as evidenced by an abnormal head-up swimming posture and confinement to the bottom of the aquar-

Table 6. Weight (g) of rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d followed by a 28-d depuration period

	Mean TCDF exposure concentration (ng/L)					
Phase and day	0	0.41	0.90	1.79	3.93	8.78
Exposure[a]						
7	0.33	0.35	0.37	0.36	0.35	0.32
14	0.39	0.40	0.43	0.42	0.31	0.41
21	0.55	0.47	0.45	0.50	0.39[b]	0.44
28	0.59	0.59	0.53	0.48[b]	0.50[b]	0.46[b]
Depuration[c]						
28	1.1	0.91	0.85[b]	0.80[b]	0.79[b]	0.71[b]

Weights represent the mean of 8 to 24 observations.
[a]Analysis of variance used for testing the effects of exposure concentration and time; $F = 4.37$ (time × exposure), $p < 0.05$.
[b]Significantly different from controls (t test; $p < 0.05$).
[c]Analysis of variance used for testing the effect of exposure concentration; $F = 5.73$ (exposure), $p < 0.03$.

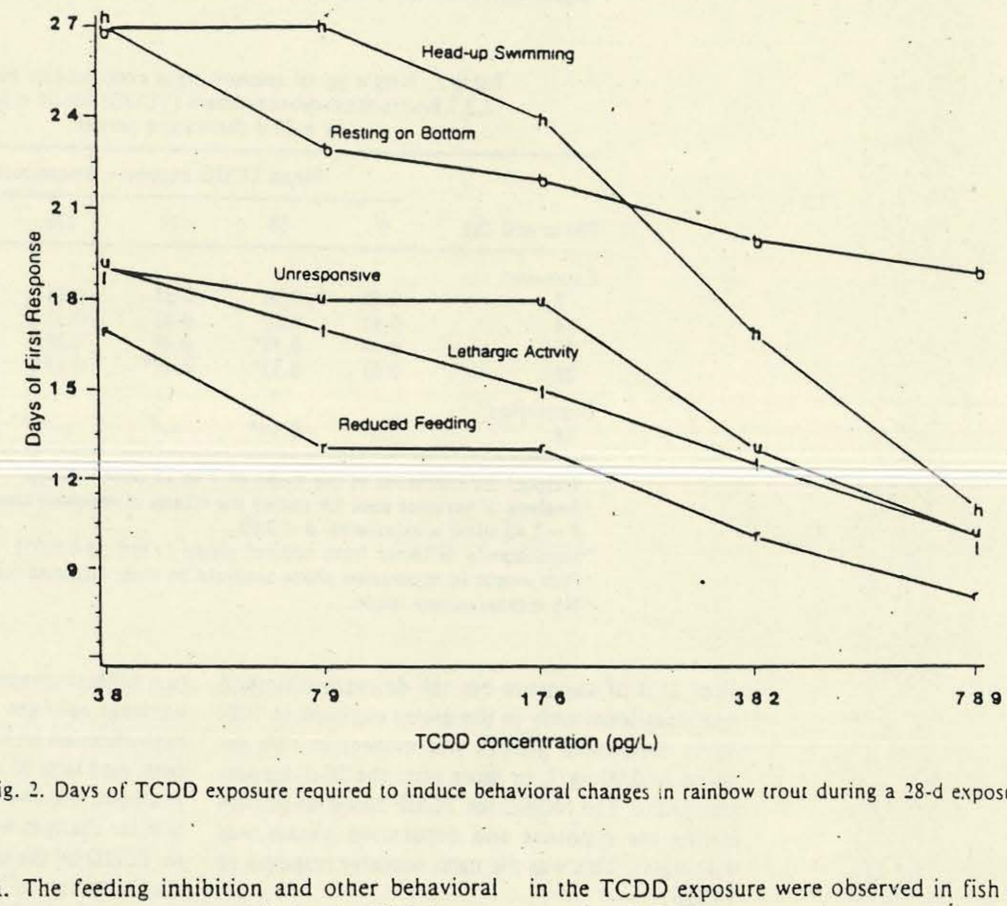


Fig. 2. Days of TCDD exposure required to induce behavioral changes in rainbow trout during a 28-d exposure.

ia. The feeding inhibition and other behavioral changes were not reversed during the 28-d depuration period.

Behavioral reactions similar to those observed in the TCDD exposure were observed in fish exposed to TCDF; however, the responses were of lesser magnitude (Fig. 3). Lethargy, unresponsiveness to external stimuli and diminished feeding

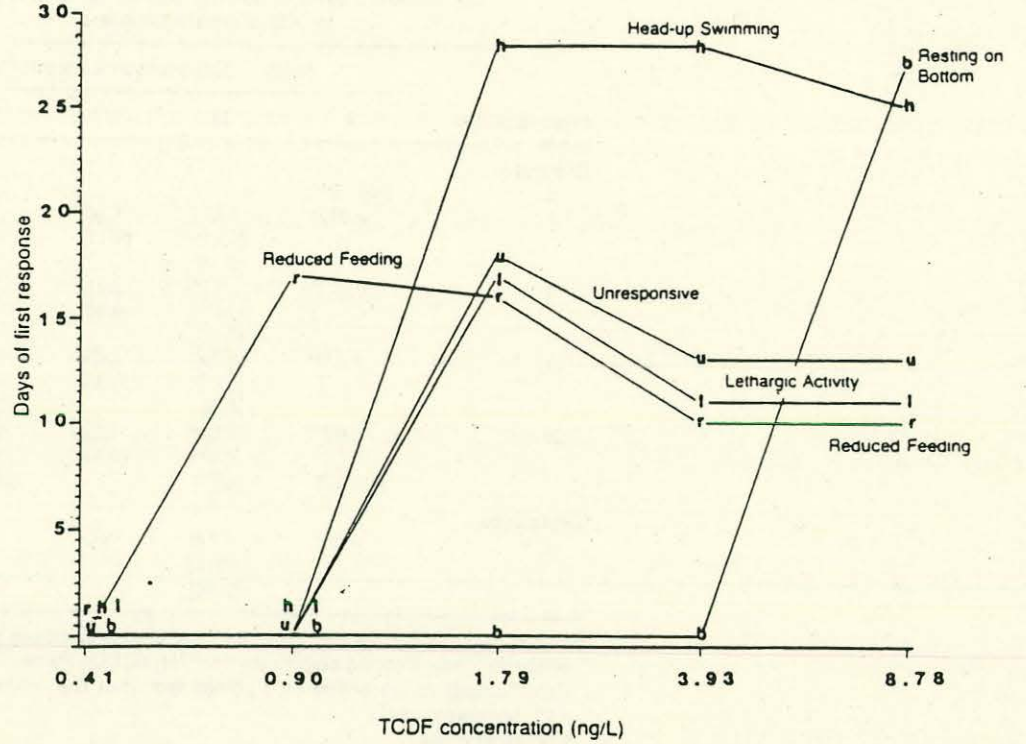


Fig. 3. Days of TCDF exposure required to induce behavioral changes in rainbow trout during a 28-d exposure.

reactions increased significantly in the three highest exposure groups. Recovery of behavioral function was evident in all but the two highest treatment groups by the end of the 28-d depuration period.

Neither TCDD nor TCDF induced observable responses in coloration or morphological characteristics such as scoliosis or lordosis; however, fin erosion was observed in fish in the lowest TCDD exposure concentration at the end of the depuration phase. In addition, exposure to both TCDD and TCDF induced observable, unique characteristics in fecal appearance. The two highest exposure concentrations of each toxicant induced long, stringy faces within the last several days of the 28-d exposure phase.

Bioconcentration

The BCFs for TCDD and TCDF differed greatly during the 28 d of continuous exposure. Whole-body residues throughout the exposure phase were in the low end of a 0.41 to 15.41 ng/g range for TCDD (Table 7). The greater the exposure concentration, the higher were the whole-body residues of TCDD during the 28-d exposures. The measured BCF for TCDD ranged from 8,558 to 28,664 during the exposure and did not appear to reach steady-state equilibrium in any of the exposure concentrations during the 28-d exposure (Table 8). The GC-MS analyses for whole-body TCDD levels agreed closely with the whole-body radiometric determinations for [^{3}H]TCDD. This similarity suggests that the ^{3}H label on the TCDD molecule was not being exchanged, and that the ^{3}H detected in the fish tissue was associated with the parent TCDD molecule. This similarity also indicates that organic extracted [^{3}H]TCDD was not being appreciably metabolized during the exposure and depuration phases. However, as judged by the results of total combustion of fish samples, it appears that about 30% of the ^{3}H label was associated with polar compounds that could have been TCDD metabolites.

Since it was apparent that a steady-state equilibrium for TCDD bioconcentration had not been reached after 28 d of exposure, we used the BIOFAC computer program [22] to estimate the bioconcentration kinetics for TCDD based only on data from the exposure phase. The estimated BCF at steady-state equilibrium was relatively consistent in fish from different exposure concentrations; the

Table 7. Whole-body residues of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout continuously exposed for 28 d followed by a 28-d depuration phase

	Mean TCDD exposure concentration (pg/L)				
Phase and day	0	38	176	382	789
Exposure					
0	[<0.02][a]				
7	0.012[a]	0.41[b] (0.05) [0.38]	1.68[b] (0.15)	3.44[b] (0.20)	6.75[b] (0.37) [6.78]
14	0.022[c]	0.77[b] (0.06) [0.71]	2.81[b] (0.18)	6.22[b] (0.67)	11.67[b] (0.68) [12.3]
21	0.023[d]	0.99[e] (0.03) [0.96]	3.87[b] (0.14)	10.10[e] (1.42) [11.3]	15.41[c] (0.86) [17.6]
28	0.027[a] [<0.02]	0.98[b] (0.05) [0.93]	4.52 (0.41)	10.95[b] (0.87) [10.8]	ND
Depuration					
28	0.22[a]	0.74[b] (0.11) [0.78]	ND	ND	ND

Values (ng/g) represent the mean (with standard deviation in parentheses) of individual fish analyzed radiometrically for [^{3}H]TCDD. Values in brackets represent GC-MS analyses performed on a pooled sample of fish, expressed as ng/g.
ND, not determined.
[a]One observation.
[b]Six observations.
[c]Two observations.
[d]Four observations.
[e]Eight observations.

Table 8. Measured bioconcentration factor (BCF)[a] for 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout exposed continuously for 28 d

	Measured TCDD exposure concentration (pg/L)			
Days of exposure	38	176	382	789
7	10,736	9,551	9,005	8,558
14	20,131	15,966	16,282	14,790
21	25,947	21,977	26,439	19,510
28	25,789	25,670	28,664	ND

[a]BCF = $(C_t/C_w) \times 1{,}000$. ND, not determined.

estimated BCF at 90% steady-state equilibrium ranged from about 37,000 to 86,000 (Table 9). Fish exposed to 382 pg/L showed somewhat different kinetics in that the estimated BCF, time to reach steady-state equilibrium and half-life were greater than in the other exposure concentrations. The relatively low K_2 value, compared with K_2 values from other exposure groups, suggested that metabolic effects may have been reducing the elimination of TCDD.

Ideally, the BCF should be estimated in fish not showing toxicity-induced responses. Inasmuch as the fish exposed to the lowest TCDD concentration of 38 pg/L showed the least toxic responses during the 28-d exposure, we suggest that the predicted BCF of 39,000 is probably the most reliable

Table 9. Estimated bioconcentration kinetics[a] of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout exposed to TCDD for 28 d

Kinetic parameter	TCDD exposure concentrations (pg/L)			
	38	176	382	702[b]
K_1, uptake rate constant (d^{-1})	1,852 (132)[c]	1,543 (69)	1,337 (61)	1,591 (53)
K_2, depuration rate constant (d^{-1})	0.047 (0.01)	0.041 (0.005)	0.015 (0.005)	0.043 (0.005)
BCF-K_B	39,000 (9,400)	37,560 (5,032)	86,000 (25,000)	36,637 (4,290)
Time to reach 90% steady state (d)	49 (11)	56 (7)	149 (43)	53 (6)
Elimination half-life, $t_{1/2}$ (d)	15 (3)	17 (2)	48 (13)	16 (2)

[a]Estimated kinetics using BIOFAC [22].
[b]Mean of TCDD measurements at days 1, 7, 14 and 21.
[c]Values in parentheses represent standard deviations.

estimate. The range in BCF we observed was substantially greater than the BCF of 7,000 to 9,270 previously reported in the literature [16,23,24]. Results from our study were perhaps better estimates of the equilibrium BCF because we used a continuous exposure in flowing water for a longer period at lower exposure concentrations. Based on the water solubility of 7.9 ng/L for TCDD [25], the predicted BCF would be about 467,000 if the regression equation, log BCF = 2.791 − 0.564 log S [26], were used; it would be about 1,000,000 if the regression equation, log BCF = 3.41 − 0.508 log S [27], were used.

We suggest from our experimental data that the overall bioconcentration from water to fish is probably much less than the theoretical estimation. The obvious toxicity-induced effects of TCDD, as well as potential influences on membrane transport and other metabolic functions, could account for the observed BCF being less than the theoretical predictions.

The estimated elimination half-life ($t_{1/2}$) from the BIOFAC ranged from 15 to 17 d among exposure concentrations, except for the estimated half-life of 48 d in fish exposed to 382 pg/L. Adams et al. [24] reported an elimination half-life of 15 d, and Branson et al. [16] reported a half-life of 58 d. In the fish exposed to 38 pg/L for 28 d and then held during the 28-d depuration phase, the whole-body residues did not decrease sufficiently to support an estimated half-life in the range of 15 to 17 d (Table 7). The whole-body residues decreased from 0.93 (±0.05) to 0.74 (±0.11) ng/g during the 28-d depuration phase. Excessive mortality in the other TCDD exposure concentrations precluded our obtaining experimental data on elimination in fish exposed to higher concentrations.

The uptake and depuration of TCDF were measured in fish exposed to 0.41 and 3.93 ng/L. In contrast to TCDD kinetics, TCDF uptake reached an apparent steady-state equilibrium after only 7 d of exposure (Table 10). Whole-body residues of TCDF did not increase after 7 d of exposure in fish exposed to 0.41 and 3.93 ng/L. In fish exposed for 28 d, the measured BCF was 6,049 at 0.41 ng/L and 2,455 at 3.93 ng/L (Table 11). The estimated bioconcentration kinetics of TCDF are shown in Table 12. Rainbow trout apparently were able to readily eliminate or metabolize TCDF. The whole-body residues in fish held during the 28-d depuration phase suggested a very short elimination half-life for this compound. Although TCDD and TCDF are structurally very similar, their bioconcentration kinetics and toxicities were found to be very different.

Table 10. Whole-body residues of 2,3,7,8-tetrachlorodibenzofuran (TCDF) in rainbow trout continuously exposed for 28 d followed by a 28-d depuration phase

Phase and day	Mean TCDF exposure concentration (ng/L)		
	0	0.41	3.93
Exposure			
0	<0.06		
7	0.17	1.63 (0.89)	11.9 (2.88)
14	0.12	1.80 (0.62)	9.30 (2.26)
21	0.19	1.05 (0.44)	10.7 (2.24)
28	0.22	2.48 (1.32)	9.65 (1.30)
Depuration			
28	<0.06	0.09 (0.06)	0.54 (0.08)

Values represent the mean (with standard deviation in parentheses) of four observations performed on individual fish, expressed as ng/g wet weight.

Table 11. Measured bioconcentration factors (BCF)[a] for 2,3,7,8-tetrachlorodibenzofuran (TCDF) in rainbow trout exposed continuously for 28 d

Days of exposure	TCDF exposure concentration (ng/L)	
	0.41	3.93
7	3,976	3,028
14	4,390	2,366
21	2,561	2,730
28	6,049	2,455

[a]BCF = $(C_t/C_w) \times 1,000$.

CONCLUSIONS

We conclude that TCDD and TCDF—especially TCDD—are extremely toxic to rainbow trout. A relative comparison of TCDD and TCDF chronic toxicities with those of several other organochlorine compounds demonstrated that TCDD is more than 10,000 times as toxic to fish as either endrin or toxaphene, and that TCDF is about 1,000 times more toxic than either of these insecticides (Table 13). Results from previous toxicity studies with fish by Helder [10,11], Miller et al. [12] and Adams et al. [24] demonstrated the toxicity of TCDD to be in the low ng/L range. However, we have shown that our lowest TCDD exposure concentration of 38 pg/L induced significant adverse effects on survival, growth, and behavioral responses. Results from our studies are perhaps more adequate estimates of TCDD toxicity because we used continuous exposure techniques for a longer time than had been used in previous studies. For similar reasons, we believe the BCF for TCDD derived from our studies is a more accurate estimate of the bioconcentration potential than are the estimates reported by Branson et al. [16] and Adams et al. [24]. Although we showed that TCDD was ex-

Table 12. Estimated bioconcentration kinetics[a] for TCDF in rainbow trout exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d

Kinetic parameter	TCDF exposure concentration (ng/L)	
	0.41	3.93
K_1 uptake rate constant (d^{-1})	1,228 (1,191)	6,852 (8,037)
K_2 depuration rate constant (d^{-1})	0.28 (0.30)	2.60 (3.04)
BCF-K_u	4,449 (6,481)	2,640 (4,379)
Time to reach 90% steady state (d)	8 (9)	0.90 (1.04)
Elimination half-life, $t_{1/2}$ (d)	3 (3)	0.27 (3.1)

Values in parentheses represent standard deviations.
[a]Estimated kinetics using BIOFAC [22].

Table 13. Chronic no effect concentrations (μg/L) for growth and survival of freshwater fish exposed to various organochlorine chemicals

Chemical and fish species	Days of exposure	Survival	Growth[a]	Source
Aroclor 1254, brook trout	118	9.0	9.0	[28]
Chlorodecone, fathead minnows	120	>0.31	>0.31	[29]
Pentachlorophenol (ultrapure), fathead minnows	90	>139	>139	[30]
Toxaphene, brook trout	90	>0.50	0.38	[31]
Toxaphene, channel catfish	90	0.096	0.20	[32]
Endrin, bluntnose minnows	30	0.1	0.1	[33]
TCDD, rainbow trout	56	<0.000038	<0.000038	This study
TCDF, rainbow trout	56	0.00179	0.00041	This study

[a]Change in weight of fish.

tremely toxic to rainbow trout, even our lowest exposure concentration was too high to derive a NOEC.

Acknowledgement – We are grateful to the many people from the Fish and Wildlife Service (FWS), Battelle and Monsanto who assisted in conducting these studies. We especially thank Mr. Dave Zumwalt for his efforts in designing the specialized diluter exposure system, and Mr. Zumwalt and Mr. George Holroyd for their outstanding efforts in constructing and calibrating the system. We appreciate the excellent advice and assistance of Dr. Mark Ellersieck and Ms. Linda Sappington in analyzing the data, and the technical assistance of Mr. Rick Archeski in analyzing the behavioral data. We give special thanks to Dr. Paul Eschmeyer, Editorial Section, Office of Information Transfer, FWS, Fort Collins, Colorado, for his review of the manuscript and for editorial advice.

REFERENCES

1. **Olie, K., M.v.d. Berg** and **O. Hutzinger.** 1983. Formation and fate of PCDD and PCDF from combustion processes. *Chemosphere* 12:627-636.
2. **Firestone, D.** 1972. Determination of polychlorodibenzo-*p*-dioxins and related compounds in commercial chlorophenols. *J. A.O.A.C.* 55:85-92.
3. **Ballschmiter, K., W. Zoller, C. Scholz** and **A. Nottrodt.** 1983. Occurrence and absence of polychlorodibenzofurans and polychlorodibenzodioxins in fly ash from municipal incinerators. *Chemosphere* 12: 585-594.
4. **Petty, J.D., D.L. Stalling, L.M. Smith** and **J.L. Johnson.** 1983. Occurrence and potential impact of PCDF's and PCDD's in aquatic ecosystems. In D.D. Hemphill, ed., *Trace Substances in Environmental Health* – XVII. University of Missouri Press, Columbia, MO, pp. 96-102.
5. **Crummett, W.B.** 1982. Environmental chlorinated dioxins from combustion: The trace chemistries of fire hypothesis. In O. Hutzinger, R.W. Frei, E. Merian and F. Pocchiari, eds., *Chlorinated Dioxins and Related Compounds Impact on the Environment.* Pergamon Press, Elmsford, NY, p. 261.
6. **Ryan, J.J., P.-Y. Lan, J.C. Pilon** and **D. Lewis.** 1983. 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and 2,3,7, 8-tetrachlorodibenzofuran residues in Great Lakes commercial and sport fish. In G. Choudhary, L.H. Keith and C. Rappe, eds., *Chlorinated Dioxins and Dibenzofurans in the Total Environment.* Butterworth, Boston, MA, pp. 87-97.
7. **Columbia National Fisheries Research Laboratory.** 1983. Impacts of contaminants on early life stages of striped bass. In P.M. Mehrle and J.L. Ludke, eds., *Progress Report.* U.S. Fish and Wildlife Service, Columbia, MO.
8. **Belton, T.J., R. Hazen, B.E. Ruppel, K. Lockwood, R. Mueller, E. Stevenson** and **J.J. Post.** 1985. A study of dioxin contamination in select finfish, crustaceans, and sediments of New Jersey Waterways. Office of Science and Research, New Jersey Department of Environmental Protection, Trenton, NJ.
9. **U.S. Food and Drug Administration.** 1981. Correspondence from FDA Commissioner Dr. Arthur Hall Hayes, Jr., to Governor Milliken of Michigan concerning the public health significance of TCDD contaminant "levels of concern" for finfish in Great Lakes. 26 August.
10. **Helder, T.** 1980. Effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on early life stages of the pike (*Esox lucius* L.). *Sci. Total Environ.* 14:255-264.
11. **Helder, T.** 1981. Effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on early life stages of rainbow trout (*Salmo gairdneri*, Richardson). *Toxicology* 19: 101-112.
12. **Miller, R.A., A.N. Logan** and **C.L. Hawkes.** 1979. Toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in aquatic organisms. *Environ. Health Perspect.* 5: 177-186.
13. **Cooper, K.R., J. Schell, P. Kahn** and **M. Gallo.** 1986. The effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on the development and survival of the Japanese medaka (*Oryzias latipes*). *Toxicologist* 6:27 (Abstract).
14. **Kleeman, J.M., J.R. Olson, S.M. Chen** and **R.E. Peterson.** 1986. Metabolism and disposition of 2,3, 7,8-tetrachlorodibenzodioxin in rainbow trout. *Toxicol. Appl. Pharmacol.* 83:391-401.
15. **Kleeman, J.M., J.R. Olson, S.M. Chen** and **R.E. Peterson.** 1986. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin metabolism and disposition in yellow perch. *Toxicol. Appl. Pharmacol.* 83:402-411.
16. **Branson, D.R., I.T. Takahashi, W.M. Parker** and **G.E. Blau.** 1985. Bioconcentration kinetics of 2,3,7, 8-tetrachlorodibenzo-*p*-dioxin in rainbow trout. *Environ. Toxicol. Chem.* 4:779-788.
17. **American Public Health Association, American Water Works Association** and **Water Pollution Control Federation.** 1980. *Standard Methods for the Examination of Water and Wastewater*, 15th ed. American Public Health Association, Washington, DC.
18. **Smith, L.M.** 1981. Carbon dispersed in glass fibers as an adsorbent for contaminant enrichment and fractionation. *Anal. Chem.* 53:2152-2154.
19. **Smith, L.M., D.L. Stalling** and **J.L. Johnson.** 1984. Determination of part-per-trillion levels of dibenzofurans and dioxins in environmental samples. *Anal. Chem.* 56:1830-1842.
20. **Drummond, R.A., C.L. Russom, D.L. Geiger** and **D.L. DeFoe.** 1986. Behavioral and morphological changes in fathead minnow, *Pimephales promelas*, as diagnostic endpoints for screening chemicals according to mode of action. In *Aquatic Toxicology and Hazard Assessment: Ninth Symposium.* American Society for Testing and Materials, Philadelphia, PA, pp. 415-435.
21. **Snedecor, G.W.** and **W.C. Cochran.** 1967. *Statistical Methods*, 6th ed. Iowa State University Press, Ames, IA.
22. **Blau, G.E., W.B. Neely** and **D.R. Branson.** 1975. Ecokinetics: A study of the fate and distribution of chemicals in laboratory ecosystems. *AIChE J.* 21: 854-861.

23. **Isensee, A.R.** 1978. Bioaccumulation of 2,3,7,8-tetrachlorodibenzo-para-dioxin. *Ecol. Bull.* 27:255–262.
24. **Adams, W.J., G.M. DeGraeve, T.D. Sabourin, J.D. Cooney** and **G.M. Mosher.** 1986. Toxicity and bioconcentration of 2,3,7,8-TCDD to fathead minnows (*Pimephales promelas*). *Chemosphere* **15**:1503–1511.
25. **Adams, W.J.** and **K.M. Blaine.** 1986. A water solubility determination of 2,3,7,8-TCDD. *Chemosphere* **15**:1397–1400.
26. **Kenaga, E.E.** and **C.A.I. Goring.** 1980. Relationship between water solubility, soil sorption, octanol-water partitioning, and concentration of chemicals in biota. In J.G. Eaton, P.R. Parrish and A.C. Hendricks, eds., *Aquatic Toxicology*. STP 707. American Society for Testing and Materials, Philadelphia, PA, pp. 78–115.
27. **Chiou, C.T., V.H. Freed, D.H. Schmedding** and **R.L. Kohnert.** 1977. Partition coefficients and bioaccumulation of selected organic chemicals. *Environ. Sci. Technol.* 11:475–478.
28. **Mauck, W.L., P.M. Mehrle** and **F.L. Mayer.** 1978. Effects of the polychlorinated biphenyl Aroclor 1254 on growth, survival, and bone development in brook trout (*Salvelinus fontinalis*). *J. Fish. Res. Board Can.* 35:1084–1088.
29. **Buckler, D.R., A. Witt, Jr., F.L. Mayer** and **J.N. Huckins.** 1981. Acute and chronic effects of Kepone and mirex on the fathead minnow. *Trans. Am. Fish. Soc.* **110**:270–280.
30. **Cleveland, L., D.R. Buckler, F.L. Mayer** and **D.R. Branson.** 1982. Toxicity of three preparations of pentachlorophenol to fathead minnows: A comparative study. *Environ. Toxicol. Chem.* 1:205–212.
31. **Mayer, F.L., P.M. Mehrle** and **W.P. Dwyer.** 1975. Toxaphene effects on reproduction, growth, and mortality of brook trout. EPA-600/3-75-013. U.S. Environmental Protection Agency, Duluth, MN.
32. **Mayer, F.L., P.M. Mehrle** and **W.P. Dwyer.** 1977. Toxaphene: Chronic toxicity to fathead minnows and channel catfish. EPA-600/3-77-069. U.S. Environmental Protection Agency, Duluth, MN.
33. **Mount, D.I.** 1962. Chronic effects of endrin on bluntnose minnows and guppies. U.S. Fish and Wildlife Service Research Report No. 58. Washington, DC.

ATTACHMENT 9

ASSESSMENT OF THE HUMAN HEALTH RISKS RELATED TO THE PRESENCE OF DIOXINS IN COLUMBIA RIVER FISH

Prepared by:

Russell E. Keenan, Ph.D.
Alan H. Parsons, Ph.D.
Ellen S. Ebert
Pamela D. Boardman, M.P.H.
Steven L. Huntley
Mary M. Sauer, M.S.P.H.

ChemRisk™
A McLaren Company
1685 Congress Street
Stroudwater Crossing
Portland, ME 04102
(207) 774-0012
(207) 774-8263

January 8, 1990

ChemRisk
A McLaren Company

An exposure pathway consists of four necessary elements: a source and mechanism of chemical release into the environment, an environmental transport medium for the released chemical, a point of potential human contact with the environmental medium, and a human exposure route (eg., inhalation, dermal contact, ingestion) at the point contact. Each pathway describes a unique potential mechanism by which a population or an individual may be exposed to a chemical. For each exposure pathway, the environmental fate and persistence of the chemical from the point of discharge to the point of human contact is an important consideration. Many factors such as adsorption onto particulates, sedimentation, and solubility influence the degree of human exposure. These factors are highly variable in the environment. Consequently, a truly valid exposure assessment can only be conducted using site-specific data. To this purpose, a study of the levels of dioxin in the edible portions of Columbia River fish has been conducted. Additionally, the rates of consumption of locally caught fish were estimated.

Columbia River fish sampling

For the purpose of determining accurate species-specific concentrations of dioxin in edible fish fillets, a variety of species of fish were collected from six different sites along the Columbia River system by an independent laboratory and consultant. A total of 680 individual fish were sampled at the six sites. Species collected included top and bottom feeders as well as resident and anadromous populations. Migratory fish sampled included coho salmon, fall chinook salmon (upriver and tule) and summer steelhead trout. Resident species sampled included white sturgeon, largescale sucker, and carp. Results of sampling data are reported below[1].

Fillet TCDD Levels in Columbia River Fish (ppt)

Species	Sampling Site					
	1	2	3	4	5	6
Coho salmon	0.08	0.10	NS	NS	NS	NS
Fall chinook salmon (Upriver)	0.08	0.09	NS	NS	NS	NS
Fall chinook salmon (Tule)	0.31	0.18	NS	NS	NS	NS
Summer steelhead trout	0.07	0.07	NS	NS	NS	NS
White sturgeon	0.09	0.12	1.09	0.88	1.68	0.55
Largescale sucker	0.32	NS	0.39	0.19	0.22	0.26
Carp	0.79	NS	1.06	1.35	1.46	0.76

At Sites 1 and 2, located downstream of NWPPA pulp and paper mills, the geometric mean concentrations of TCDD in salmon ranged from 0.08 to 0.31 parts per trillion (ppt) and steelhead trout averaged 0.07 ppt. Sturgeon, sucker, and carp collected from sites 1, 2, 3, and 4 had fillet TCDD levels averaging

[1] Note: 80% of the anadromous and 45% of all species sampled had nondetectable levels of TCDD. Nondetectable samples were assigned a value equal to one half the limit of detection per EPA protocol. This results in a more conservative estimation of tissue TCDD levels because actual values could equal zero.

DRAFT ATTACHMENT 10

ANALYSIS OF THE POTENTIAL POPULATIONS AT RISK FROM THE CONSUMPTION OF FRESHWATER FISH CAUGHT NEAR PAPER MILLS

Craig McCormack
Office of Policy Planning and Evaluation

David Cleverly 202-382-7891 (D.C)
Office of Research and Development

April 23, 1990

INTRODUCTION:

OTS, OSW, and OW have conducted a detailed human and ecological risk assessment of environmental loadings of dioxin from bleached pulp and paper mills. In that analysis only maximum lifetime cancer risk and average lifetime cancer risk to the hypothetically exposed individual was estimated for various exposure scenarios. No estimation of potential population risk, especially to sensitive subgroups, was provided in the analysis. Since draft publication of these results, we have identified populations of Asians, and tribal Native Americans that reside along the banks of the Columbia River in Oregon. The State government indicates that there are eight bleached pulp and paper mills that directly discharge to the Columbia River. The State also indicates that freshwater fish caught from the Columbia river are the main source of animal protein for these people. They consume an average of 100 to 150 grams of fish flesh each day over the course of the year. These individuals are much more likely to catch and consume fish that has been contaminated with dioxin from the effluent discharged from the mills than other populations in the area. The Native Americans number about 15,000, and the Asians number about 30,000 people.

In addition to these subpopulations exposed by diet to dioxin, we have estimated that approximately 610,000 people living in the vicinity of pulp and paper mills have family incomes at or below the poverty level. These individuals are also expected to derive a significant portion of animal protein from both subsistence and sports fishing in rivers near paper mills. Subsistence fishermen consume about 100 grams of fish per day/1, and sports fishermen consume about 69 grams fish per day/2.

For purposes of the assessment of potential cancer risk, we have employed monitoring data of dioxin contamination in fresh water fish caught in the vicinity of bleached pulp and paper mills. This was developed by the Environmental Research Laboratory in Duluth Minnesota as part of the National Bioaccumulation Study of freshwater fish in the U.S. The range of detected TCDD equivalent concentration in the edible fish fillet was from 0.1 ppt - 24 ppt. The weighted

average fillet concentration was 6.5 ppt (6.5 pg/gm). For purposes of estimating incremental lifetime cancer risk to the most exposed individual, a fillet concentration of 24 ppt was used. The weighted average dioxin concentration in the fillet of 6.5 ppt was used to derive the approximate average lifetime risk to subsistence and sports fishermen. The average exposure and average lifetime risk was used to estimate the annual cancer incidence in these sensitive subpopulations. In addition a human body weight of 70 kilograms was assumed to compute estimates of excess cancer risk.

CONCLUSIONS:

It is currently not possible to directly measure the association between the chronic dietary intake of dioxin contaminated freshwater fish, and the occurrence of specific forms of cancer in the exposed populations. The epidemiologic studies of these populations with a high dependency for subsistence fishing as a source of dietary animal protein have not been conducted. Therefore we have mathematically estimated lifetime excess cancer risk to the population residing near the Columbia River, as well as to low-income populations living in the vicinity of other mills in the U.S. This analysis is not intended to replace any previous risk assessments involving the human consumption of fish that has been contaminated with dioxin from the effluent discharged from paper mills, but is merely to illustrate that methodologies can be developed to estimate total populations at risk in the U.S.

The following are the results:

	Pop.	MIR(a)	AVG Risk(b)	Cancer Inc.(c)
Native Americans	**15,000. . . .**	**$8.6 X 10^{-3}$**	**$1.5 X 10^{-3}$**	**0.33**
Asian Americans	**30,000**	**$8.6 X 10^{-3}$**	**$1.5 X 10^{-3}$**	**0.67**
Total Risk	**45,000**	**$8.6 X10^{-3}$**	**$1.5X 10^{-3}$**	**1.0**
Low income families	**610,000**	**$5.4X 10^{-3}$**	**$1.0 X 10^{-3}$**	**9.3**

(a) MIR is the maximum individual risk, and is associated with the highest fish consumption rate and the highest dioxin concentration in fish caught near paper mills.

(b) Average lifetime cancer risk is the excess cancer risk based on the average fish consumption rate for subsistence and sports fishermen, and the weighted average dioxin concentration in fish caught near paper mills.

(c)Cancer incidence is the estimated number of cancer cases per year within the

defined exposed population. This was computed using average lifetime risk.

1/ U.S. Environmental Protection Agency (1988). Risk Assessment for Dioxin Contamination Midland, Michigan. Region 5. EPA-905/4-88-005.

2/Estimated consumption by the U.S. Food and Drug Administration, assuming substitution of average U.S. population daily consumption of red meat with fish.

Calculations of Risk

1. Native Americans

Assumptions:

a. MEI consumes 150 gms fish/day.
b. Average consumption is 100 grms fish/day.
c. 70 kilogram person.
d. Lifetime exposure.
e. Max. dioxin concentration in fish fillet = 24 pg/gm.
f. Weighted average dioxin in fish fillet = 6.5 pg/gm.
g. Population of 15,000.
h. Risk Specific Dose of Dioxin = lifetime cancer risk of one in a million is: 0.006 pg/kg/day.

Max. Daily Dose= (150 gms/day X 24 pg/gm) / 70 kg person
= 51.43 pg dioxin/kg/day

MIR ={(51.43 pg/kg/day) / (0.006 pg/kg/day)} X 10^{-6}
MIR = 8.6 X 10^{-3}

Avg. Daily Dose= (100 gms/day X 6.5 pg/gm)/ 70 kg person
= 9.28 pg dioxin/kg/ day

Avg. lifetime risk = {(9.28 pg/day)/(0.006 pg/kg/day)} X 10-6
= 1.5 X 10^{-3}

Annual Cancer Incidence = (Avg risk * population)/ 70 year lifespan
= (1.5 X 10^{-3} * 15,000)/ 70 yrs
= 0.33

2. Asian Americans

Assumptions are the same as with Native Americans. The population size is

MEI = maximally exposed individual

30,000.

Max. Daily Dose = 51.43 pg dioxin/kg/day.
MIR = 8.6 X 10-3

Avg. Daily Dose = 9.28 pg dioxin/kg/day
Avg. lifetime risk = 1.5×10^{-3}

Annual Cancer Incidence = (1.5×10^{-3} * 30,000)/70 yr lifespan
= 0.67

3. Low income families.

Assumptions:

a. MEI consumes 100 gms fish/day.
b. Average consumption is 69grms fish/day.
c. 70 kilogram person.
d. Lifetime exposure.
e. Max. dioxin concentration in fish fillet = 24 pg/gm.
f. Weighted average dioxin in fish fillet = 6.5 pg/gm.
g. Population of 610,000.
h. Risk Specific Dose of Dioxin = lifetime cancer risk of one in a million is: 0.006 pg/kg/day.

Max Daily Dose = (100 gms/day) X (24 pg dioxin/gm)/ 70 kg person
= 34.28 pg dioxin/kg/day

MIR = {(34.28 pg/kg/dy)/(0.006 pg/kg/dy)} X 10^{-6}
= 5.7×10^{-3}

Avg. Daily Dose = (69 gms/day) X (6.5 pg/gm)/70 kg person
= 6.41 pg dioxin/kg/day

Avg. lifetime risk = { (6.41 pg/kg/dy)/(0.006 pg/kg/dy)} X 10-6
= 1.0×10^{-3}

Annual Cancer Incidence ={ (1.0×10^{-3}) * (610,000)}/ 70 year lifespan
=9.3

The Bottom Line:

• The "Forest through the trees" is that the environmental loadings of dioxin from the mills may result in high levels of risk to humans.

• The analysis of the regulatory options suggests that this particular industrial source category fits the mold for a regulatory pollution prevention initiative through use of the CWA, TSCA, and RCRA.

* could require substantial reduction in the overall use of chlorine
* BACT seems to be oxygen delignification

OREGON
INSIDER
A BIWEEKLY DIGEST OF ENVIRONMENTAL NEWS

Inside the Dioxin Standard: Is it Defensible?

CONTENTS

■ The Environmental Quality Commission (EQC) will decide Nov. 2 whether to hold public hearings on a complex proposal to update the state's water quality standards. The proposal covers an enormous number of topics including a new "anti-degradation standard" to protect pristine waterways, a new "wetlands" definition, and new standards for dissolved oxygen, bacteria, toxic pollutants, particulate matter and bacteria (see Issue 20).

Tucked somewhere in the middle of the package, the Department of Environmental Quality (DEQ) has proposed to keep unchanged the current and seemingly incomprehensible water quality standard for dioxin: 0.013 parts per quadrillion (ppq). In addition, the agency has for the first time proposed a standard limiting the amount of dioxin that can accumulate in fish tissue. Both proposals are sure to draw the attention of the pulp and paper industry and environmentalists.

Industry representatives have long questioned the scientific underpinnings of the dioxin standard. They have even challenged the assertion that dioxin poses any threat to human health or the environment, comparing it to broccoli in one study. On the other hand, environmentalists see a standard that leaves completely unregulated hundreds of closely related toxic organo-chlorine compounds that are discharged from bleach kraft pulp mills every day. Based only on protecting human populations from cancer, they also see a standard that ignores documented impacts on fish and wildlife and fails to address non-cancerous affects on human health such as reproductive interference and immune system suppression.

Each side contends that the standard for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) -- the only compound regulated by DEQ's dioxin standard -- should be changed in some way. For now, DEQ has decided to keep the standard as it is.

The standard "answers" a very narrow question for DEQ and the public: How much 2,3,7,8-TCDD can exist in the water column without creating more than a 1-in-a-million cancer risk?

The standard does not regulate the amount of dioxin in river bottom sediments, where a seemingly significant percentage of these insoluble compounds settle. It does not take into account the natural loss, or "attenuation," of dioxin through breakdown and binding with particles suspended in the water column. And, since compliance with the standard is measured down river at the edge of the "mixing zone," it isn't even used to directly regulate the amount of dioxin coming out of pulp mill discharge pipes.

There are significant gaps in the scientific understanding of this toxin and in the regulatory mechanism by which it is controlled. While it is impossible to resolve the many questions surrounding dioxin, it is not particularly difficult to understand the guts of the standard and how the federal government came up with the result of 0.013 parts per quadrillion.

An Understandable Formula

For all the rhetoric, battling experts, and discussions of "linearized multistage models," "LD_{50} values" and all the rest, the standard is surprisingly understandable. The Environmental Protection Agency developed the dioxin standard using a relatively simple formula that includes six factors:

$$\text{Dioxin Standard} = \frac{\text{RISK} \times \text{WT}}{[\text{WCR} + (\text{BCF} \times \text{FCR}) \times \text{CPF}]}$$

The Six Factors

RISK: The cancer risk society is willing to tolerate from dioxin.

WT: The weight of the average adult.

WCR: The amount of water ingested by the average person each day – called the water consumption rate.

BCF: The extent to which fish concentrate dioxin in their tissues by swimming in contaminated water – called the bio-concentration factor.

FCR: The amount of fish ingested by the average person each day – called the fish consumption rate.

CPF: The chemical's cancer potency, a measure of how harmful the toxin really is – called the cancer potency factor.

The Overall Debate

Agency officials, industry representatives and environmentalists seem to agree that the formula itself is scientifically defensible. The debate rages over what numbers go into the formula and to many broader issues surrounding dioxin regulation.

EPA/DEQ Numbers

Through laboratory tests and simple assumptions, EPA assigned values to each of these factors, plugged them into a formula, and came up with the dioxin standard. DEQ adopted all of EPA's recommended values. With estimates of potential compliance costs running in the hundreds of millions of dollars and predictions of disastrous human health and environmental impacts, there is a surprisingly high degree of "play" in the numbers used to calculate the final standard. As a result, experts on both sides have been free to tweak the

THE EPA/DEQ NUMBERS:

RISK	1-in-a-million
WT	70 kilograms*
WCR	2 liters/day
BCF	5,000
FCR	6.5 grams/day*
CPF	156,000

* 6.5 grams per day is about ¼ of an ounce of fish. 70 kgs is about 155 pounds.

OREGON INSIDER (ISSN 1043-7142) is published biweekly (twenty-four times a year) as a news service of the Oregon Environmental Foundation, 2637 SW Water Avenue, Portland, Oregon 97201 (503) 222-2252. The Foundation is a non-profit corporation dedicated to education and research. Executive Editor: Peter A. Ravella, OSB No. 86264. Staff Writers: Jeff Bernstein & Sarah McCoy. Business Manager: Greg Tozian. Advisory Board Members: Roy Hemmingway, Consultant; Margaret Kirkpatrick, Attorney, Stoel, Rives, Boley, Jones & Grey; Judy Roumpf, Publisher, Resource Recycling magazine; Connie Taylor, Associate, HartCrowser; Dan Saltzman, President, Environmental Management Solutions and Diane Dimon Snow, Assistant to Earl Blumenauer. Subscription Rates: $245 per year including first-class delivery, $135 for private, non-profit 501(c)(3) organizations. Multiple subscription rates available. Letters to the Editor and comments welcome at above address.

numbers to better fit their view of the relative risks and benefits of dioxin regulation.

Three of the six factors are generally accepted and attract little attention. These are the water consumption rate, body weight, and the acceptable risk (RISK) determination.

THE "ACCEPTED" NUMBERS

WCR - 2 liters/day

Water Consumption Rate (WCR). Because of how the formula works, this factor has virtually no affect on the final standard and consequently draws little attention. If DEQ were to eliminate drinking water as a route of dioxin exposure altogether -- and plug in a "0" for the WCF -- the final standard would not change.

WT - 70 kilograms

Body Weight Factor (WT). EPA used 70 kilograms for the body "weight" factor. At about 155 pounds, this seems to be a pretty good approximation of the average adult's weight. The dioxin standard would be stricter if the agency plugged in a smaller number for body weight. For example, had EPA used 50 kilograms -- about 110 pounds -- the final dioxin standard would be .009 PPQ instead of .013 PPQ.

All else being equal, people weighing less than 155 pounds, such as children and women would, on average, face a slightly greater risk of cancer than their heavier counterparts under the .013 PPQ standard.

RISK - 1-in-a-million

Acceptable Cancer Risk (RISK). There is no magic behind DEQ's decision to base the state's dioxin standard on a 1-in-a-million cancer risk. It is not mandated by federal or state law; it is a policy decision. According to Lydia Taylor, administrator of the Water Quality Division, all DEQ water quality standards have been based on this risk level since 1987.

1-in-10-million?

Reasonable people differ whether it would be appropriate to set environmental regulatory policy on a less demanding cancer risk limit. John Bonine, a professor of environmental law at the University of Oregon, questioned whether the general population should be subjected to any greater cancer risk for the sake of industry profits. "EPA has developed guidance for dioxin based on a 1-in-10-million cancer risk. Oregon is free to adopt it but hasn't," he said.

A standard based on a 1-in-10-million cancer risk would be ten times tougher than the current one, or .0013 PPQ.

1-in-10,000?

According to Doug Morrison, environmental counsel for the Northwest Pulp & Paper Association, using a 1-in-a-million cancer risk level can be overly protective. Morrison said it would be statistically sound to accept cancer risks as high as 1-in-100,000 or 1-in-10,000 for certain sub-populations -- such as Native Americans, Asians and recreational fisherman who eat more river fish -- because there are fewer than 1 million in the group. "You can allow a higher risk factor for these smaller groups and still not cause any additional cancers," he said.

Other States Vary

At least one other state has decided to accept greater risks. Maryland's dioxin standard is based on a 1-in-100,000 cancer risk and is 1.2 PPQ, about 100 times less stringent than Oregon's.

DEQ Uses 1-in-a-million

Because DEQ's Water Quality Division has uniformly set its standards based on a 1-in-a-million cancer risk, it seems unlikely that the state would follow Maryland's lead. The EQC has made it an agency-wide goal to apply a uniform risk level to all regulatory programs, but that level has not been defined, (see DEQ 1990 "Strategic Plan."

THE "CONTROVERSIAL" NUMBERS

The remaining three factors -- fish consumption (FCR), cancer potency (CPF), and bio-concentration (BCF) -- have attracted the most debate for a couple of reasons. Not only do these factors have the greatest impact on the final standard, but the information on them is less developed. The bio-concentration and cancer potency numbers are based on laboratory studies that remain open to interpretation in the scientific community. Definitive surveys on consumption of Columbia River fish have not been done.

FCR: Who Does the Standard Protect?

Fish Consumption Rate (FCR). The debate over this factor is not complicated. Because different people eat different amounts and kinds of fish, a simple question arises: What single number best represents the public's average fish consumption? The answer may be, "There isn't one."

EPA's Number

In adopting the dioxin standard, DEQ accepted EPA's estimate that the average person consumes 6½ grams of freshwater or estuarine fish per day. That's a little less than one-quarter of an ounce per day, or about 5 pounds of fish and shellfish per year. According to Gene Foster, DEQ's expert on the dioxin standard, EPA based its estimate on a limited nationwide market survey of consumer buying habits.

Complete Data is Unavailable

"Complete fish consumption data has not been compiled specifically for the Columbia River system -- where the pulp mills discharge their effluent -- or for the fish most commonly consumed," said Foster. With the help of the Columbia River Intertribal Fish Commission, EPA is studying the diets of Native Americans along the river. Results could be available by year's end.

Accounting for Sub-Groups

Foster said differences between identifiable sub-groups cannot be overlooked when compiling fish consumption data. Native Americans -- particularly those living along the river -- Asians, commercial and recreational fisherman, and low-income subsistence fisherman all eat more fish than the general population.

FCR Range: 6.5 to 150 g/day

According to a preliminary risk assessment done by EPA this Summer, members of some sub-groups along the Columbia consume as much as 100 to 150 grams or about 3½ to 5¼ ounces of fish per day. "These rates are not off the wall," added Foster.

Industry says 13 - 16 g/day

Even the Northwest Pulp and Paper Association (NWPPA) -- an industry trade group -- acknowledges that EPA's 6.5 g/day figure is too low. The NWPPA estimates that recreational fisherman and Native Americans eat a little more than 13 and 16 grams of fish per day, respectively.

Most Agree 6.5 g/day is Low

The table at right shows how the dioxin standard would change if higher fish consumption numbers were plugged into the formula. No one claims that the average fish consumption rate in the Northwest is less than the 6.5 g/day. While

HOW MUCH FISH DO YOU EAT?

Grams Per Day	No. of 6 oz. Meals / Wk.	New Standard*
6.5	.2	0.013
10	.4	0.089
25	1.0	0.0035
50	2.0	0.0017
75	3.0	0.0012
100	4.0	0.0009
150	6.0	0.0006

* This is how the standard would change if DEQ used a higher FCR.

individuals may consume as much as 150 g/day, the overall average for the population would be lower.

BCF: Inadequate Science

Bio-concentration Factor (BCF). Dioxin in the environment tends to concentrate in living organisms, but in different ways and in different amounts. This factor quantifies the amount of dioxin fish concentrate in their tissues by swimming in contaminated water. Surprisingly, it does not take into account dioxin entering the fish through the food chain, just absorption through the skin.

Simplistic Studies

Based on simplistic laboratory experiments, EPA concluded that some fish concentrate 5,000 times as much dioxin in their tissues as is found in the water column. As with all other factors, DEQ adopted EPA's conclusion rather than conduct its own experiments.

Food Chain Ignored

Environmentalists argue a BCF of 5,000 grossly underestimates the amount of dioxin in fish tissue and therefore, the amount ingested by humans. "This is a significant oversight in the standard," said Bonine. "Scientists have documented dioxin accumulation in fish through the food change – called "bio-accumulation" – and it is a more important route of exposure than absorption through the skin," he said.

BCF Could Go Higher

Agency officials, industry representatives, and environmentalists generally agree that the BCF should be higher. The debate is over how much higher. Studies conducted for the NW Pulp & Paper Association indicate the BCF for sturgeon ought to be 10,600, over twice as high as the number EPA plugged into the formula.

BCF for Non-Resident Fish at Issue

"We acknowledge that our effluent is responsible for elevated dioxin levels in local, resident fish populations near our discharge pipes, said Llewellyn Matthews, executive director of the NWPPA. "We are not convinced that pulp mill effluent contributes to dioxin levels found in non-resident fish such as salmon. There are other sources of dioxin," she said.

HOW MUCH DIOXIN DO FISH ACCUMULATE?

BCF Values	New Standard*
10,000	0.0069
25,000	0.0027
50,000	0.0013
75,000	0.0009
100,000	0.0006
150,000	0.0004

* This is how the standard would change if DEQ used a higher BCF.

BCF Range: 5,000 to 150,000

According to Bill Diamond, director of EPA's Water Quality Criteria and Standards Division, EPA studies suggest the bio-concentration factor could range as high as 159,000.

Environmentalists have even argued the BCF could be as high as 500,000 for some species, if contamination of the food chain is taken into account.

DEQ Leans to 50,000

DEQ seems to be leaning toward a moderate increase in the bio-concentration factor. "The conclusions on this factor are very crude at this point," said Foster. "My guess is it will settle in somewhere around 50,000 to 60,000." The table at right shows how the dioxin standard would change if a higher bio-concentration factors were used. According to Foster, DEQ is planning to conduct field studies to develop a more accurate BCF for Columbia River fish.

CPF: How Toxic is Dioxin?

Cancer Potency Factor. Most of the debate has focused on this factor, which indicates dioxin's human cancer-causing potential. All arguments by industry and the environmental community regarding dioxin's dangerousness are subsumed in this factor. A closer look at this factor reveals that even if the industry's lowest cancer potency number is plugged into the formula, the dioxin

standard is still less than 1 part per quadrillion.

EPA selected a CPF of 156,000 mg/kg/day. The higher the CPF, the more dangerous the chemical, and the lower the water quality standard.

The Kociba Study . . .

The federal agency based its CPF on a single, two-year rat liver study completed in 1978 by Dr. R.J. Kociba. Since then, industry representatives and some members of the scientific community have challenged the Kociba study. Critics point out that the model used to develop the CPF is too simplistic. They argue Dr. Kociba improperly counted "precancerous liver tumors," failed to incorporate a "no observable affect level" in the test, and made other errors.

Under Attack

Dr. Robert Squire, a John Hopkins researcher and participant in the original study, recently reevaluated Dr. Kociba's data and concluded that the CPF was too high, possibly by a factor of 10 or more. EPA and DEQ acknowledge that legitimate questions surround the Kociba study but they are not prepared to change the CPF yet.

Other Agencies Use Lower CPFs

Other federal agencies use cancer potency factors much lower than EPA's. The U.S. Food and Drug Administration uses a CPF of 17,500 and the federal Center for Disease Control uses 36,000. According to Lydia Taylor, the administrator of DEQ's Water Quality Division, it would not be appropriate for DEQ to regulate dioxins based strictly on these cancer potency factors. "FDA is required to take economics into account when developing their cancer potency factor and we are not," she said.

Industry Wants State Review

The NWPPA has repeatedly urged DEQ to conduct its own review of dioxin's cancer potency. "The upshot is we believe they have over estimated the cancer potency of dioxin and that the states should do their own independent analysis of this factor," said Matthews.

The Washington Department of Health — with help from University of Washington researchers — has undertaken its own study of dioxin's cancer potency. EPA also has a study underway but Oregon does not.

DEQ May Respond

"We will be looking at the cancer potency factor when the new data is available from EPA, but for now we are satisfied with the value we are using," said DEQ's Foster.

CPF Range: 6,700 to 250,000

The range of CPF values seems to be between 6,700 and 250,000. The NWPPA says 6,700 to 9,700 is justified based on the Squire re-analysis and other studies. Environmentalists have challenged the objectivity of the Squire re-analysis and argue that there is no compelling reason to lower the CPF. They also assert that the CPF could be as high as 250,000.

HOW POTENT IS DIOXIN?

CPF Values	New Standard*
6,700	0.321
9,700	0.222
17,500	0.123
36,000	0.059
250,000	0.008

* This is how the standard would change if DEQ used a lower CPF.

DEQ Leans to 15,000

According to Foster, some studies suggest that the CPF could be as low as 15,000. If such a CPF were used, the dioxin standard would be about 0.12 PPQ, or about 10 times less strict than the current standard.

The table at right shows how the dioxin standard would change if lower CPF values were plugged into the formula. None of the new standards exceeds a single part per quadrillion.

PULLING IT TOGETHER

How Does the Standard Change?

The large table on page 8 shows how the dioxin standard changes as the various parameters are "tweaked" one at a time. It also shows what happens if the controversial factors were all changed at the same time, rather than independently of each other. With the help of industry, the environmental community and DEQ, four new dioxin standards were developed – two "NWPPA Numbers," the "Bonine Numbers" and the "DEQ Lean To."

Industry's Scenario

NWPPA Numbers. These numbers were provided by Doug Morrison, an attorney for the NW Pulp and Paper Association. If DEQ were to assume a fish consumption rate of 13.4 grams per day, a bio-concentration factor of 10,600 and a cancer potency factor of 6,700, the final dioxin standard would be .073 PPQ, about 5 times less strict than the current standard but still less than 1 PPQ. If the CPF were 9,700 – the NWPPA's upper end estimate – the final standard would be .050 PPQ.

Environmentalists' Scenario

Bonine Numbers. As an "exercise in number crunching," John Bonine agreed to provided his estimates for the factors: a fish consumption rate of 100 grams per day to protect Native Americans; a body weight of 50 kilograms – about 110 pounds – to better protect women and children; a risk factor of 1-in-10-million; and a bio-concentration factor of 50,000. Based on these assumptions, the dioxin standard would be 0.0000021 PPQ or 0.0021 parts per quintillion.

Bonine is actively engaged in the dioxin debate, representing the Northwest Coalition for Alternatives to Pesticides (NCAP) in litigation over DEQ's dioxin regulations.

FOUR POSSIBLE STANDARDS

Source of Values	New Standard*
NWPPA Numbers	.050
NWPPA Numbers	.073
Bonine Numbers	.0000021
DEQ 'Lean To'	.0037

* This is how the standard would change if EPA used the unofficial values provided by industry, environmentalists and DEQ.

DEQ's 'Lean To' Scenario

DEQ 'Lean To'. This scenario was developed with DEQ's help but does not reflect the agency's position on the dioxin standard. These numbers used are values the agency may "lean to" if the standard is eventually reviewed. The values are a fish consumption rate of 25 grams per day (about 1 fish meal per week), a bio-concentration factor of 50,000, and a cancer potency factor of 15,000 (over 10 times smaller than EPA's current CPF of 156,000, and smaller than any CPF employed by other federal agencies). Based on these assumptions, the final dioxin standard would be .0037 PPQ, or about 3½ times more strict than the current standard.

CONCLUSION

No Silver Bullets

All parties to the controversy acknowledge that the .013 PPQ dioxin standard is based on rough guesses and uncertain science.

Whether DEQ's dioxin standard is too strict, or not strict enough, depends on each individual's personal sense of comfort with levels of acceptable risk, and the economics of reaching the standard. As Dr. Donald Barnes, Director of the

TWEEKING THE NUMBERS: A LOOK AT HOW THE STANDARD CHANGES

	Fish Consumpt (FCR)	Water Consumpt (WCR)	Body Weight (WT)	Accepted Risk (RISK)*	Bioconcen-tration (BCF)	Cancer Potency (CPF)*	Final Standard
DEQ's Standard	6.5 (g/day)	2 (l/day)	70 (kg)	1.00E-06	5,000	156,000 (mg/kg/day)	.013 PPQ
	10	2	70	1.00E-06	5,000	156,000	.0089 PPQ
Tweeking	25	2	70	1.00E-06	5,000	156,000	.0035 PPQ
the	50	2	70	1.00E-06	5,000	156,000	.0017 PPQ
FCR	75	2	70	1.00E-06	5,000	156,000	.0012 PPQ
	100	2	70	1.00E-06	5,000	156,000	.0009 PPQ
	150	2	70	1.00E-06	5,000	156,000	.0006 PPQ
	6.5	2	70	1.00E-06	10,000	156,000	.0069 PPQ
Tweeking	6.5	2	70	1.00E-06	25,000	156,000	.0034 PPQ
the	6.5	2	70	1.00E-06	50,000	156,000	.0013 PPQ
BCF	6.5	2	70	1.00E-06	75,000	156,000	.0009 PPQ
	6.5	2	70	1.00E-06	100,000	156,000	.0006 PPQ
	6.5	2	70	1.00E-06	150,000	156,000	.0004 PPQ
	6.5	2	70	1.00E-06	5,000	6,700	.321 PPQ
Tweeking	6.5	2	70	1.00E-06	5,000	9,700	.222 PPQ
the	6.5	2	70	1.00E-06	5,000	17,500	.123 PPQ
CPF	6.5	2	70	1.00E-06	5,000	36,000	.059 PPQ
	6.5	2	70	1.00E-06	5,000	250,000	.008 PPQ
NWPPA Numbers	13.4	2	70	1.00E-06	10,600	9,700	.050 PPQ
	13.4	2	70	1.00E-06	10,600	6,700	.073 PPQ
Bonine Numbers	100	2	50	1.00E-07	150,000	156,000	.0000021
DEQ's 'Lean To'	25	2	70	1.00E-06	50,000	15,000	.0037 PPQ

*NOTE: The RISK FACTOR is expressed in Lotus 1-2-3 scientific notation. A 1.00E-06 notation means a 1-in-a-million risk and 1.00E-07 means 1-in-10-million.

EPA's Science Advisory Board, told the EQC this summer, "When it comes to dioxin, there are a lot of uncertainties; there are no silver bullet answers."

Standard Unlikely to Exceed 1 PPQ

Whatever else is decided, a few conclusions can be drawn. First, no single factor will be changed in isolation. Both DEQ and EPA are committed to a full review all the factors, not just the just the cancer potency, bio-concentration, or fish consumption numbers. Second, even if adjustments are made, it appears the final standard will remain below a single part per quadrillion, far below the detectable limits of today's instruments. Third, under all the scenarios presented, it appears the Columbia River will remain "water quality limited," forcing the mills to make expensive improvements to control dioxin.

Status & References

If approved by the EQC Nov. 1, eight public hearings on DEQ's entire water quality regulatory package, including the dioxin standard, will be held between Jan. 14 and Jan. 22 (watch *OI Calendar* for details). For more information, contact Eugene Foster (DEQ) at 229-6982. References: ORS 468.735, OAR 340-41 Table 20 (proposed water quality standards for toxic substances).

AIR QUALITY

Advisory Committee to Recommend Few Changes to Protect Wilderness Area Visibility

■ After some 18 months of work, it appears a Department of Environmental Quality (DEQ) advisory committee will recommended few if any significant changes in the way the agency protects visibility and other "air quality related values" in wilderness areas. Even though the group will recommend adding some new wilderness areas to the program, it will be years before that occurs.

Low Priority

"This is a slow moving process – it's not on the front burner," said John Core, visibility program coordinator and liaison to the advisory committee.

The recommendations are being developed as part of a federally-mandated review of the state "Visibility Protection Program." The VPP is supposed to protect air quality related values such as scenic vistas, air chemistry, aquatic biology and even sensitive plants in certain designated wilderness areas.

Triennial Review Underway

First completed in 1986, the VPP was approved by the Environmental Protection Agency in 1987. The program is unique because it requires air pollution control measures even where air quality is generally very high. The idea is to "preserve, protect, and enhance" the pristine air quality often found in wilderness areas, national parks, national seashores and similar areas.

DEQ appointed a 15-member Visibility Protection Advisory Committee last April to help review the program. The group includes representatives of the public, federal land management agencies, timber and agricultural industries, environmentalists and the tourism industry.

Field & Slash Burning at Issue

The primary threat to air quality in these areas is smoke from grass seed industry field burning, forest industry slash burning, and natural forest fires. The VPP restricts field and slash burning during certain months so smoke does not interfere with recreational uses.

Twelve Areas Protected Now

Some of Oregon's most noteworthy attractions are among the 12 wilderness areas currently protected under the program. These include Crater Lake National Park, Mt. Hood Wilderness Area, and popular wilderness areas near Bend. Designated "Class I," these areas receive the greatest air quality protection under the Clean Air Act and DEQ regulations.

Two Questions

There are two general questions before the committee. First, should DEQ expand the VPP to include areas set aside as wilderness since 1977? Second, should DEQ change the way visibility and other related values are protected?

DIOXINS, FURANS AND PCBs: THE TRUE STORY

Dioxins, furans and PCBs have become some of the most controversial chemicals of modern society. Dioxin in particular has been labelled the most toxic chemical ever produced by man. More than $1 billion has been spent so far on dioxin research[1], yet at the same time, industry and government officials insist that not enough evidence on the toxicity exists to justify elimination of the sources.

This paper explores some of the myths and facts surrounding these environmentally dangerous chemicals and explains why the scientific debate has become of an increasing political nature.

What Are 'Dioxins'

The term 'dioxins' usually refers to a whole chemical family with 75 individual members, which more correctly should be termed chlorinated dibenzo-p-dioxins. The most toxic member of this family is 2,3,7,8-Tetra-Chloro-Dibenzo-p-Dioxin, often abbreviated as 2,3,7,8-TCDD.

Often, the term 'dioxins' also includes a closely related chemical family called chlorinated dibenzofurans. The most toxic among the 135 known furans is 2,3,7,8-Tetra-Chloro-Dibenzo-Furan (TCDF), which is one tenth as toxic as the corresponding dioxin, TCDD.

Of the 210 dioxins and furans, twelve are extremely toxic and are commonly referred to as the 'Dirty Dozen'. Their individual toxicity is ranked by comparing them to 2,3,7,8-TCDD via internationally agreed upon Toxic Equivalence Factors (TEFs). Box 1 (next page) shows the chemical structures of dioxins and furans, and their toxicity ranking.

PCBs are another chemical family closely related to dioxins. Due to their similar chemical structure, some PCBs can act through exactly the same pathways in organisms as dioxins, but are much less potent. However, due to their chemical nature, PCBs are inevitably contaminated with furans and dioxins, and will form these more toxic chemicals during fires.

How Toxic Are Dioxins [2]

a) Extreme Ability to Kill

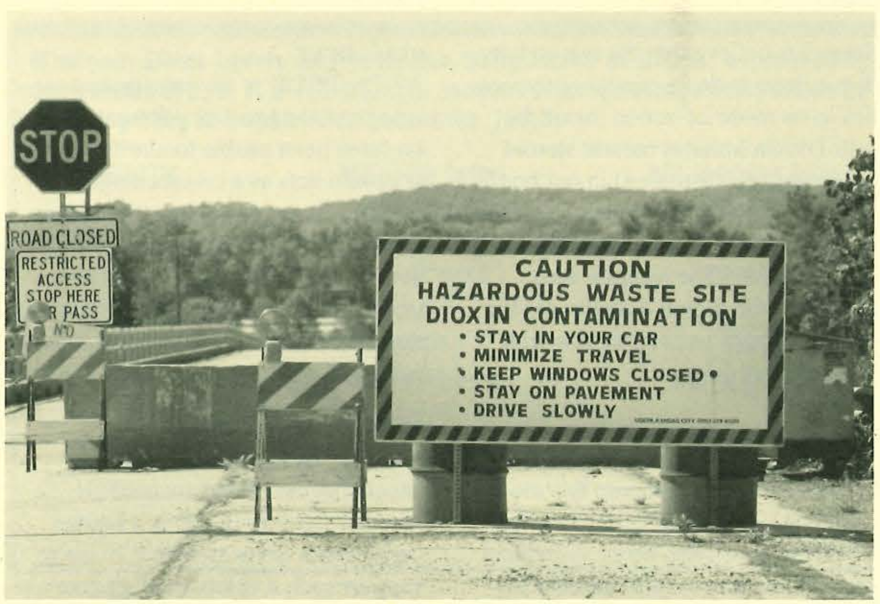
Dioxin TCDD is the most toxic man-made chemical ever tested on laboratory animals. Acutely lethal doses are measured in micro-grams per kilogram animal weight, in the parts per billion range. [2e] Though the lethal dose varies considerably from species to species, dioxin has been found to be extraordinarily toxic to all species tested.

Characteristic of lethal dioxin exposure is the 'wasting syndrome': animals seem to waste away, and eventually die, without displaying any overt pathological symptoms. The exact reason why dioxin can cause death in these minute quantities is not yet known.[2e]

b) Extremely Bio-Accumulative

Dioxins are some of the most persistent and bio-accumulative man-made chemicals released into the environment. While dioxins can be broken down under certain conditions, in particular when exposed to intensive sunlight, they cannot be broken down once absorbed by soil or dust. When they enter the food-chain, they will bio-magnify, often to levels many thousands of times higher than their surroundings.[2d,3]

It is this combination of dioxin's extreme toxicity and its bio-magnification in the environment that makes Greenpeace believe that there can be no safe level of dioxin emissions.



Conclusions and Greenpeace Demands

Enough research exists to prove that dioxin is extremely toxic and persistent, and that levels in our environment and in human milk are increasing. Given that many health effects occur from exposure to even minute quantities over time, and that widespread contamination of our environment and the build-up of these chemicals in the food chain has already led to dangerously high levels in human milk and in marine mammals, all energy must be devoted toward preventing any further releases of dioxins into the environment.

The elimination of man-made dioxin sources would go hand-in-hand with the elimination of a much larger group of environmentally dangerous organochlorines, which would be extremely desirable from an overall environmental point of view. Elimination of all dioxin sources would mark a turning point in our dealings with pollution control, since a holistic approach would have to include the phase-out of an entire class of anthropogenic chemicals presently discharged in large quantities into the environment.

In 1983, after two years of research, the Ministers' Expert Advisory Committee on Dioxins stated that [15]:

"Regardless of arguments about the significance of species differences in sensitivity, the validity of risk assessments, and other uncertainties which may take years to resolve, it is quite clear that dioxins are very unpleasant things to have in our environment and the less we have of them the better. It is, in fact, imperative to reduce dioxin exposure to the absolute possible minimum."

Despite these recommendations, the Canadian government has failed to eliminate even such outstanding dioxin sources as pentachlorophenol, but has instead actually added new dioxin sources to the Canadian environment by building further municipal and hazardous waste incinerators.

Greenpeace demands that the Canadian government follow the leadership provided by forward thinking European governments, and:

establish a five-year plan to eliminate all known industrial dioxin sources,

and in particular:

- **ban import and use of chlorophenols immediately;**
- **establish an indefinite moratorium on construction of new municipal and hazardous waste incinerators;**
- **phase out disposable products made of PVC or PVDC;**
- **phase out PVC coating of copper wire;**
- **phase out chlorinated solvents;**
- **eliminate the use of chlorine in the pulp and paper industry and metallurgical industry;**
- **establish a mass-balance of chlorine and organochlorines in Canada; i.e. determine the amount of chlorine gas and organochlorines produced, and their fate in the environment. This mass balance should extend to other halogens and organohalogens;**
- **commission a feasibility study on phase-out of all production and use of organochlorines.**
- **Fund research to find clean production technologies and alternatives to chlorinated products, as well as safe methods of destroying the existing piles of dioxin and other chlorinated waste.**

This paper was researched and written by Renate Kroesa, M.Sc., Toxic Project Co-ordinator.

REFERENCES

1) Report from Conferences, the 5th Int'l Dioxin Symposium, Bayreuth, 1985; Chemosphere, 1986, 15, N1-2.

2) This entire section is based on the following five overview reports/books published on the toxicology of dioxin. All reports/books give an excellent overview and provide many detailed references to the interested reader.
   a) 'Human Health Aspects of Exposure to PCDDs and PCDFs'; UAREP, Bethesda, Maryland, June 1988 (funded by the American Paper Institute).
   b) 'The Chemical Scythe', by Alistair Hay; Plenum Press 1982.
   c) 'A Cancer Risk-Specific Dose Estimate for 2,3,7,8-TCDD'; US-EPA/600/6-88/007Ab, June 1988, plus Appendices A-F.
   d) 'Dioxins in the Environment' by the UK Dept of the Environment; Pollution Paper No. 27, 1989.
   e) S.A. Skene et al, Human Toxicol, 1989, 8, 173-203.

3) P.M. Mehrle et al, Environmental Toxicology and Chemistry, 1988, 7, 47-62.

4) F. Rohleder, Presentation to the 9th Int'l Dioxin Symposium, Toronto, 1989.

5) T. Sinks, Presentation to the 7th Int'l Symposium on Epidemiology in Occupational Health, Tokyo, 1989.

6) a) R.E. Bowman et al, Neurotoxicology, 1986, 7, 637-650.
   b) J.R. Allen et al, Toxicology and Applied Pharmacology, 1979, 48, A180.
   c) J.R. Allen et al, Bulletin of Environmental Contamination and Toxicology, 1979, 21, 463-469.

7) 'Who do you believe?', Jock Ferguson; Chemosphere, 1985, 14 791-796.

8) PCBs, PCDDs and PCDFs in Breast Milk: Assessment of Health Risks; WHO, Regional Office for Europe; EH 29 (1988).

9) W.R. Swain; Aquatic Toxicology, 1988, 11, 357-377.

10) Monitor 1988, Sweden's Marine Environment - Ecosystems Under Pressure; National Swedish Environmental Protection Board.

11) a) R.R. Bumb et al (Dow Chemical), Science, 1980, 210, 385.
   b) Nestrick et al (Dow Chemical), Chemosphere, 1983, 12, 617-626.

12) J.M. Czuczwa, R.A. Hites, Chemosphere, 1986, 15, 1417-1420.

13) a) A. Schector et al, Chemosphere, 1988, 17, 627.
   b) A. Schector et al, poster at the 9th Int'l Dioxin Symposium, Toronto, 1989.

14) W.V. Ligon et al (General Electric), Environ. Sci. Technol. 1989, 23, 1286-1290.

15) Report of the Joint Health and Welfare Canada/ Environment Canada Advisory Committee on Dioxins, November 1983.

GREENPEACE

Founded in Canada, 1971
Fondé au Canada, 1971

Vancouver

1726 Commercial Drive,
Vancouver
British Columbia
Canada V5N 4A3
✆ 604 253-7701
FAX 604 253-0114

Toronto

578 Bloor Street West
Toronto, Ontario
Canada M6G 1K1
✆ 416 538-6470
Fax 416 538-6479

Montréal

2444 Notre-Dame Ouest
Montréal (Québec)
Canada H3J 1N5
✆ 514 933--0021
Fax 514 933-1017

Press Gang Printers - a feminist worker-controlled collective

IF YOU THINK WHITER IS BETTER...

GREENPEACE

...THINK

This paper is white. It was bleached with oxygen.

AGAIN.

This paper is whiter. It was bleached with chlorine.

A SMALL DIFFERENCE TO YOU...

...MAKES A BIG DIFFERENCE TO OTHERS.

Chlorine-bleached pulp is bad for the environment. There can be no doubt about that. Studies have shown again and again that effluents from kraft or sulphite mills using chlorine technology lead to reduced reproductivity in fish, suppressed immune systems, impaired metabolism, and a multitude of other long-term effects. Chlorine-bleached paper is also bad for you. Many of the chlorinated poisons discharged by the mills will also be found in paper - like the page you are now holding in your hand. Even dioxin, one of the most toxic chemicals ever produced, is likely to be present in this chlorine-bleached paper. Dioxin has been proven to leach from bleached paper products, such as milk cartons and coffee filters. Yet, dioxin is only the tip of the iceberg when it comes to organochlorine pollution from pulp and paper mills. Up to 1,000 different chemicals can be found in the effluent of mills employing chlorine-bleaching. Many of these cause cancer or genetic damage

and are persistent and accumulate in the environment. On average, pulp mills discharge around 35 tons of toxic organochlorines every single day. Even those mills that already have up- graded their process to reduce formation of the most notorius organochlorine, dioxin, will still discharge between 10 and 20 tons of other chlorinated poisons every single day. These discharges must stop now. The page you are now reading was printed on sulphite pulp bleached with oxygen-based agents. Such chlorine-free bleaching technology is readily available and must be employed immediately by mills using the sulphite process. Chlorine-free bleaching technology available for kraft mills will yield a cream-colored pulp. That brightness is entirely sufficient for most purposes, particulary since kraft pulp is mainly used in paper products that need to be strong, not white, such as packaging, stationery or envelopes.

THINK TWICE BEFORE YOU BUY WHITE, AND SUPPORT GREENPEACE IN ITS DEMANDS FOR

- Complete elimination of all chlorine-based bleaching chemicals.
- Use of the right fiber for the right product, i.e. the use of off-white kraft and off-white sulphite pulp, or completely unbleached pulp whenever possible.

CHLORINE-FREE BY 1993!

For more information about different pulp and paper making technologies and their impact on the environment, please ask us for the Greenpeace Guide to Paper.

B.R.O., Stockholm. Werzäta, Göteborg.

Agenda Item L. **Petition for Rule Amendment - Dioxin Standard**

Date	Date Received	Item Description
May 23, 1991	May 23, 1991	Petition from **James River II** and **Boise Cascade** (supported by Associated Oregon Industries, the Northwest Pulp and Paper Association, the City of St. Helens, the Association of Western Pulp and Paper Workers, Local 1, and the United Paper Workers International Union, Local 1097)
June 2, 1991	June 4, 1991	Letter from **Roger and Mary Thompson** (opposed)
June 4, 1991	June 7, 1991	Letter from **Robert J. Thompson** (reject petition)
June 6, 1991	June 7, 1991	Letter from **Northwest Pulp & Paper** (support)
June 6, 1991	June 7, 1991	Letter from **Oregon Salmon Commission** (opposed)
June 7, 1991	June 10, 1991	Letter and attachments from **Greenpeace** (deny petition)
June 7, 1991	June 11, 1991	Memorandum from **DEQ** (recommends rejection of petition)
June 10, 1991	June 10, 1991	Letter from **Northwest Environmental Advocates** (deny petition)
June 10, 1991	June 10, 1991	Memorandum from **Sierra Club Legal Defense Fund** (deny petition)
Undated	June 11, 1991	Letter from **Environmental Protection Agency** (deny petition)
June 11, 1991	June 12, 1991	Letter from **Representative Norris** (support)
June 11, 1991	June 12, 1991	Letter from **Oregon Health Division** (deny petition)
June 11, 1991	June 13, 1991	Letter from **Representative Van Leeuwen** (support)

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
MAY 23 1991
OFFICE OF THE DIRECTOR

May 23, 1991

HAND DELIVERED

Mr. Fred Hansen, Director
Oregon Department of Environmental Quality
811 S.W. Sixth Avenue
Portland, Oregon 97204

Re: Petition for Rule Amendment

Dear Mr. Hansen:

Enclosed is a petition to amend Oregon's ambient water quality criterion for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The petitioners are James River II, Inc., and Boise Cascade Corporation. Also supporting the petition are the Associated Oregon Industries, the Northwest Pulp & Paper Association[1], the City of St. Helens, the Association of Western Pulp and Paper Workers, Local 1, and the United Paper Workers International Union, Local 1097.

As you know, Oregon's present ambient water quality criterion for TCDD is 0.013 parts per quadrillion (ppq). The Environmental Quality Commission adopted this criterion in 1987 from an EPA guidance criterion developed in 1984. Since the criterion's adoption, and particularly within the last several months, a substantial body of new scientific evidence has shown that the assumptions upon which EPA relied in developing its guidance criterion were incorrect and that EPA's guidance criterion enormously overstated the risks posed by TCDD. The new evidence prompted EPA Administrator William Reilly in April of this year to order a complete reevaluation of the risks posed by TCDD and of EPA's TCDD-related programs.

The supporting documents appended to the petition describe in detail the latest scientific information concerning the risks posed by TCDD, as well as information concerning environmental exposures to TCDD in Oregon. Based on this information, the petition proposes an Oregon water quality criterion for TCDD of 2.3 ppq.

---

[1] Pope & Talbot, Inc., is a member of the Northwest Pulp & Paper Association but takes no position on the petition.

mrcpay24 15760/133

In submitting this petition, the petitioners are mindful of the Department's triennial review recommendation to retain the existing water quality criterion of 0.013 ppq. It is the petitioners' understanding, however, that the Department's recommendation was made without the benefit of the very recent scientific information that prompted EPA Administrator Reilly's April decision to reevaluate the risks posed by TCDD. This information includes the reassessment of the animal studies on which EPA relied in developing its guidance criterion for TCDD, the results of the Banbury Conference on TCDD risks, and recently published epidemiologic studies of workers and others exposed to TCDD.

The petitioners are also mindful of the limited resources of the Commission and the Department and their extensive obligations with respect to other matters. Given these constraints, the Commission may be tempted not to take any action until EPA has undertaken the lengthy process of revising its guidance criterion for TCDD. Unfortunately, by the time that EPA has acted, Oregon's existing TCDD criterion may have resulted in tens of millions of dollars of additional pollution control expenditures that the latest scientific information shows will produce no environmental benefit. Maryland and Virginia have recently averted this wasteful result by adopting, with EPA approval, water quality criteria for TCDD that are nearly 100 times less stringent than EPA's now outdated 1984 guidance criterion.

By granting the petition, the Commission will not, of course, have committed itself to revising the TCDD criterion. The petitioners ask only for an opportunity to present the latest scientific evidence on TCDD to the Commission and the public in the open forum provided by the Commission's procedures for rulemaking. In presenting this evidence, the petitioners would make available to the Commission, as well as the public, national experts in the risks posed by TCDD, including Dr. Robert Squire, whose evaluation of the tissues of rats fed TCDD was the primary basis for EPA's present guidance criterion. The petitioners are confident that this evidence will convincingly demonstrate that a TCDD criterion of 2.3 ppq

will fully protect human health and all designated beneficial uses of the waters of the state.

Very truly yours,

John W. Gould

John W. Gould
Lane Powell Spears Lubersky
800 Pacific Building
520 S.W. Yamhill Street
Portland, Oregon 97204
(503) 226-6151
Of Attorneys for
Petitioner James River II, Inc.

Richard Baxendale by MRC

Richard Baxendale
506 National Building
1008 Western Avenue
Seattle, Washington 98104
(206) 623-2848
Of Attorneys for
Petitioner Boise Cascade
Corporation

cc: Chair William P. Hutchison, Jr.
Commissioner Emery N. Castle
Commissioner Henry Lorenzen
Commissioner Carol A. Whipple
Commissioner William W. Wessinger
Mr. John E. Bonine
Mr. Larry Edelman
Mr. Michael Huston
Mr. Peter Linden
Ms. Lydia Taylor
Ms. Linda K. Williams
Mr. Jay T. Waldron
Mr. James M. Whitty, Associated Oregon Industries
Ms. Llewellyn Matthews, Northwest Pulp & Paper Association
Mr. William Taylor, United Paper Workers International Union, Local 1097
Mr. Gordon Simpson, Association of Western Pulp and Paper Workers, Local 1

mrcpay24 15760/133

BEFORE THE ENVIRONMENTAL QUALITY COMMISSION
OF THE STATE OF OREGON

In the matter of the petition of James River II, Inc., and Boise Cascade Corporation to amend subparagraph (2)(p)(B) of Oregon Administrative Rules chapter 340, division 41, sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965.	)	PETITION FOR RULE AMENDMENT (ORAL PRESENTATION REQUESTED)

May 23, 1991

I. INTRODUCTION

James River II, Inc. (James River) and Boise Cascade Corporation (Boise Cascade) petition the Commission to amend subparagraph (2)(p)(B) of OAR chapter 340, division 41, sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965. Supporting the Petition are the Associated Oregon Industries, the Northwest Pulp & Paper Association[1], the City of St. Helens, the Association of Western Pulp and Paper Workers, Local 1, and the United Paper Workers International Union, Local 1097.

The sections of the Oregon Administrative Rules listed above establish water quality criteria for all of Oregon's water basins. Subparagraph (2)(p)(B) of each section is identical:

> Levels of toxic substances shall not exceed the most recent criteria values for organic and inorganic pollutants established by EPA [the U.S. Environmental Protection Agency] and published in **Quality Criteria for Water** (1986). A list of the criteria is presented in Table 20.

The most stringent of EPA's published criteria for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), as set forth in Table 20, is 0.000013 nanograms per liter, or 0.013 parts per quadrillion (ppq), for the protection of human health.

---

[1] Pope & Talbot, Inc., is a member of the Northwest Pulp & Paper Association but takes no position on the Petition.

A substantial body of new scientific evidence concerning the toxicity of TCDD has become available since EPA published its guideline TCDD criteria in 1984.[2] This new evidence overwhelmingly shows that TCDD is far less harmful than was originally assumed and that EPA's TCDD criterion of 0.013 ppq for the protection of human health is no longer scientifically defensible. The new evidence, together with evidence concerning TCDD that is specific to Oregon, is discussed in the "Supporting Document for the Establishment of an Ambient Water Quality Criterion for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin in the State of Oregon," attached as Appendix A, and in "An Assessment of Potential Carcinogenic Risk from 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)," attached as Appendix B. In accordance with the recommendations set forth in Appendix A, the Petitioners request that the Commission initiate rulemaking proceedings to amend subparagraph (2)(p)(B) of the sections listed above to provide that concentrations of TCDD shall not exceed 2.3 ppq in Oregon waters.

The Petitioners submit this Petition for Rule Amendment pursuant to ORS 183.390, OAR 340-11-046, and OAR 137-01-070. As provided in OAR 137-01-070(3)(b), the Petitioners

---

[2] EPA's Quality Criteria for Water 1986, EPA 440/5-86-001, was published in 1986, but EPA's criteria for TCDD were published in 1984, 49 Fed. Reg. 5831 (Feb. 15, 1984).

request an opportunity to make an oral presentation to the Commission on whether to grant the Petition.

II. PETITIONERS

Petitioner James River owns and operates a bleached kraft pulp and paper mill at Wauna, Oregon. The mill discharges process wastewater into the Columbia River pursuant to a National Pollutant Discharge Elimination System (NPDES) permit issued by the Oregon Department of Environmental Quality (DEQ). On November 14, 1990, DEQ issued a renewed NPDES permit for the mill which contained effluent limits for TCDD. James River subsequently requested a contested case hearing on the TCDD effluent limits and other conditions of the renewed permit. The contested case is now pending before the Commission. James River's address is:

James River II, Inc.
Wauna Mill
Route 2, Box 2185
Clatskanie, Oregon 97016

Boise Cascade owns and operates a bleached kraft pulp and paper mill at St. Helens, Oregon. The mill discharges process wastewater into a publicly owned treatment works operated by the City of St. Helens. The treatment works discharges effluent into the Columbia River pursuant to an NPDES permit issued by DEQ. On November 14, 1990, DEQ issued a renewed NPDES permit for the City which contained effluent limits for TCDD and which required the City to limit TCDD

discharges from the mill into its treatment works. The City subsequently requested a contested case hearing on the TCDD effluent limits and other conditions of its renewed permit. Boise Cascade is a party to that contested case. The contested case has been consolidated with the contested case concerning James River's renewed NPDES permit and is now pending before the Commission. Boise Cascade's address is:

Boise Cascade Corporation
1600 S.W. Fourth Avenue
Portland, Oregon 97201

All correspondence concerning this petition should be directed to

John W. Gould
Lane Powell Spears Lubersky
800 Pacific Building
520 S.W. Yamhill Street
Portland, Oregon 97204

and

Richard Baxendale
506 National Building
1008 Western Avenue
Seattle, Washington 98104

III. OTHER INTERESTED PARTIES

The Petitioners believe that the other parties to the contested cases described above may be interested in the petition. In addition to DEQ, those parties and their attorneys are:

City of St. Helens

Represented by: Peter M. Linden
City Attorney
City of St. Helens
P.O. Box 278
St. Helens, Oregon 97051

Northwest Coalition for Alternatives to Pesticides
Columbia River United

Represented by: John E. Bonine
Western Environmental Law Clinic
School of Law
University of Oregon
Eugene, Oregon 97403

Pope and Talbot, Inc.

Represented by: Jay T. Waldron
David F. Bartz, Jr.
Schwabe, Williamson & Wyatt
1600-1950 Pacwest Center
1211 S.W. Fifth Avenue
Portland, Oregon 97204

UA Local 290, Plumbers and Steamfitters
Mike Jerkiewicz

Represented by: Linda K. Williams
1744 N.E. Clackamas Street
Portland, Oregon 97232

IV. RULE TO BE AMENDED

The Petitioners request that the Commission amend subparagraph (2)(p)(B) in each of the following sections of Oregon Administrative Rules chapter 340, division 41: 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965. Subparagraph (2)(p)(B) of each of these sections is identical:

> Levels of toxic substances shall not exceed the most recent criteria values for organic and inorganic pollutants

> established by EPA and published in **Quality Criteria for Water** (1986). A list of the criteria is presented in Table 20.

Table 20 lists these EPA criteria for TCDD: 0.010 micrograms per liter (ug/l) (10,000 ppq) for the acute protection of freshwater aquatic life; 0.00001 ug/l (10 ppq) for the chronic protection of freshwater aquatic life; 0.000014 nanograms per liter (ng/l) (0.014 ppq) for the protection of human health from fish consumption; 0.000013 ng/l (0.013 ppq) for the protection of human health from fish consumption and water ingestion. The most stringent EPA TCDD criterion, then, is 0.013 ppq.

Petitioners request that the Commission amend subparagraph (2)(p)(B) of each of the sections of OAR chapter 340, division 41, listed above to read as follows (matter to be added is highlighted):

> Levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin shall not exceed 0.0023 nanograms per liter (2.3 parts per quadrillion). Levels of other toxic substances shall not exceed the most recent criteria values for organic and inorganic pollutants established by EPA and published in **Quality Criteria for Water** (1986). A list of the criteria is presented in Table 20.

Thus, following the requested amendment, subparagraph (2)(p)(B) of each of the amended sections of OAR chapter 340, division 41, would read:

> Levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin shall not exceed 0.0023 nanograms per liter (2.3 parts per quadrillion). Levels of other toxic substances shall not exceed the most recent criteria values for

organic and inorganic pollutants established by EPA and published in **Quality Criteria for Water** (1986). A list of the criteria is presented in Table 20.

V. LEGAL BACKGROUND

The Commission's function is "to establish the policies for the operation of the department [DEQ]." ORS 468.015. In particular, the Commission is to "establish standards of quality and purity for the waters of the state." ORS 468.735(1).

The federal Clean Water Act also requires the Commission, as the state agency responsible for water pollution control, to adopt water quality standards for the waters of the state. See 33 U.S.C. § 1313(c)(1). Water quality "standards" "consist of the designated uses of the . . . waters involved and the water quality criteria for such waters based upon such uses." 33 U.S.C. § 1313(c)(2)(A). For substances such as TCDD that are listed as toxic pollutants under the Clean Water Act, states must adopt "specific numerical criteria" for the pollutants. See 33 U.S.C. § 1313(c)(2)(B). All water quality criteria adopted by a state are subject to review by EPA for consistency with the Clean Water Act. See 33 U.S.C. § 1313(c)(3).

Section 304 of the Clean Water Act requires EPA to "develop and publish . . . criteria for water quality." 33 U.S.C. § 1314(a)(1). The most recent collection of these

criteria, including those for TCDD, are published in the EPA document Quality Criteria for Water 1986, EPA 440/5-86-001.

EPA's water quality criteria are intended only as guidance for other federal agencies and the states; the states are not required to adopt EPA's criteria as their own. The preamble to Quality Criteria for Water 1986 emphasizes:

> These criteria are not rules and they do not have regulatory impact. Rather, these criteria present scientific data and guidance of the environmental effects of pollutants which can be useful to derive regulatory requirements based on considerations of water quality impacts.

So long as a state's water quality criteria are derived through "scientifically defensible methods," EPA will approve the criteria although the criteria may differ from EPA's guidance criteria. See 40 C.F.R. § 131.11(b)(1) (1990). Indeed, EPA recently approved Maryland's (1990) and Virginia's (1991) TCDD water quality criteria of 1.2 ppq, which are nearly 100 times greater than EPA's guidance criterion of 0.013 ppq.[3]

VI. REASONS FOR THE RULE AMENDMENT

A. Basis for the Present TCDD Criterion of 0.013 ppq

Oregon's present TCDD criterion of 0.013 ppq was adopted directly from EPA's guidance criterion for the protection of human health from the consumption of fish and the

---

[3] EPA's approval of Maryland's TCDD water quality criterion is attached as Appendix C; EPA's approval of Virginia's water quality criterion is attached as Appendix D.

ingestion of water. EPA's guidance criterion was based on studies of tumors in rats that had been fed high doses of TCDD. Appendix A, p. 2-11. EPA assumed that the incidence of tumors in rats fed high doses of TCDD would be linearly related to the incidence of tumors in humans exposed to low doses of TCDD and that there was no threshold dose below which TCDD would not pose some risk of cancer, i.e., any exposure to humans greater than zero posed a risk of cancer. See Appendix A, p. 2-12.

Using these assumptions, the incidence of tumors in rats fed high doses of TCDD, and a "risk level" of 1 in 1,000,000 (1×10^{-6}), EPA derived an acceptable daily intake (ADI) for TCDD of 0.006 picograms per kilogram of body weight per day (pg/kg/d). That is, EPA's water quality criterion for TCDD is based on the assumption that humans can with reasonable risk consume up to 0.006 pg/kg/d of TCDD. See Appendix A, p. iv.

To derive a guidance water quality criterion for TCDD from an ADI of 0.006 pg/kg/d, EPA used the following simple formula:

$$WQS = (ADI \times BW)/[(BCF \times FCR) + WCR]$$

where

WQS = water quality standard (criterion), expressed in picograms per liter (pg/L), or ppq

ADI = acceptable daily intake, expressed in pg/kg/d

BW = body weight, expressed in kilograms (kg)

BCF = bioconcentration factor

WCR = water consumption rate, expressed in liters per day

FCR = fish consumption rate, expressed in kilograms per day (kg/d).

Appendix A, p. iv.

The bioconcentration factor (BCF) is the concentration of a substance in fish tissue divided by its dissolved concentration in the water in which the fish lives. <u>See</u> Appendix A, p. 4-1. It is a measure of the degree to which a fish takes up a dissolved substance in the water and concentrates the substance in its tissues. Thus, if a dissolved substance is present in water at a concentration of one part per million and is present in the tissues of fish that live in the water at a concentration of 100 parts per million, the BCF is 100.

Employing the formula set forth above, it may be seen that the appropriate water quality criterion (the WQS) will increase as either the ADI or body weight increases and that it will decrease as either the BCF or fish or water consumption increases. In deriving its TCDD water quality criterion of 0.013 ppq, EPA assumed an ADI of 0.006 pg/kg/d, an average body weight of 70 kilograms, a BCF of 5000, average fish consumption of 0.0065 kilograms per day, and average water consumption of 2.0 liters per day. Appendix A, p. iv.

B. New Scientific Information and Region-Specific Exposure Data

New scientific information concerning TCDD and region-specific TCDD exposure information support the adoption of a substantially less stringent TCDD criterion for Oregon. This information and its use in the development of a TCDD criterion for Oregon are described in detail in Appendices A and B. The following is a summary.

1. Acceptable Daily Intake of TCDD

New scientific information concerning the mechanism by which TCDD causes toxic effects, epidemiologic studies of TCDD exposures, and the recent reevaluation of the animal studies on which EPA relied in developing its guidance TCDD criterion, demonstrate that EPA's ADI for TCDD is unwarrantedly stringent by several orders of magnitude. Whereas EPA assumed an ADI for TCDD of 0.006 pg/kg/d, this new scientific information demonstrates that an ADI for TCDD of 1 to 10 pg/kg/d would fully protect human health, even under conservative assumptions. See Appendix A, section 2; Appendix B, pp. 8-9.

EPA's guidance TCDD criterion assumed that any exposure to TCDD above zero produced a risk of cancer. Recent scientific research, however, shows that the toxic effects associated with exposure to TCDD are "receptor mediated." See Appendix A, pp. 2-9 to 2-10; Appendix B, pp. 5-8. This, in turn, indicates that there is a threshold dose of TCDD below which TCDD has no toxic effects. See id. The existence of such a threshold is also supported by animal research and by epidemiologic studies. The latter studies have not shown evidence of increased cancer risk from low-level environmental exposures to TCDD. See Appendix A, pp. 2-9.

In addition to the evidence for a TCDD toxicity threshold, a recent reevaluation of the animal study on which EPA relied in developing its ADI for TCDD shows that EPA's ADI is scientifically unsound. A 1978 study by Dr. R. J. Kociba and others showed that rats fed high doses of TCDD developed liver lesions. Appendix A, p. 2-11; Appendix B, pp. 3-5. At EPA's request, Dr. Robert Squire in 1980 evaluated these lesions and reported that a number of the lesions were cancerous tumors. Id. EPA used these results to classify TCDD as a "probable" human carcinogen and to develop its ADI for TCDD of 0.006 pg/kg/d. Id. Since that time, however, the methodology for evaluating rat liver lesions has changed considerably. Using this new methodology, which is the methodology accepted by EPA, Dr. Squire and an independent pathology working group (PWG) in 1990 reevaluated the results of the 1978 Kociba study. See Appendix A, pp. 2-11 to 2-12; Appendix B, pp. 3-5. Upon reevaluation, substantially fewer cancerous tumors were found. Id. Moreover, the tumors were associated with large TCDD doses that also induced extensive liver damage. Id.

Although the recent scientific information discussed above and in Appendices A and B suggests that EPA's use of a nonthreshold, linear model to estimate the risk of exposure to TCDD is not scientifically valid, Dr. R. E. Keenan and others have applied the results of the Kociba study, as reevaluated by the PWG in 1990, to the model used by EPA. See Appendix A, p. 2-12. Using this and other recent scientific information, Dr. Keenan calculated a cancer potency for TCDD that was 16 times lower than that calculated by EPA. At an appropriately conservative 10^{-5} risk level, Dr. Keenan's calculated cancer potency for TCDD equals an ADI of 1.0 pg/kg/d, i.e., an ADI approximately 167 times larger than EPA's ADI of 0.006 pg/kg/d. See id. Dr. Squire, as set forth in Appendix B, also believes that 1.0 pg/kg/d is an appropriate ADI for TCDD.

A model for calculating an ADI for TCDD that is more consistent with the latest scientific knowledge, however, is one that recognizes that TCDD acts through a threshold mechanism. See Appendix A, p. 2-13; Appendix B, pp. 5-8. The 1978 Kociba rat study reported no observable adverse effects in rats fed 1000 pg/kg/d of TCDD. Applying the widely accepted safety factor of 100 to this "no observable adverse effect level" (NOAEL) of 1000 pg/kg/d, one obtains an ADI of 10 pg/kg/d for TCDD. Id.

Many North American and European governments, including those in Canada, the Netherlands, Germany, and the United Kingdom, have used a threshold model and safety factors

to calculate an ADI for TCDD. See Appendix A, pp. 2-12 to 2-13. Most recently, this approach was used by a working group of the World Health Organization to recommend an ADI for TCDD of 10 pg/kg/d and by the Washington Department of Health to develop an ADI for TCDD of 20 pg/kg/d. Appendix A, p. 2-13.

In sum, the weight of the most recent scientific evidence supports an ADI for TCDD of between 1.0 and 10.0 pg/kg/d rather than EPA's now outdated ADI of 0.006 pg/kg/d. As set forth in Appendices A and B, an ADI of 1.0 pg/kg/d is fully protective of human health from all forms of TCDD-induced toxicity, including cancer, reproductive effects, and immunotoxicity.

2. Regulatory Bioaccumulation Multiplier (RBM)

EPA's TCDD criterion was calculated using a bioconcentration factor (BCF) of 5000. A BCF, however, takes into account only the uptake of dissolved compounds through fish gill surfaces. Other means of accumulating substances in fish tissues, such as ingestion of food and sediment, are not addressed. Appendix A, pp. 4-1 to 4-2.

Section 4.3 of Appendix A describes the development of a regulatory bioaccumulation multiplier (RBM). The RBM is the concentration of a substance in the edible portion of fish tissues divided by the total amount of the substance (dissolved and adsorbed to particulates) added to the water body per unit volume of water. Appendix A, p. 4-6. Thus, the RBM is the degree to which a substance will be concentrated in the edible

portion of fish tissues through all accumulation methods. Id. The advantage of the RBM is that increases in discharges of a substance to a water body can be directly related to increases in the concentration of that substance in edible fish tissues in that water body. See Appendix A, p. 4-7.

A wide variation in BCFs and bioaccumulation factors (BAFs) has been reported for TCDD. See id. When converted into RBMs, however, the reported BCFs and BAFs fall within a relatively narrow range of 600 to 6440 and average 3600. Id. Therefore, the multiplier of 5000 used by EPA as a BCF is scientifically sound as an RBM, albeit for different reasons. Appendix A, p. 4-8.

3. Fish Consumption

The principal route by which humans are exposed to TCDD discharged into water bodies is through the consumption of fish that live in those water bodies. Appendix A, p. 5-1. The study set forth in Appendix A chose the Columbia River as a representative river to characterize Oregon fish consumption patterns. In addition to characterizing the fish consumption patterns of the general population, it also characterizes the fish consumption patterns of two subpopulations likely to be greater consumers of fish: recreational anglers and Native Americans.

The mean consumption rate of Columbia River fish for the general population is 0.91 grams per day. Appendix A, p. 5-3. For recreational anglers, the median consumption

estimate is 5.8 grams per day, and for Native Americans, the mean consumption estimate is 16.4 grams per day. Appendix A, pp. 5-7 to 5-8. Native Americans, however, consume a larger proportion of anadromous fish than do recreational anglers. Appendix A, p. 5-8. Reported TCDD concentrations of anadromous fish, which spend little time within the river, are far below those of resident fish species. Id. If this difference in consumption patterns is taken into account, recreational anglers are the most exposed population. Id. For this reason, the most appropriate fish consumption rate to employ in setting a TCDD water quality criterion for Oregon is 5.8 grams per day. Appendix A, p. 5-9.

4. Consumption of Water

EPA's water quality criterion for TCDD is based on an assumed daily consumption of water of 2.0 liters per day. This consumption rate is derived from the daily ration of water required by U.S. Army field personnel. Appendix A, p. 6-1. Section 6 of Appendix A demonstrates that, although 2.0 liters per day of liquids may be a reasonable consumption rate, only approximately 60 percent of liquids consumed are water or water-based soups or beverages. Thus, a more realistic water consumption rate is 1.2 liters per day. Id.

C. <u>Calculation of an Oregon TCDD Water Quality Criterion</u>

Substituting only a regulatory bioaccumulation multiplier (RBM) for the bioconcentration (BCF) used by EPA, the formula for deriving an Oregon water quality criterion for TCDD is as follows:

$$WQS = (ADI \times BW)/[(RBM \times FCR) + WCR]$$

where

WQS	=	water quality standard (criterion), expressed in picograms per liter (pg/L), or ppq
ADI	=	acceptable daily intake, expressed in pg/kg/d
BW	=	body weight, expressed in kilograms (kg)
RBM	=	regulatory bioaccumulation multiplier
WCR	=	water consumption rate, expressed in liters per day
FCR	=	fish consumption rate, expressed in kilograms per day (kg/d).

Appendix A, p. 9-3.

As discussed above, a scientifically sound ADI for TCDD is 1.0 to 10.0 pg/kg/d, not the 0.006 pg/kg/d used by EPA. Appendix A uses the most conservative of the ADIs within this range, 1.0 pg/kg/d. <u>Id.</u> Appendix A retains EPA's assumption that average body weight is 70 kg, and uses an RBM of 5000, which is equal to EPA's BCF of 5000. <u>Id.</u> Using fish consumption data for the Columbia River and protecting recreational anglers, the most exposed population group, Appendix A uses a fish consumption rate of 0.0058 kg/d, rather than EPA's assumed fish consumption rate of 0.0065 kg/d. <u>Id.</u>

Finally, Appendix A uses a realistic water consumption rate of 1.2 liters per day rather than EPA's assumed water consumption rate of 2.0 liters per day. Id. Inserting these values into the formula above yields a TCDD water quality criterion of 2.3 picograms per liter or 2.3 ppq. Id.

D. A TCDD Water Quality Criterion of 2.3 ppq for the Protection of Human Health Also Protects Other Designated Beneficial Uses

Section 3 of Appendix A discusses the reported effects of TCDD on aquatic life. For long-term exposures to fish, the lowest TCDD concentration for which adverse effects have been reported is 38 ppq in a study of rainbow trout. Appendix A, p. 3-6. No adverse effects for long-term exposure have been reported at concentrations ranging from 1.1 ppq to approximately 3000 ppq. Id. Recent experimental stream studies have shown no adverse effects in cold-water fish species at TCDD concentrations of 3.5 ppq. Id. Moreover, evidence suggests that fish are more sensitive to TCDD than other aquatic organisms. Appendix A, p. 3-7. For these reasons, a TCDD water quality criterion of 2.3 ppq would protect designated beneficial uses other than those involving human health. See Appendix A, p. 9-3.

VII. EFFECTS OF ADOPTION OF THE PROPOSED AMENDMENTS

Because, as shown above and in more detail in Appendix A, a TCDD water quality criterion of 2.3 ppq would fully protect human health and designated beneficial uses of

Oregon waters, no adverse effects would follow from the adoption of this criterion. On the other hand, adoption of a less stringent criterion for TCDD may substantially reduce compliance costs for the pulp and paper industry, other industries, municipal sewage treatment plants, and other suspected sources of TCDD discharges. Adoption of a less stringent TCDD criterion would also help maintain the competitiveness of Oregon industries against industries in other states that have already adopted TCDD water quality criteria that are orders of magnitude less stringent than Oregon's existing criterion of 0.013 ppq.

VIII. CONCLUSION

For the foregoing reasons, the Commission should initiate rulemaking proceedings to adopt the amendments proposed by the Petitioners. The amendments would establish a water quality criterion for TCDD of 2.3 ppq in all waters of the state.

DATED: May 23, 1991.

John W. Gould
John W. Gould
Lane Powell Spears Lubersky
800 Pacific Building
520 S.W. Yamhill Street
Portland, Oregon 97204
(503) 226-6151

Of Attorneys for Petitioner
James River II, Inc.

Richard Baxendale by MRC
Richard Baxendale
506 National Building
1008 Western Avenue
Seattle, Washington 98104
(206) 623-2848

Of Attorneys for Petitioner
Boise Cascade Corporation

June 2, 1991

Environmental Quality Commission
Directors Office
811 S. W. 6th Ave.
Portland, Oregon 97204

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 04 1991
OFFICE OF THE DIRECTOR

Dear Commission Member,

In reference to the giant pulp and paper manufacturers, notably James River Corporation and Boise Cascade, who brashly now request the Oregon E.Q.C. to set lower ambient water quality standards.

Needless to say, the Oregon standard is absolutely necessary to the maintenance of our waterways now and for the future. Certainly industrial needs must be given some consideration. However all members of the state's citizenry should also be granted the highest water quality standards in our great Northwest. Oregon as a leader in all environmental concerns is a model for the nation.

As owners of property on the Columbia River in Columbia County, we implore the E.Q.C. to reject the proposed change in water quality standards. Industry cannot provide any real evidence that would support any modification of the D.E.Q. standard.

Thank you for your vote against such a negative approach to our water quality.

Sincerely,

Roger and Mary Thompson

Roger and Mary Thompson
4144 S. E. Boardman Ave.
Milwaukie, Oregon 97267

Environmental Quality Commission
Directors Office
811 SW 6th Avenue
Portland, OR 97204

June 4, 1991

Dear Commission Member,

I urge you to please reject the latest proposal by the pulp industry to reduce the water quality standards in Oregon.

In a time of increased environmental awareness, it seems indefensible that certain companies would propose to lessen the standards for economic reasons, while neglecting and potentially harming a very large and complex ecological system.

My interest as a partner in land in Clatskanie prompts me to write this letter not only for myself, but for everyone who lives on or near the rivers in Oregon. You have the opportunity to effect a positive result for the people of Oregon. Please do so.

Respectfully,

Robert J. Thompson

Robert J. Thompson

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED

MILES
SAND AND GRAVEL COMPANY
P.O. BOX 130, AUBURN, WASHINGTON 98071

AUBURN
JUN 5 '91
WASH.

U.S. POSTAGE
0 5
METER
8219

Environmental Quality Commission
Directors Office
811 S.W. 6th Ave.
Portland, OR 97204

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 07 1991

OFFICE OF THE DIRECTOR

NORTHWEST PULP&PAPER

June 6, 1991

Fred Hansen, Director
Department of Environmental Quality
811 SW Sixth Avenue
Portland, OR 97204

Dear Mr. Hansen:

The Northwest Pulp and Paper Association is writing to support the James River Corp. and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Oregon's current water quality standard of 0.013 parts per quadrillion (ppq) is a human-health-based standard. However, the science upon which this standard was developed has been challenged — and its conclusions radically altered — by the very scientist who conducted the original research. Therefore, the premise for the current standard is now highly questionable.

In addition, the Environmental Protection Agency has recently approved water quality standards 100-times less stringent than its guideline criterion (which Oregon adopted, along with a variety of other EPA recommendations for toxic discharges). Thus, EPA has indirectly conceded that, when taking new science and regional factors into consideration, its criterion of 0.013 ppq may be more restrictive than necessary to protect human health.

In recognizing this apparent conflict, EPA has announced a review of the science on dioxin. I have enclosed a May 17 report from *Science* that notes the one-year time frame EPA Administrator William Reilly has established for this review. However, should Oregon decide to wait on the EPA review before commencing a review of its standard — and not suspend its imposition of dioxin discharge restrictions — the two mills in question are bound by state law to invest millions of dollars in what may prove to be unnecessary environmental controls.

Oregon needs a scientifically-based water quality standard for dioxin that is fully protective of human health. The Clean Water Act delegates this responsibility to the states, in part so that states may incorporate regional data, such as fish consumption information, into their decision. It is time for Oregon to develop such a state-specific water quality standard for dioxin. We hope that the Environmental Quality Commission will accept the James River and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Sincerely,

Kathy E. Gill

Kathy E. Gill, CAE
Public Affairs Director

enclosure
c: EQC members

NORTHWEST PULP & PAPER ASSOCIATION 1300 114TH AVENUE SOUTHEAST, SUITE 110 BELLEVUE, WASHINGTON 98004 (206) 455-1323

EPA Moves to Reassess the Risk of Dioxin

Urged on by the scientific community, EPA is developing a new model for estimating dioxin's risk

GALVANIZED BY THE RESULTS OF A RECENT scientific meeting on dioxin's molecular actions, Environmental Protection Agency (EPA) administrator William K. Reilly has launched a major new effort to reassess the toxicity of this ubiquitous—and infamous—chemical.

Responding to criticism that the model EPA now uses to assess dioxin's risk is obsolete, Reilly has asked agency scientists to come up with a new "biologically based" model that will draw on an emerging understanding of the first steps that take place as dioxin enters a cell (for example, see pages 924 and 954). Reilly and others call the new effort "precedent-setting" not only for how the agency regulates carcinogens but also for EPA's quick response to new scientific developments—not its strong suit in the past.

Until now, EPA has gauged the risk of dioxin exposure by using the same model it applies to most carcinogens: the linear multistage model, which assumes that risk rises in proportion to dose. Agency officials have long viewed the model as a "default"—one adopted for lack of a real understanding of how carcinogens work—and their intent was always to replace it with something more realistic once mechanisms were understood. But so far, they say, such evidence has been lacking. Now it may at last be in hand, at least for dioxin and perhaps a handful of other chemicals that behave similarly.

The turning point came in an 8 March briefing for Reilly and his top deputies given by three agency scientists: William Farland and Peter Preuss, both at EPA headquarters in Washington, D.C., and Linda Birnbaum of EPA's Health Effects Research Laboratory in North Carolina. Part of the briefing was devoted to recent epidemiologic studies, including the new one by Marilyn Fingerhut of the National Institute for Occupational Safety and Health (NIOSH), which found perhaps the strongest link yet between high doses of dioxin and human cancer (see *Science*, 8 February, page 625). The EPA scientists also discussed a reanalysis of data from a 1976 study of cancer in dioxin-exposed rats that figured heavily in EPA's original risk assessment. After re-examining the original slides of liver tissue, investigators have concluded that the animals developed fewer tumors than was originally believed.

But it was Birnbaum and Farland's description of a meeting last November at the Banbury Center at Cold Spring Harbor Laboratory that Reilly says made the most compelling case for change. At that meeting a group of dioxin experts agreed that before dioxin can cause any of the ill effects it has been linked to—cancer, immune system suppression, chloracne, and birth defects—one "necessary but not sufficient" event must occur: the compound must bind to and activate a receptor, known as the aryl hydrocarbon or AH receptor (see *Science*, 8 February, p. 625). After that, the dioxin-receptor complex is transported to the nucleus, where it binds to specific sequences of DNA and turns genes on and off, thereby causing its myriad effects. It had long been known that dioxin binds to a receptor, but before the Banbury meeting it had been unclear whether all of dioxin's effects or just some were mediated this way.

Key mover. *Linda Birnbaum had been urging EPA to change how it does dioxin risk assessment.*

The Banbury group also agreed that dioxin has to occupy a certain number of AH receptors on a cell before any biological response can ensue. The result is a practical "threshold" for dioxin exposure, below which no toxic effects occur. That conclusion flies in the face of the linear model's underlying assumption: that the risk of harmful effects begins with exposure to a single molecule and increases from there. Faced with this new picture of dioxin's action, the Banbury participants urged EPA to develop a new, receptor-based model for dioxin risk assessment.

Reilly bit. He has now asked scientists in EPA's Office of Research and Development, in collaboration with academic researchers around the country, to come up with just such a model. The goal, explains Michael Gallo of the Robert Wood Johnson Medical School, one of the organizers of the Banbury meeting who is now working with EPA, is to pinpoint the threshold or "safe" dose below which none of dioxin's ill effects should occur.

In building the model, Gallo and his EPA colleagues hope to draw on work on the dioxin receptor now under way in a number of labs around the country. In this issue of *Science*, for example, a group headed by Oliver Hankinson of the University of California at Los Angeles reports on the cloning of a protein that is necessary for the receptor to function. Various roles have been proposed for the new protein; one intriguing possibility is that it is part of the receptor itself. The dioxin receptor thus might contain at least two proteins, one that binds to dioxin (and presumably whatever natural molecule dioxin mimics) and another that binds to DNA. "Boy, is that exciting," says Gallo, who adds that the new findings will feed directly into the model.

Until the model is complete, no one can say for sure whether it will show dioxin to be more or less risky than EPA now calculates, though Gallo and others speculate that it will turn out to be less risky. One of the major questions is how close the presumed "safe" dose is to the background levels of dioxin to which the general population is exposed. If background exposure is already near the "safe" dose, then there may not be much room for additional exposure.

Those background levels are largely unknown, so Reilly has added that question to the EPA scientists' assignment. Over the next year Birnbaum and other EPA scientists, in collaboration with researchers from NIOSH, the Centers for Disease Control, and the Air Force, hope to get a fix on blood levels of dioxin and the handful of polychlorinated biphenyls that behave similarly and thus could increase its risk. Meanwhile, other researchers will be studying the sources and routes of dioxin exposure—most of which are dietary—and how it is passed up the food chain.

Reilly wants the new model and related work complete within a year, at which time the results will go on to EPA's Scientific Advisory Board (SAB) for peer review. Three years ago, the SAB sent EPA scientists back to the drawing board when they tried to revise the dioxin standard, saying the science wasn't sound enough. Birnbaum and other EPA researchers predict a different outcome this time. ■ LESLIE ROBERTS

313 S.W. 2nd Street, Suite D
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON SALMON COMMISSION

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 07 1991
OFFICE OF THE DIRECTOR

June 6, 1991

Office of the Director
Department of Environmental Quality
811 SW 6th Ave.
Portland, OR 97204

RE: Petition for reduction of Oregon's ambient water quality standard

Dear Mr. Fred Hansen:

At a very late date I was advised that this petition is once again before your department. I understand the EQC will consider and possibly act upon the petition submitted to you by James River Corporation and Boise Cascade at its June 14th meeting. For some reason this Commission has been excluded from any official notification by your department or by the petitioners. Instead I have been advised by a local citizen that this action has been about to take place.

This Commission remains opposed to lowering of our ambient water quality standards until and unless it can be shown that there will be zero negative effect upon the health of salmon runs in the affected waters. The basis of our concern is primarily for effects on the juvenile salmon who must use the fresh water habitat enroute to the ocean. We remain especially concerned in view of the recent petitions for endangered species status on several northwest salmon runs.

I include copies of testimony and correspondence already submitted to your department which I would like to have attached to the record for this particular petition.

In short, the Commission remains extremely concerned that even current loading of dioxins into the fresh water habitat may have deliterious effects on juvenile salmon survivability. Until it can be shown that those effects do not exist and until it can be shown that a reduction of our water quality standards will not further the problem, we remain opposed to any lessening of the standards.

Thank you for your considerations. I hope the oversight which led to the lack of communication with this Commission about these petitions will be corrected.

Sincerely yours,

Tom Robinson, Manager
Oregon Salmon Commission

TR/nf

313 S.W. 2nd Street, Suite D
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON
TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

May 10, 1990

Llewellyn Matthews
Northwest Pulp & Paper Association
1300 114th Ave. SE, Suite 110
Bellevue, WA 98004

Dear Mr. Matthews:

Thank you for your letter and overview statement pertaining to the dioxin issue. Although I was not personally in attendance, this Commission was represented at your Astoria briefing by Commissioner Robert Finzer. Mr. Finzer is a North Coast commercial fisherman and wholesaler. He gave a brief report on the situation at our last Commission meeting.

We are sensitive to your problems and we support your stated commitment to a solution which can allow a healthy pulp industry within a healthy environment. To us that continues to mean operations which do not pose risk to salmon food products nor to salmon survival, health or reproduction. It also means maintaining standards of water quality which are equal to those of our competitors in other nations which provide salmon to the world market.

So far, we are fairly comfortable with the food safety issue. Our public salmon are pure, clean food with all agencies finding salmon as the least likely of all fishes to be contaminated with toxins.

However, we remain steadfast in our position that standards equivalent to those in Europe and Canada be maintained here. Also, we continue to insist that our standards be met in fact. These are critical market demands.

We continue to be extremely concerned about salmon reproduction, smolt mortality, and immune systems, when exposed to effluent materials throughout the inland waterways they use. Even small percentages of mortality or fecundity loss represent large numbers of salmon losses at the harvest end. For example a 1% loss of down stream coho smolts represents a number of salmon roughly equal to the entire Oregon commercial troll harvest. We must learn the true impact on smolts and learn how to control it. I have not read the reports you cite as showing "no adverse affects on fish reproduction or fish tissue." Perhaps your staff can supply us with a copy.

Your offer to meet with us may be something we can explore later this fall, after our harvest season. We, like you, are an industry which supplies a valuable commodity to the market, relying on a healthy natural resource for the raw material. In the past, salmon resources industries have not viewed the wood products industry as a friend. I think you will agree that there is basis in fact for that view. Too much of our salmon resource has been lost to forest industries already. If that stops, perhaps we can ally as fellow industries, in common cause. If it does not, then our position is clear, and probably adversarial.

Sincerely yours,

Tom Robinson, Manager
Oregon Salmon Commission

cc: Dalton Hobbs, Department of Agriculture
Jill Zarnowitz, OR Dept. of Fish & Wildlife
Bob Eaton, Salmon for All
Oregon Salmon Commissioners

313 S.W. 2nd Street, Suite D
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON
TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

Date: May 1, 1990

To: DEQ
Water Quality Division
811 SW 6th Ave.
Portland, OR 97204

From: Tom Robinson, Manager
Oregon Salmon Commission

RE: Proposed Rule Changes Affecting Pulp Mill/Dioxin Effluents Standards.

Please be advised that the Oregon Salmon Commission on behalf of Oregon's commercial salmon trollers and on behalf of the consuming public which we serve under OAR 576.305 does not support any of the options for rule changes affecting standards applied to pulp mill effluents/dioxin contamination. The Oregon Salmon Commission has provided formal oral and written testimony to DEQ and to the Environment Quality Commission on this subject. Our position remains unchanged. We adamantly support stringent standards which will fully protect both food quality and the smolt survivability of salmon which use the Columbia River corridor. While we are satisfied that no danger to consumers of salmon food fish is imminent, we see this as no reason to relax any of the standards. We continue to be greatly concerned about mortality of juvenile salmon and about biological effects on adult salmon's immune systems and reproductive capacities when exposed to these effluents. Those biological and mortality concerns have not yet been addressed nor answered satisfactorily.

Attached are copies of written testimony already supplied to you by this Commission. Please apply them to this record.

On behalf of the Commission I also express a great dissatisfaction with the notification processes being used as this issue continues to run a gauntlet of meetings and reviews. I have not been formally contacted on a regular basis by your department about the schedule of hearings and comment deadlines. I remind you that we are a state agency which is very much affected by the decisions you will make. I find it extremely remarkable that my best source of up-to-date information continues to be the "grapevine" rather than official communications from your department. Furthermore, I know that the Pacific Fisheries Management Council and the states of Oregon and Washington fisheries divisions are greatly concerned about this issue. Are they not being directly contacted? Please take prompt action to correct this oversight in notification.

cc: William P. Hutchinson EQC
Randy Fisher ODFW
Joe Blum WDF
Richard Schwarz PFMC
Frank Warrens PFMC
Bob Eaton Salmon for All

313 S.W. 2nd Street, Suite C
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

Date: December 15, 1989

To: Fred Hansen, Director
Department of Environmental Quality
811 SW Sixth
Portland, OR 97204

From: Tom Robinson, Manager
Oregon Salmon Commission

Re: Proposed Rule Changes

We understand that Oregon's EQC is reviewing proposed rule changes on pulp mill pollution effluents January 1990. As you know we continue to provide comment on this matter as we find it to have significant impact on our industry through degradation of the environment. The details of our concern are outlined in previous communications and testimony submitted to you.

We also have some specific concerns and comments regarding proposed rule changes.

1. We ask for a return to full, open disclosure of all proceedings between the state and pulp mill industry representatives as this matter is resolved.
2. We support the status-quo of rules which require formal findings on pollution before EQC makes approvals. We recommend that food fish studies should be independently performed by other than industry contractors, to assure the objectivity of required findings.
3. We call your attention to the following items from the proposed rule changes:
   a) Proposed changes in paragraph 3, section (a) are alarming in that they appear to weaken existing permit processes, allowing too much subjective opinion, changing the phrase "would not", to read, "is not expected to", is clearly a move away from the level of control and protection which we must have through your commission, to assure safe, quality habitat for food fish in Oregon.
   b) Likewise, we support the status-quo for procedures which determine WQL status. There must not be a relaxing of processes which would remove the burden of positive proof of compliance with effluent standards, prior to removing a waterway, or a facility, from corrective activity. Speculative statements that compliance is expected may be encouraging news, but should not be substituted for actual achievement.

Thank you for your attention to our requests. We continue to rely on EQC, and DEQ to protect the habitat of Oregon's salmon resource as you execute your difficult tasks.

cc See attached sheet

GREENPEACE

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 10 1991
OFFICE OF THE DIRECTOR

7 June, 1991

Oregon Environmental Quality Commission
c/o Oregon DEQ Director's Office
811 S.W. 6th Avenue
Portland, OR 97204

Director
Oregon Department of Environmental Quality
811 S.W. 6th Avenue
Portland, OR 97204

Dear Commissioners and Director:

We understand that James River, Inc. and Boise Cascade Corp., along with several co-petitioners have asked the Commission and the DEQ to amend the state's ambient water quality standard for 2,3,7,8-TCDD from a current level 0.013 ppq to 2.3ppq.

We wish to offer comments regarding the wisdom of honoring such a petition that we hope you will make part of the public record in this decision.

INADEQUATE PUBLIC NOTICE

First we must question the lack of public notification involved in this pending decision. We have, on more than one occasion, asked to be placed on the DEQ notification list for any water quality actions the Department has pending, particularly with respect to pulp mills.

Our requests have to date been ignored, and we find that the only way to obtain a copy of a notice or a draft permit is to hear of its existence from a third party and then to call the DEQ to request a copy be sent us. Nor have we received word of final decisions regarding permits or any response to permit comments we have offered. To say that this archaic and haphazard method of public notice is deficient is an understatement. It is certainly not consistent with the mandate for public participation inherent in EPA's having delegated the water quality program to the state of Oregon.

That the petitioners themselves have the temerity to suggest they have identified all interested parties as the few listed in item 2 of the Commission Chair's notice, is absurd. A gutting of the state's water quality standard for the most potent chemical known to mankind is not something to be decided privately after consultation with just a few individuals.

Even the more narrow decision the Commission intends to make about whether or not to initiate a rulemaking that could potentially weaken the standard should have received broader notice, e.g. tribal governments, fishing interests, the state health department and those state and federal agencies charged with protecting wildlife (e.g. the U.S. Fish and Wildlife Service).

THRESHOLD MODEL CITED BY PETITIONERS AS FAVORING THE WEAKENING OF A STANDARD HAS NOT BEEN PEER REVIEWED

We remind the Commission that the much touted theory regarding a supposed threshold mechanism for 2,3,7,8-TCDD has not yet been peer reviewed. The forum in which it was first advanced, at a Banbury conference last fall, has itself become known for the controversy it created among attendees (see attachment 1). No version of the theory has yet been published in the scientific literature, and the theory has been challenged by other dioxin scientists (see attachments 2, 3).

EPA's own review of it's dioxin standard is still underway and far from finalization, and any attempt by the state of Oregon to presuppose EPA's conclusions would be ill-advised. EPA Administer William Reilly himself warned against second guessing the Agency's dioxin review, advising that in the interim state governments should go on with business as usual.

There is also new evidence coming from other quarters that tends to refute the threshold theory cited so enthusiastically by the petitioners. Abstracts for two papers to be presented at this fall's dioxin symposium are attached which argue against reliance on such a theory (see attachment 4).

Moreover, a paper by Sargent, et al published in a recent issue of <u>Carcinogenesis</u> (see attachment 5) suggests alarmingly that even non-planar PCB's can act by a mechanism identical to that of coplanar compounds such as 2,3,7,8-TCDD, and that exposure to mixtures resulted in superadditive effects. The authors further state that humans already are exposed to levels at which adverse effects would certainly be occurring. This in turn suggests why the epidemiology concerning exposure to 2,3,7,8-TCDD is at best equivocal, except in very exaggerated doses, as was indeed the case for a recently published NIOSH study (see attachment 6).

EVIDENCE CITED BY PETITIONERS REGARDING BIOCONCENTRATION IN FISH AND FISH CONSUMPTION RATES DIFFERS DRAMATICALLY FROM THAT OFFERED BY MORE CREDIBLE SOURCES

Petitioners suggest that the prevailing way of estimating bioconcentration (BCF) factors in fish used to calculate the current standard should be scrapped, and that a different (less conservative) method for estimating BCF's should be substituted. The method they suggest yields a number in the same ballpark as

the existing one. Yet there is much evidence from EPA's lab in Duluth to suggest that fish are far better at taking up and storing dioxin than the 5000 factor now in use supposes (see attachments 7, 8), and the Agency has requested funds in its 1992 budget to re-evaluate its BCF assumptions.

In fact it has been shown that even Columbia River salmon, species thought to be more protected from uptake because of their mobility and feeding patterns, are harboring levels of dioxin in their edible tissues (see attachment 9).

Patterns of human fish consumption in the Pacific Northwest also argue for a much stronger standard. EPA has long acknowledged that the average fish consumption rate of 6.5 grams per day per person assumed in the setting of its current standard seriously underestimates actual eating patterns, and this has been confirmed by surveys in several states. Moreover, work by EPA's Cleverly and McCormack indicates that Columbia River sports and subsistence fishers, Native Americans, and Asian Americans eat far more fish than the levels suggested by petitioners (see attachment 10). One wonders how petitioners could have arrived at the impossibly low figures they suggest.

Petitioners also make the illogical claim that only fish consumption from the Columbia River need be considered, irrespective of the rest of one's fish diet, as if to suppose that all other sources of fish (or food) are free from contamination.

THE STATE HAS A DUTY TO PROTECT US FROM OTHER HARM THAN JUST CANCER, AND FROM OTHER POLLUTANTS THAN JUST 2,3,7,8-TCDD

Petitioners make mention of Keenan, et al's re-evaluation of the Kociba rat study from which EPA's current acceptable daily intake is derived. They suggest that we should take heart from the fact that slightly more than half a team of 9 scientists funded by the industry should find that many of the liver lesions identified by Kociba as cancerous might only be pre-cancerous after all. A critique of this study is enclosed.

In any case, it is hardly reassuring to expect that one's liver be riddled with dioxin-induced lumps and bumps of any kind. We similarly find no comfort in the fact that women thoughout the industrialized world are passing dioxins and other organochlorines on to future generations through the placenta and via breast-feeding.

Studies on primates have shown that dioxins can cause profound behavioral and reproductive effects at very low doses. The petitioners ignore all non-cancerous effects in arguing for a weaker standard.

It must also be noted that 2,3,7,8-TCDD never occurs in

isolation. Discharges from the pulp and paper industry include other dioxins and furans and numerous other compounds which exhibit similar mechanisms of toxicity. The Sargent study mentioned above gives added weight to the likelihood that these compounds can act synergistically.

THE STATE HAS A DUTY TO PROTECT THE ENVIRONMENT AS WELL AS HUMAN HEALTH

Petitioners have offered no evidence to suggest that a weakened ambient water quality standard will be sufficiently protective of aquatic life or fish-eating birds and mammals.

Nor have petitioners demonstrated that a weakening of the current dioxin standard will not adversely effect bald eagle populations on the lower Columbia River, as required under the Endangered Species Act. Much evidence already exists to suggest that dioxins and other organochlorines are negatively impacting these birds. The pending listing of various wild salmon species will further increase the burden of proof necessary to justify any continued discharge of dioxin and other organochlorines.

A RELAXING OF THE DIOXIN STANDARD AS PROPOSED BY INDUSTRY WILL NOT RELIEVE THE INDUSTRY OF ANY FINANCIAL BURDEN FOR POLLUTION CONTROL

The same technologies that must be implemented by petitioners to meet the state's current dioxin standard will in any case be required in order to meet the technology-based standards already in their NPDES permits. Indeed, the longer the industry waits to install new bleaching technology, the greater will be their ultimate financial burden.

Capital costs for equipment will only be more expensive, and the money invested in stopgap measures such as chlorine-dioxide generators will only be money wasted. The U.S. industry can also be expected to lose market share in Europe as a result of its recalcitrance, as is already proving the case in Canada. Fletcher Challenge's failure to produce chlorine-free pulp for its foreign market has already cost them an estimated $ 5 million dollars in loss of sales.

THE ONLY ACCEPTABLE STANDARD FOR DIOXIN IS ZERO, AND THE STATE OF OREGON SHOULD TAKE IMMEDIATE STEPS TO ELIMINATE ALL KNOWN SOURCES

Dioxin is the most intensively studied compound in history, and will doubtless remain the darling of the scientific community for years to come. Even so we still do not know its precise toxicity to humans, and given the degree to which we are all already contaminated with dioxin and dioxin-like compounds, we probably never will. There is simply no such thing as a control group to serve as a baseline.

But what we do know is serious enough to make moot any further quibbling about precisely how much is too much dioxin. What we know is more than enough to justify elimination of all known sources.

We urge the Department and the Commission to deny the petition to set a weaker dioxin standard, and instead use your limited resources to moving the pulp and paper industry into chlorine-free technology. The technologies exist, and only await implementation.

Sincerely,

Shelley Stewart

Shelley Stewart
U.S. Pulp/Paper Project

***

Please note that these comments are printed on chlorine-free paper imported from Europe. No North American manufacturer has yet been willing to produce chlorine-free bleached office or printing paper.

Attachment I

UNIVERSITY OF MARYLAND AT BALTIMORE

The University Program In Toxicology
660 West Redwood Street
Howard Hall, Room 544
Baltimore, Maryland 21201-1596
(301) 328-8196

January 29, 1991

Dr. Jan Witkowski
Director
Banbury Center
Cold Spring Harbor Laboratory
P O Box 534
Cold Spring Harbor, NY 11724

Dear Dr. Witkowski:

I was a participant in the recent Banbury Conference on "Biological Basis for Risk Assessment of Dioxins and Related Compounds" held at the Banbury Center in October 1990. I am writing you becuase I have just been informed of a very disturbing result of that conference, a press release sent out by a public relations firm along with statements by Drs Scheuplein, van der Heiden, and Gallo purporting to represent the "consensus" views of the participants at that conference with espect to regulatory conclusions related to risk assessment of dioxins. I only learned of this press release from a reporter who called me last week (Marguerite Holloway of Scientific American).

This press release, copy enclosed, was never shown to me or to most of the participants in the conference, as far as I know. Thus, in terms of process alone, it should not be represented as a "consensus" document. Morover, its contents do not accurately reflect the views of all participants, or even a consensus of those views, as best I can determine. I resent the circulation of this press release as reflecting the views of a meeting in which I was a participant, and I feel that my name attached to it somehow implies my agreement with it.

I am in fact rather astounded by such a product from a Banbury Conference. While it was rather obvious to some of us that the organizers, and some of the sponsors, of this confernece had some trans-scientific objectives in mind related to regulations concerning dioxin, I had expected that the Banbury Center would be able to keep these motives under control. The press releases and statements imply that a major focus of the conference was a discussion of the regulatory risk assessments that have been applied to the dioxins; this was not the focus of this meeting. I agreed to participate based upon my previously held high regard for Banbury and Cold Spring Harbor. I did not expect to be manipulated by industry and government spokespeople

(who are not dioxin researchers, incidentally) to be made into a supporter of their political views on dioxins and risk assessment. This is particularly annoying to me because I was invited to present the main conference paper on the topic of the scientific basis for dioxin risk assessment. In this paper, I have attempted to present the complexity of integrating the basic molecular biology of dioxins into a receptor-based model. I do not feel that the state of knowledge on this complex topic can be reduced to a simplistic press release.

The preparation and release of these documents by Drs Scheuplein, van der Heijden, Carlo, and Gallo, with the assistance of a public relations firm, discredits all of us. It challenges the precious institution of free scientific discussion, epitomized by such places as Banbury, Dahlem, and the Gordon conferences. I hope you believe that I would be just as angry if this action had been taken by an environmental group. I trust you will take aciton to dissociate Banbury from this attempt to manipulate science and scientists. Because these people have acted without consulting the rest of us, and because I have heard about this only through the press, I am with great regret also sending this letter to the persons shown under my signature, as well as to my colleagues at the conference, an action not taken by these people.

Yours sincerely,

Ellen K Silbergeld

Ellen Silbergeld, PhD
Visiting Professor of Toxicology and
Adjunct Professor of Pharmacology
and Experimental Therapeutics

cc: Leslie Roberts, Science
Marguerite Holloway, Scientific American
Cristine Russell, Washington Post
Chris Joyce, New Scientist
Judy Randall, The Economist
Betty Mushak, NIEHS
William Farland, EPA

attendees, Banbury Conference on Dioxins

History Lessons

Warfare analysts offer some disturbing—and hopeful—news

Political leaders always claim to be steering us by the lights of history toward a peaceful future. But what does a comprehensive analysis of our past actually reveal about our present course? A pessimist could conclude that our leaders are completely misreading—or misrepresenting—history. An optimist could find hope that warfare might become obsolete anyway—if the tentative spread of democracy worldwide continues.

These conclusions are both supported by the Correlates of War project, a computerized storehouse of information on 118 wars (defined as conflicts leading to at least 1,000 deaths) and more than 1,000 lesser disputes from the early 1800s to the present. Researchers at the University of Michigan created the data base in the 1970s to find statistical associations between warfare and various economic, political and social factors.

The data offer no support for the bromide "peace through strength," according to J. David Singer, a political scientist at Ann Arbor who oversees the Correlates project. A buildup of military armaments, far from deterring war, is one of the most frequent precursors of it. At the very least, Singer says, such a finding suggests that the U.S. policy of supplying arms to nations in an unstable region—such as the Middle East—is seriously flawed.

There is also no evidence that alliances help to keep the peace. In fact, a nation's participation in one or more alliances increases its risk of warfare, Singer says, particularly against its allies. History even casts doubt on the argument—used by the U.S. to justify both its current war against Iraq and its past one against Vietnam—that allowing aggression to proceed unchecked always leads to more aggression. Although Hitler's Europe certainly provides an important counterexample, Correlates of War data yielded little statistical correlation between warfare in a given region and prior unchecked aggression, Singer says.

A somewhat more hopeful finding

A Press Release on Dioxin Sets the Record Wrong

When the Chlorine Institute shopped around for a place to hold a scientific conference, they did not want just any host. "We were looking for an organization that was squeaky clean, that would not in any way, shape or form be questioned about the conference," says Robert G. Smerko, president of the Washington, D.C.–based Institute, which is supported by some 170 chemical, paper and other manufacturers.

Smerko seemed to have met his requirements when he finally landed Cold Spring Harbor Laboratory. Last October the laboratory's respected Banbury Center held a conference—jointly sponsored by the Chlorine Institute and the Environmental Protection Agency—on the toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, or TCDD. That chlorinated compound achieved notoriety during the Vietnam War, when it was identified as a contaminant of the defoliant Agent Orange. It remains controversial because it is found in some commercial herbicides and is produced in other chemical processes, such as paper bleaching.

Cold Spring Harbor Laboratory may have been squeaky clean, but the conference apparently was not. And the outcome of that meeting—attended by 38 of the world's dioxin experts, few of whom say they knew it was industry sponsored—is every bit as controversial as the substance that was the topic of discussion.

The issue is a press release sent out at the conclusion of the meeting by the Chlorine Institute's public relations firm, Daniel J. Edelman, Inc. It announced that the experts had agreed on a model for the toxicity of dioxin that "allows for the presence of a substance in the environment, with no risk experienced below a certain level of exposure." The release said that the scientists had rejected a linear exposure model, in which any level of exposure would have a biological effect, in favor of a receptor-based model that implies a threshold level. (This part of the release was approved by Cold Spring Harbor Laboratory, says the Banbury Center's director, Jan A. Witkowski—although he now says Edelman made several changes after he saw it.)

Such a consensus, of course, would have implications for setting permissible levels of the substance in the environment. But those at the conference insist that no such agreement was reached. "There was no consensus in terms of risk assessment," says George W. Lucier of the National Institute of Environmental Health Sciences. In addition, none of the scientists saw the press release, although their names accompanied it. "We were being used, clearly, and that's unfortunate," declares Arnold J. Schecter, professor of preventive medicine at the State University of New York at Binghamton. "Political layering is not particularly good, especially when it is unbeknownst," Lucier adds.

Few of the participants seem to dispute that the receptor-based mechanism of dioxin is relevant to human exposure. Nor did they before the conference, observes Alan P. Poland of the University of Wisconsin at Madison, who discovered the receptor in 1976. "The basic tenets were all known since 1981 or 1982," Poland says. But Lucier notes that now "we are at the point where we can reevaluate the linear model."

Indeed, the EPA intends to explore the question of whether there is a threshold response. The agency will investigate the receptor-based model with Michael A. Gallo, one of the conference organizers and a professor of toxicology at the University of Medicine and Dentistry of New Jersey–Robert Wood Johnson Medical School. But Gallo and others agree that discussion of thresholds in a regulatory context may be premature. At the conference, "some regulators got real excited by back-of-the-envelope calculations" and thought dioxin standards could be eased, says Linda S. Birnbaum, director of the EPA's environmental toxicology division. "Clearly, we don't know that."

Although many of the Banbury attendees were the last to know about the consensus they reportedly reached, news about the conference traveled quickly in political circles. At a recent hearing on dioxin standards in Alabama, expert witness for the pulp and paper industry Russell E. Keenan invoked the Banbury results in his testimony. "There was general agreement among the attending scientists that dioxin is much less toxic to humans than originally believed," Keenan claimed. Obviously, "it is not useless to tout Banbury results if you have a political ax to grind," comments Cate Jenkins, a chemist in the EPA's hazardous waste division. —*Marguerite Holloway*

Attachment 2

To: Dioxin Nerds, et al.
From: Tom Webster, CBNS Queens College, Flushing NY 11367
Date: 3/14/91
RE: Banbury Dioxin Model, Part 1 A Critique

A recent two article series in Science[1] covered the infamous Banbury conference on dioxin toxicity. The second article addresses the scandal aspect of the story, particularly the involvement of the Chlorine Institute. The first article (attached) addresses some of the scientific aspects, but does so in what I consider a rather opaque fashion.

In particular, the article shows an S-shaped graph which appears to show why dioxin has a threshold. Science indicates, using the graph, that "responses to dioxin increase slowly at first but then shoot up after passing a critical concentration."

However, all is not as simple as it seems at first. Since there has been some confusion regarding this business, I will address the graph in this memo.

(1) Background: The Ah receptor

First, a bit of background. 2,3,7,8-TCDD and other dioxin-like compounds (PCDFs, co-planar PCBs, chlorinated naphthalenes, etc.) are generally thought to cause toxicity through a receptor mediated mechanism. This receptor also binds aromatic hydrocarbons such as 3-methylcholanthrene and other non-halogenated aromatic hydrocarbons; hence it is termed the Ah receptor.

The Ah receptor is a protein which is normally found in the fluid (cytosol) of the cell (There is some controversy here; some people think it is found solely in the nucleus). Only certain molecules ("ligands") with certain properties (size ,shape, etc.) fit it, like a key into a lock. 2,3,7,8-TCDD has the best fit of any known compound. When this occurs, the receptor-ligand complex changes shape and moves into the nucleus. The change in shape helps it to recognize and bind to certain sequences in the DNA. This in turn causes the transcription and translation of adjacent DNA into protein. (This is quite similar to the mechanism of steroid hormones.)

The most well understood effect is the production an enzyme called P450IA1 which makes aromatic hydrocarbons more water soluble--and therefore easier to excrete--by adding hydoxyl (-OH) groups. One measure of this enzyme activity is called aryl hydrocarbon hydroxylase (AHH).

Many of the types of toxicity associated with dioxin-like compounds correlate with binding to the Ah receptor or AHH activity (also with EROD, a related enzyme activity). This provides good evidence that dioxin toxicity is mediated by the Ah receptor, i.e., binding to Ah is the first (but not only) step. It also provides both a theoretical justification and a measurement technique for 2,3,7,8-TCDD equivalents. If all dioxin-like compounds act through the receptor, then the potency of a given compound can be rated against 2,3,7,8-TCDD by their relative ability to bind Ah and induce AHH or EROD activity.

Nevertheless, other experiments show that many toxic effects are probably not directly caused by enzyme induction. Hence, other genes are probably being turned on by the Ah receptor as

well. The nature of these other genes and the biochemical mechanism of many toxic responses is not so well understood. I'll discuss some of this in a future memo.

(2) Receptor Kinetics

If the toxicity of dioxin-like compounds is mediated by the Ah receptor, clearly we need to understand this first step. Receptor-ligand relationships are mathematically described by the Michaelis-Menten equation, a standard tool for describing enzymes. This is schematically described as:

$$L + R \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} LR \qquad (1)$$

where "R" is the unbound receptor, "L" is the ligand (molecule binding to the receptor) and "LR" is the receptor-ligand complex. k_1 and k_{-1} are, respectively, the association and dissociation rate constants. At equilibrium, we find

$$K_D = [L][R]/[LR] \qquad (2)$$

$$K_D = k_{-1}/k_1$$

where the items in the brackets "[ ]" are concentrations and K_D is the dissociation equilibrium constant. The constant K_D tells us, in an inverse way, about the strength of the binding between the ligand and the receptor. A small K_D means the binding is strong, and thus the receptor-ligand complex is less likely to dissociate. Conversely, a large K_D means that the receptor-ligand binding is weak.

Equation (2) can be solved in terms of the amount of occupied (bound) receptor:

$$[LR] = [L]*R0/(K_D + [L]) \qquad (3)$$

where R0 is the total amount of receptor, bound and unbound.

Equation (3) gives the relationship between the amount of 2,3,7,8-TCDD (or other ligand) and the amount of bound receptor (LR). Remember that the toxic activity of 2,3,7,8-TCDD (and other dioxin-like compounds) is thought to be associated with the concentration of dioxin-receptor complexes. We could infer a dose-response curve with two additional pieces of information: 1) the relationship between external dose (e.g., amount of exposure per day) and [L] and ii) the relationship between [LR] and toxicity.

Note that when the concentration of 2,3,7,8-TCDD is significantly less than K_D, the relationship is linear:

$$[LR] = [L]*R0/K_D \qquad \text{for } [L] \ll K_D \qquad (4)$$

Indeed, this equation indicates that even one molecule of 2,3,7,8-TCDD could bind to the receptor, indicating that there may be no theoretical threshold for activity. The slope of the curve is governed by the number of Ah receptors (R0) and the dissociation constant (K_D). Since 2,3,7,8-TCDD has a very small K_D compared to

other dioxin-like compounds, it binds tightly, and has a large slope.

For a high concentration of 2,3,7,8-TCDD, the curve saturates. One can't produce more receptor-dioxin complexes than there are receptors:

$$[LR] = R0 \qquad \text{for } [L] >> K_D \qquad (5)$$

(We'll ignore for now so-called "supermaximal" induction as well as circumstances which alter the number of receptors).

Finally, note that when the concentration of a compound equals its K_D, the number of bound receptors is equal to one-half the total number of receptors.

$$[LR] = R0/2 \qquad \text{for } [L] = K_D \qquad (6)$$

(3) Analysis of the Science graph

When equation (3) is plotted on normal graph paper it looks like my Figure 1, linear at low levels of 2,3,7,8-TCDD--the concentration of receptor-ligand complexes directly proportional to the concentration of ligand--and plateauing--at 100% bound receptor--at high levels of 2,3,7,8-TCDD.

When the same equation is replotted using the logarithm of the concentration of 2,3,7,8-TCDD, the graph looks like Figure 2, the same S-shaped curve seen in Science. Note that the horizontal axis in the Science graph gives concentration of 2,3,7,8-TCDD increasing by a factor of ten at each step; this is equivalent to using logarithms.

Finally, 50% of the receptors are shown as occupied in the Science graph when the concentration of 2,3,7,8-TCDD equals about 10^{-9} (Although not given, the units are undoubtably the standard moles per liter). This is the old K_D value for 2,3,7,8-TCDD. Actually, recent experiments indicate that the K_D is probably even smaller, on the order of 10^{-12} to 10^{-11} moles per liter. This means that 2,3,7,8-TCDD binds Ah more tightly than previously thought.

(4) Discussion

As a result, it should be clear that the graph in Science does not by itself indicate a threshold. The S-shape of the curve is an artifact of the graphing technique. Plotted on linear axes, the equation for ligand-receptor interaction indicates that the number of occupied receptors rises linearly from zero. In other words, this response should theoretically be linear at low doses with no threshold.

What then is really going on? Clearly, there must be more to the story. I'll be writing another memo on this, but let me give a few hints.

i) There may be other compounds inside the cell which bind to Ah, albeit with less affinity, complicating the picture.

ii) Binding to the receptor is just the first step. The other steps, binding to DNA, generation of protein, action of protein, etc., might not be linear. Hence, even though the first step might be linear, the final toxic response might not be.

ii) Binding to the receptor is reversible. However, the long half-life of dioxin-like compounds and the background exposure to them diminishes the strength of this argument.

iv) The Birnbaum[2] memo makes the following assumptions: 1) all toxicity is mediated by the Ah receptor binding; 2) induction of P450IA1 (AHH activity) is the most sensitive response of this system; 3) no effect occurs until one can measure an increase in enzyme activity. This defines a "practical" threshold that one can use to determine no-effect levels, etc.

In response to this last argument (briefly), enzyme induction may be the most sensitive response, but we don't really know. Also, lack of measurable activity doesn't necessarily mean no activity. Ability to measure a response is determined by many things including the sensitivity of the assay, the statistical power of the experiment, etc. In addition, 2,3,7,8-TCDD has a very long lifetime in the human body. Finally, the already existing body-burden of dioxin-like compounds in humans and other animals needs to be taken into consideration when examining such threshold models.

<u>References</u>

(1) Roberts, L. (1991a). Dioxin Risks Revisited. <u>Science</u> <u>251</u>: 624-626. February 8.
Roberts, L. (1991b). Flap Erupts Over Dioxin Meeting. <u>Science</u> <u>251</u>: 866-867. February 22.

(2) Birnbaum, L. (1990). Memo to E. Bretthauer (EPA-ORD) regarding Consensus at Banbury Dioxin Conference. October 31.

Figure1 : Linear Plot

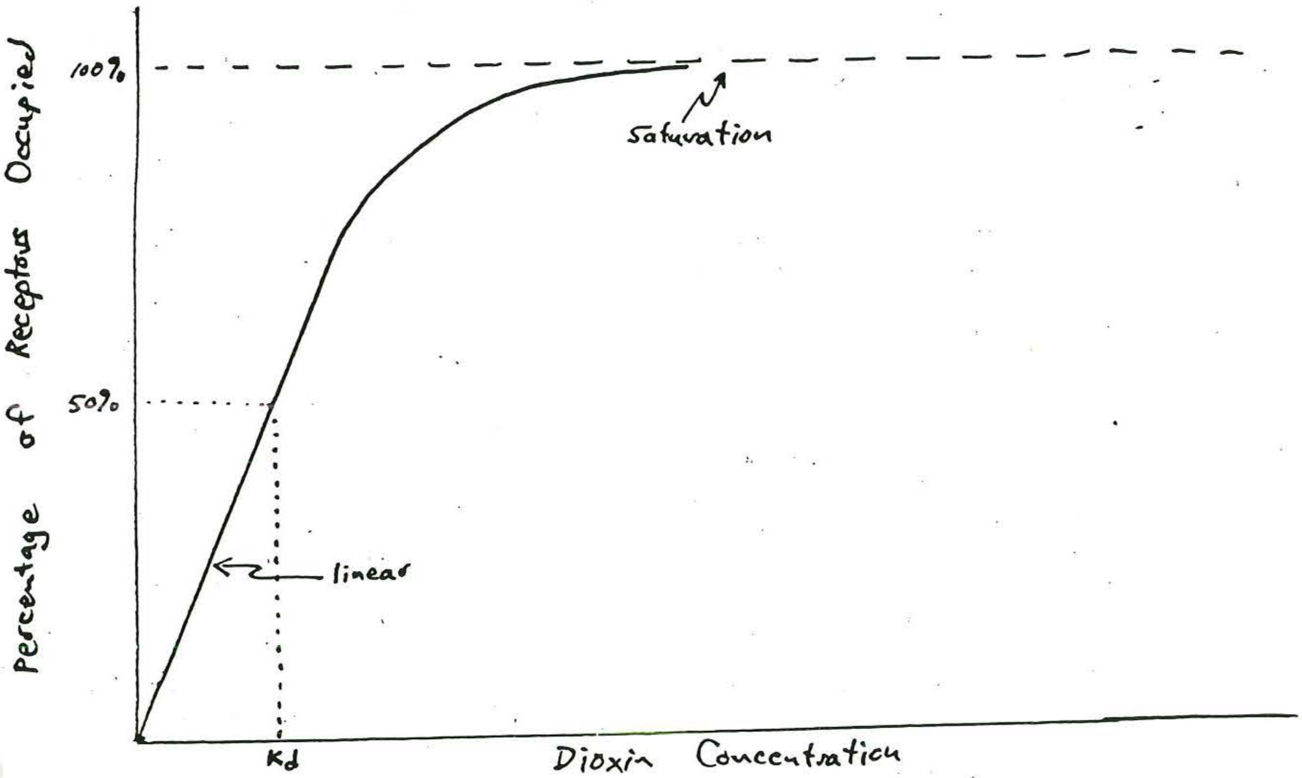
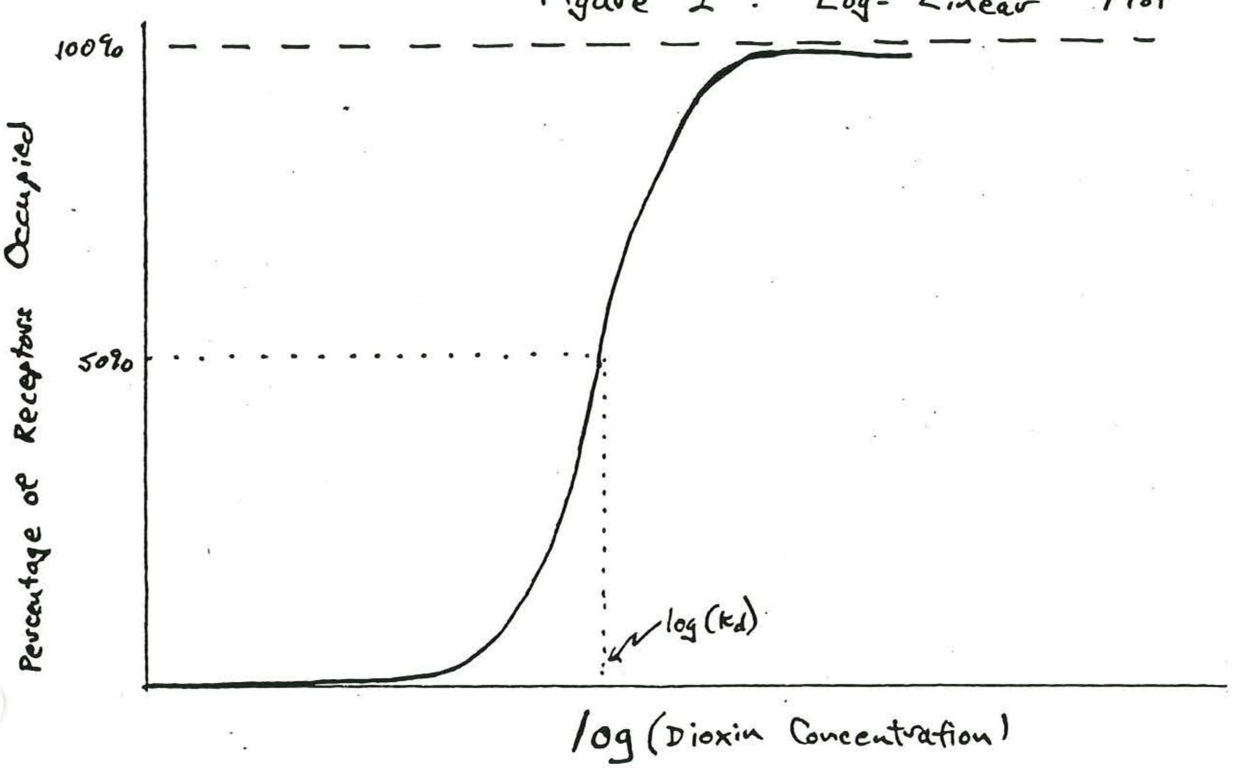


Figure 2 : Log-Linear Plot



Attachment 3

Downgrading Dioxin's Cancer Risk: Where's the Science?

By Tom Webster

Some of the concerns about the toxicity of the wood preservative pentachlorophenol have resulted because of its contamination with dioxins and furans. During manufacturing, pentachlorophenol is contaminated with several members of this family of compounds, with hexadioxins being most abundant.[1] 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD, commonly called dioxin), the most toxic dioxin, has been found in commercial pentachlorophenol formulations[1] and is often found in the soil and waste products from wood treatment plants.[2,3] This article discusses recent attempts to weaken regulatory standards for 2,3,7,8-TCDD.

-Ed.

The pulp and paper industry and certain consultants are once again attempting to relax the regulatory standards for dioxin. The consulting company ChemRisk has proposed an increase in the so-called "acceptable" dose of 2,3,7,8-TCDD by a factor as large as one thousand.[4,5] Many states are currently setting water quality standards for dioxin,[6] a regulation that depends on the "acceptable" dose.[7]

Despite assertions that the proposed change is based on new scientific evidence showing that dioxin "may be far less dangerous than previously imagined,"[8] the new information is actually a reinterpretation of the 1978 rat experiment that forms the basis for the U.S. Environmental Protection Agency's (EPA's) current estimate of dioxin's ability to cause cancer. In this reanalysis, a group of pathologists voted, according to a new set of guidelines, on the classification of tumors found in the test animals.[9]

However, if all other assumptions are left unchanged, recounting the tumors according to the revised rules [10] would result in an "acceptable" daily dioxin dose that is only two to three times larger than the current estimate. This is an insignificant change given the uncertainty in risk assessment. 2,3,7,8-TCDD is currently rated as millions of times more carcinogenic than many other compounds.

> *"Indeed, new scientific evidence on the amount of fish people consume, the degree to which dioxin is concentrated in fish, and the toxic equivalencies of other dioxins and furans supports stronger, not weaker, dioxin standards."*

The much larger change proposed by ChemRisk was derived by altering a number of other assumptions without proper justification. Indeed, new scientific evidence on the amount of fish people consume, the degree to which dioxin is concentrated in fish, and the toxic equivalencies of other dioxins and furans (JPR 10(2):23-27) supports stronger, not weaker, dioxin standards.[7]

Human Health Effects Controversy

This episode is neither the first nor last attempt to downgrade or dismiss the toxicity of dioxin. Perhaps the best known and continuing controversy surrounds Agent Orange. 2,3,7,8-TCDD was a contaminant in the herbicide 2,4,5-T, a component of Agent Orange, which was sprayed in parts of the United States as well as in Vietnam.

Despite the claim by some that the only long-term effect of dioxin on humans is chloracne, a serious skin disorder, the compound has been hypothesized to cause a number of other health effects in humans. Several recent epidemiological studies support this position. The Agent Orange Scientific Task Force[11] linked phenoxyacetic acid herbicides (such as Agent Orange) and their dioxin contaminants to a number of diseases including certain cancers. Dioxin's close chemical relatives PCBs and dibenzofurans may cause birth defects and learning/behavioral changes in the children of exposed women.[12,13] Certain key earlier studies that found no increase in cancer in chemical workers exposed to dioxin are faulty or possibly even fraudulent,[14,15] a charge now under investigation by EPA. Recent studies of German and American chemical workers exposed to dioxin found statistically significant increases in cancer rates.[16,17]

EPA rates cancer-causing compounds qualitatively (how good is the evidence for cancer causation in humans?) and quantitatively (how much cancer is caused by a given dose?). As a result of the recent epidemiology, it is likely that EPA will upgrade the qualitative standing of 2,3,7,8-TCDD to a Class B1 probable human carcinogen (limited human data and sufficient animal data),[18] an action with important regulatory ramifications.[19]

Constructing an "Acceptable" Daily Intake of Dioxin

EPA typically assumes that cancer-causing agents have no threshold, meaning that any amount of exposure can cause damage. Some people argue that there is no acceptable exposure for dioxin, an unintentional chemical by-product with no use or benefit, and that the goal should be zero exposure to this compound. EPA, however, has stated that some level of risk is "acceptable," a decision that is a matter of policy, not science. In setting ambi-

Tom Webster is a researcher with the Center for the Biology of Natural Systems (CBNS) of Queens College. He is currently working on a project for Greenpeace concerning chlorinated compounds.

CBNS; Queens College; City University of New York; Flushing, NY 11367; (718) 670-4180.

ent water quality standards, EPA often uses an acceptable lifetime risk of cancer of one case in a million (10^{-6}).

Based on this policy, the acceptable daily dose of a chemical is established by dividing the acceptable risk level by the "potency" of the compound. EPA calls such values risk specific doses (RsD). The potency is the quantitative estimate of the strength of the carcinogen. The more potent a chemical is, the smaller the dose that is required to pose a certain level of risk.

For dioxin, as with the overwhelming majority of toxic chemicals, there are insufficient human data to establish a potency. (The new study cancer among chemical workers[17] may, however, prove sufficient.) Consequently, dioxin's potency is based on laboratory experiments with animals. The current estimate for 2,3,7,8-TCDD[1] was based on a 1978 experiment on female rats, the most sensitive sex and species tested.[20]

EPA projected from the number of tumors found in animals at experimental doses to effects at the lower doses that people might encounter using a standard mathematical technique, the linear multistage model. This model assumes that the carcinogen has no threshold and that effects at low doses are linear, i.e., directly proportional to dose.

Finally, the potency in humans is estimated by multiplying the animal value by a "scaling factor." This adjusts for differences between the experimental animal and humans. For dioxin, EPA employed the default "surface area" scaling factor, since many differences between animals and humans (e.g., metabolism) depend on relative surface area.[1,21]

The 1988 Attempt to Downgrade Dioxin

In 1988, a proposal was made by EPA's Dioxin Workgroup to decrease the carcinogenic potency of 2,3,7,8-TCDD by a factor of sixteen. The Workgroup argued that dioxin might cause cancer through several mechanisms rather than being simply a complete carcinogen (the basis of the 1985 estimate). It might, therefore, be a less potent cancer-causing agent than previously thought. The Workgroup concluded that there was "no definitive scientific basis" for determining how much less potent dioxin might be.[22]

They noted that other agencies (the Center for Disease Control, the Food and Drug Administration) as well as other countries have less stringent "acceptable" levels of dioxin. They argued that "for strictly policy purposes, there is great benefit in federal agencies adopting consistent positions in the absence of compelling scientific information" and that an order of magnitude (factor of ten) estimate conveys the uncertainty involved. Based on this somewhat arbitrary logic, the Working Group recommended increasing the "acceptable" level (RsD) from 0.006 picograms (one picogram is one trillionth of a gram) per kilogram per day (pg/kg/day) to 0.1 pg/kg/day.

In their review of this proposal, EPA's Science Advisory Panel acknowledged some criticisms of the application of the linear multistage model to dioxin. However, they rejected the Workgroup's proposal, stating that "there is no reason to necessarily believe that a new mechanism model would lead to a relaxation of the risk specific dose for 2,3,7,8-TCDD induced cancer...The Panel therefore finds no scientific basis at this time for the proposed change."[23]

Acceptable Doses of Dioxin: ChemRisk versus EPA

At about the same time that the Science Advisory Panel was rejecting the 1988 case for increasing the "acceptable" risk of dioxin by a factor of sixteen, ChemRisk's new proposal supported an increase by as much as a factor of one thousand.[4,5] Three main factors are used by ChemRisk and EPA in their respective dioxin computations (see Table 1):

> *"ChemRisk selects an "acceptable" risk of 10^{-5}. Since the level of acceptable risk is a question of policy, not science, ChemRisk's choice of this factor is arbitrary."*

• **"Acceptable" Lifetime Cancer Risk:** For water quality standards, EPA recommends an "acceptable" lifetime cancer risk ranging from one in ten million (10^{-7}) to one in one hundred thousand (10^{-5}). However, one in one million (10^{-6}) is both the default and most commonly used value.[6,24] ChemRisk selects an "acceptable" risk of 10^{-5}. Since the level of acceptable risk is a question of policy, not science, ChemRisk's choice of this factor is arbitrary.

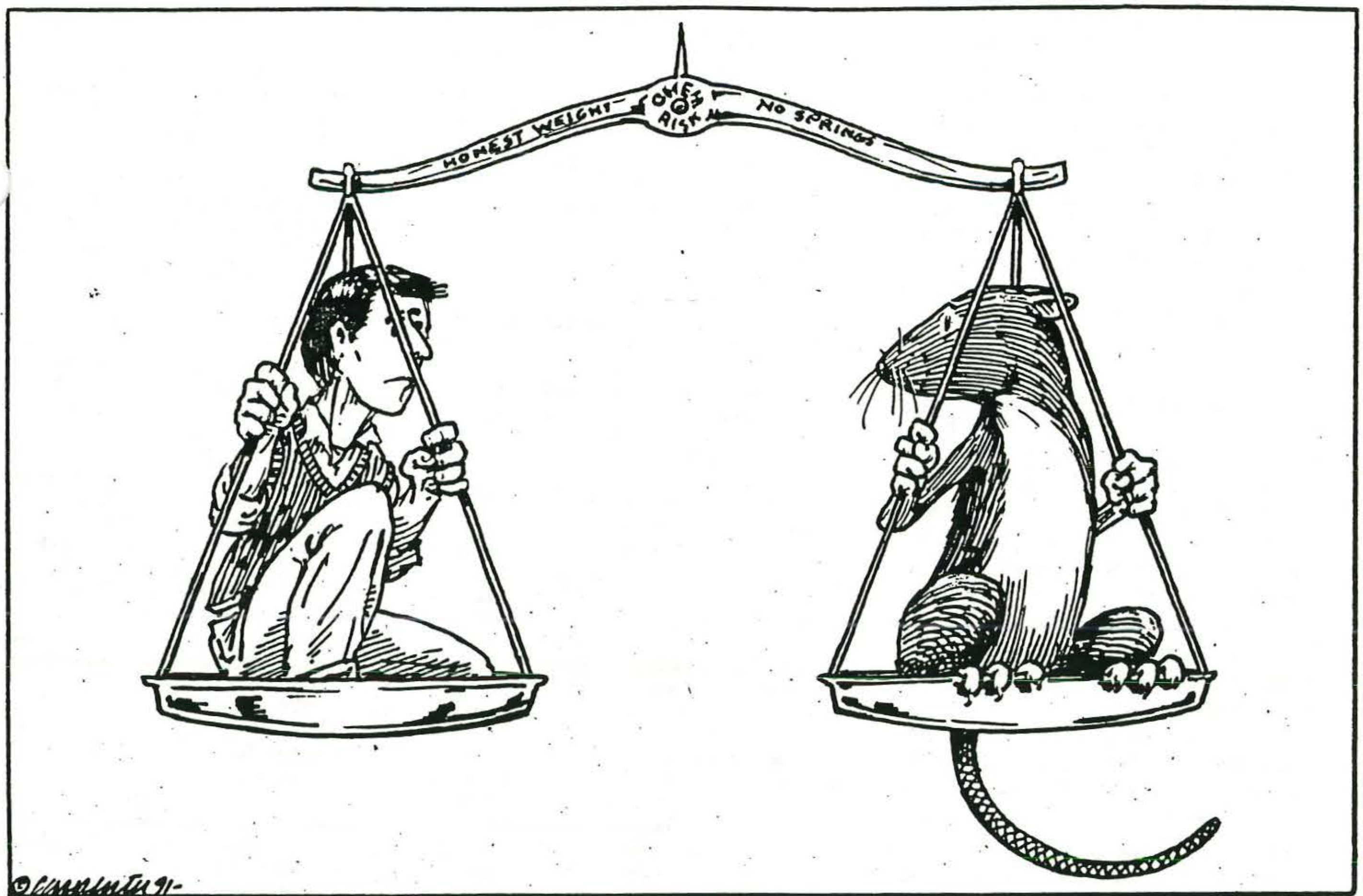
• **Interspecies Scaling Factor:** ChemRisk uses a body weight scaling factor to extrapolate from rats to humans. Since dose is commonly expressed as an amount per kilogram of body weight, ChemRisk's approach assumes that humans and rats are equally sensitive. EPA's surface area scaling factor assumes that humans will be more sensitive than rats per unit body weight by a

Table 1
Constructing an "Acceptable" Dose of Dioxin

	USEPA[1]	ChemRisk[4,5]	Factor[a]
1. Cancer potency in rats $(mg/kg/day)^{-1}$ (95% upper-bound estimate with linear multi-stage model)	29000	1500	19.3[b]
2. Scaling factor, rat to human (surface area)	5.38 (body weight)	1	5.38
3. "Acceptable" Lifetime Cancer Risk	10^{-6}[c]	10^{-5}	10
4. Risk-Specific Dose of 2,3,7,8-TCDD (pg/kg/day)	0.006[d]	6.74	1040

a. Factor by which ChemRisk is less stringent.
b. This factor would be 2-3 if the only change was the reclassification of tumors.
c. One in a million is a default and common value for water quality standards.[6,25]
d. An earlier draft by ChemRisk proposed an acceptable dose of 2.5 pg/kg/day.[4]

Note: RsD = (acceptable risk)/(rat potency * scaling factor)



Jim Carpenter

factor of about five.

ChemRisk argues that the use of the dose per body weight scaling factor is "more biologically relevant" because 2,3,7,8-TCDD is itself the active compound rather than any metabolite as is common with many carcinogens. EPA has disagreed with this line of reasoning in general,[25] but the case against body weight scaling is even stronger for 2,3,7,8-TCDD.

Since EPA's 1985 dioxin potency estimate, 2,3,7,8-TCDD half-life in humans has been determined to be 5-10 years, much longer than previously thought. In rats, the half-life of 2,3,7,8-TCDD is only about one month. Taking into account differences in tissue distribution, a scientist with EPA's Carcinogen Assessment Group estimated a scaling factor for the liver of as high as 37, much higher than ChemRisk's body weight scaling factor of one as well as EPA's surface area scaling factor of 5.38.[25] ChemRisk's reliance on the body weight scaling factor is not supportable.

• **Cancer Potency in Rats:** EPA's 1985 computation of dioxin potency was based on the occurrence in the 1978 rat study of carcinomas (cancerous tumors) and neoplastic nodules (lesions which may develop into cancerous tumors) in the liver, as well as tumors in other organs where the increase over control animals was statistically significant. In 1986, researchers proposed dividing neoplastic nodules into two groups: hepatocellular hyperplasia (a noncancerous proliferation of liver cells caused by toxicity) and hepatocellular adenomas (benign liver tumors).[10] This change has been questioned by some toxicologists.[26]

ChemRisk used the new classification system to argue in 1989 that the EPA's 1985 analysis was incorrect.[4]

At about the same time, Dr. Squire, a consulting pathologist involved in the original analysis of the female rat cancer data, was asked to re-examine the in conjunction with the setting of a water quality standard for Maine.[27] (Squire was involved earlier in a controversy over dioxin contaminants of pentachlorophenol: see article beginning on p. 4). After an initial review of the rat data, Dr. Squire helped convene a group of pathologists to re-examine the liver tissue slides from the experiment using the new classification system.

During this re-evaluation, in which "consensus" was defined as agreement by four out of seven pathologists (not all votes were unanimous), the group identified fewer carcinomas as well as fewer total tumors (carcinomas plus adenomas) than EPA's earlier analyses. The group concluded that because "the tumors were predominantly benign and usually associated with lesions of hepatic [liver] toxicity" the rat study demonstrated "a weak oncogenic [cancer-causing] effect of TCDD."[9] The implication of this controversial conclusion is that liver toxicity somehow caused or magnified the carcinogenic response.

ChemRisk used these results to calculate a new potency factor for 2,3,7,8-TCDD in rats, but counted only carcinomas in the liver (the primary target organ in this animal). They ignored carcinomas in other tissues as well as all adenomas, benign tumors that may progress into carcinomas. Both omissions are contrary to EPA guidelines for carcinogen risk assessment.[21]

ChemRisk also failed to adjust for early mortality of some test animals, a another correction used by EPA.[1]

If the revised tumor pathology criteria are applied, eliminating liver hyperplasias, but all other standard EPA assumptions are employed, the calculated rat potency is reduced by only a factor of two to three from the current value. Again, ChemRisk's calculation of a new dioxin carcinogenic potency factor is indefensible.

Conclusion

A proposed acceptable daily dose for 2,3,7,8-TCDD is claimed to be based on new science regarding the classification of tumors. However, if this change alone is made, the "acceptable" dose of dioxin would only be altered by a factor of two to three. ChemRisk's proposed reduction by a factor of as much as a thousand is fundamentally based on scientifically indefensible changes in a number of other unrelated assumptions.

This series of events shows many of the problems with quantitative risk assessment. There is uncertainty about even the most basic questions such as the classification of tumors in laboratory animals. A large number of assumptions are required, each of which must be independently justified. Because of the uncertainty and the number of assumptions, it may be possible, in the absence of checks and balances, to construct nearly any result. ■

References and Notes

1. U.S. Environmental Protection Agency. 1985. *Health assessment document for polychlorinated dibenzo-p-dioxins.* EPA/600/8-84/014F. Washington, D.C.: Office of Health and Environmental Assessment.
2. U.S. Environmental Protection Agency. 1987. National dioxin study. EPA/530-SW-87-025. Washington, D.C.: Office of Solid Waste and Emergency Response.
3. State Water Resources Control Board. 1988. Chlorinated dibenzo-p-dioxin and dibenzofuran contamination in California from chlorophenol wood preservative use. Report 88-5WQ. Sacramento, CA: Division of Water Quality.
4. Keenan, R., R. Wenning, A. Parsons. 1989. Sensitivity analysis for dioxin risk assessment and implications for determining acceptable daily exposure: Executive summary. Portland, ME.: ChemRisk, October 20.
5. Keenan, R. Letter to Dr. R. Loehr, Chair, Executive Committee, Science Advisory Board, U.S. Environmental Protection Agency. March 20, 1990.
6. U.S. Environmental Protection Agency. 1990. *Tracking report: State water quality criteria for dioxin (2,3,7,8-TCDD).* Washington, D.C.: Office of Water Regulations and Standards. May.
7. Where people can consume both fish and water, the water quality standard is computed as:
   C = (RsD*BW)/((FC*BCF)+WC)
   RsD = risk specific dose ("acceptable" dose at a given risk level)
   BW = human body weight
   FC = fish consumption
   BCF = bioconcentration factor, the ratio between the concentration of the compound found in the fish and the concentration in water.
   WC = water consumption rate by humans (negligible when BCF is large).

   The current EPA water quality standard for 2,3,7,8-TCDD assumes a fish consumption rate of 6.5 grams per day (0.23 oz.) and a bioconcentration factor of 5000.[6,24] Both of these factors are low. New data indicate that sport fishermen can consume 30 grams per day of fish while subsistence fishermen may consume 140 grams per day.[24,28] These values are about five and twenty two times higher than the current EPA value. Recent studies of the bioconcentration of 2,3,7,8-TCDD have found values from 39,000 to 140,000.[29,30] Thus, even if the RsD for 2,3,7,8-TCDD was raised by a factor of two to three to account for changes in tumor classification, a water quality standard tens to hundreds of time lower could be constructed.

   Furthermore, water quality standards are set compound by compound, ignoring the fact that compounds closely related to 2,3,7,8-TCDD—such as 2,3,7,8-tetrachlorodibenzofuran, also emitted by pulp and paper mills that bleach with chlorine—are added together in other regulatory contexts, after adjusting for relative potency using the 2,3,7,8-TCDD equivalence methodology.
8. Gladwell, M. 1990. Scientists temper views on cancer-causing potential of dioxin. *Washington Post*, May 31, p. A3.
9. Sauer, R. and PATHCO, Inc. 1990. Pathology Working Group 2,3,7,8-tetrachlorodibenzo-p-dioxin in Sprague-Dawley Rats. 10075 Tyler Place #16, Ijamsville, MD 21754. March 13.
10. Maronpot, R., C. Montgomery, G. Boorman, and E. McConnell 1986. National Toxicology Program nomenclature for hepatoproliferative lesions of rats. *Toxicologic Pathology* 14(2): 263-273.
11. Agent Orange Scientific Task Force. 1990. *Human health effects associated with exposure to herbicides and/or their associated contaminants - chlorinated dioxins.* Washington, D.C.: National Veterans Legal Services Project.
12. Rogan, W., B. Gladen, C. Hsu, Y. Chen, and H. Ko. 1990. Yucheng: Studies in children. Presented at Dioxin '90, The Tenth International Meeting. Bayreuth, Germany.
13. Jacobson, J., S. Jacobson, and H. Humphrey. 1990. Effects of in utero exposure to polychlorinated biphenyls and related contaminants on cognitive functioning in young children. *J. Pediatrics* 116: 38-45.
14. Rohleder, F. 1989. Dioxins and cancer mortality: Reanalysis of the BASF cohort. Ninth International Symposium on Chlorinated Dioxins and Related Compounds, Toronto, Ontario, Sept. 17-22.
15. Van Strum, C. and P. Merrell. 1990. Dioxin human health damage studies: Damaged data? *Journal of Pesticide Reform* 10(1): 8-12.
16. Zober, A., P. Messerer, and P. Huber. Thirty-four-year mortality follow-up of B employees exposed to 2,3,7,8-TCDD after the 1953 accident. *International Archives of Occupational and Environmental Health.* 62: 139-157.
17. Fingerhut, M., et al. (1991). Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324(4): 212-218.
18. "EPA likely to upgrade dioxin cancer classification to reflect new data." *Inside EPA.* February 1, 1991. p.4.
19. Jenkins, C. 1991. U.S. Environmental Protection Agency Memorandum. January 24.
20. Kociba, R., D. Keyes, J. Beyer, R. Carreon, C. Wade, D. Dittenber, R. Kalnins, L. Frauson, C. Park, S. Barnard, R. Hummel, and and C. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicology and Applied Pharmacology* 46: 279-303.
21. U.S. Environmental Protection Agency. 1986. Guidelines for carcinogen risk assessment. *Federal Register* 51(185): 33991. September 24.
22. U.S. Environmental Protection Agency. 1988. *A cancer risk-specific dose estimate for 2,3,7,8-TCDD: Draft.* EPA/600/6-88/007Aa. June. pp. 49-50.
23. Goldstein, B., N. Kim. 1989. Letter from the Chair and Co-Chair of the Ad Hoc Dioxin Panel to Dr. R. Loehr, Chair, Science Advisory Board Executive Committee, U.S Environmental Protection Agency. Noven. 28.
24. U.S. Environmental Protection Agency. 1990. EPA's position on Georgia's adoption of a dioxin water quality standard. Region IV. March.
25. Bayard, S. 1988. Quantitative implications of the use of different extrapolation procedures for low-dose cancer risk estimates from exposure to 2,3,7,8-TCDD. Appendix A of reference 22.
26. Alsen-Hinrichs, C, Department of Toxicology, University of Kiel School of Medicine, Kiel, Germany. Letter to the *Washington Post* (unpublished). June 21, 1990.
27. Squire, R. 1990. Letter to Dr. Robert Michaels acknowledging the request of November 28, 1989. January 8.
28. U.S. Environmental Protection Agency (1989). *Exposure factors handbook.* Versar, Inc. EPA 600/8-89-043. Washington, D.C.: EPA.
29. Mehrle, P., et al. 1988. Toxicity and bioconcentration of 2,3,7,8-tetrachlorodibenzo-p-dioxin and 2,3,7,8-tetrachlorodibenzofuran in rainbow trout. *Environ. Toxicol. Chem.* 7: 47-62.
30. Cook, P., A. Batterman, and B. Butterworth. 1990. *Laboratory study of TCDD bioaccumulation by lake trout from Lake Ontario sediments, food chain and water.* Duluth, MN: U.S. Environmental Protection Agency Environmental Research Laboratory.

Eleventh International Symposium on Chlorinated Dioxins and Related Compounds

MAR 20 1991

cc Steve
CR
[illegible]
Jim N

DIOXIN '91

September 23-27, 1991

Conference Information

School of Public Health
Office of Continuing Education
The University of North Carolina at Chapel Hill
CB# 8165, Miller Hall
Chapel Hill, NC 27599-8165
Phone: 919/966-1104
Fax: 919/966-7141

Organizing Committee

Memo

To: Conference Participants Who Plan to Submit Papers

From: Sharon Johnson Wills
Program Assistant

Date: February 10, 1991

Re: Abstract Format Instructions

The Organizing Committee of Dioxin '91 invites you to submit your abstract for the 11th International Symposium on Chlorinated Dioxins and Related Compounds. The conference will be held in Research Triangle Park, North Carolina, Sept. 23-27, 1991. Enclosed please find one instruction sheet and two forms for submitting your abstract. Also enclosed is an acknowledgment card that you should send back with your completed package. Fill in the lines marked "title" and "author" and return it with your abstract package to the Office of Continuing Education. I will return the card to you to acknowledge receipt of your abstract.

Please read the instructions carefully and take note of all mailing advisories so that we may include your abstract in this year's program. Remember that all abstracts must be received no later than April 1, 1991. Abstracts received after this date will not be considered for acceptance, published or printed.

If you have any questions or concerns, please call or write.

P.S. A complete brochure describing this program will be mailed to you in April. To register for Dioxin '91 before that time, please call me at 919/966-1104.

DOSE RESPONSE RELATIONSHIPS FOR CHRONIC EXPOSURE TO 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD) IN A RAT TUMOR PROMOTION MODEL: 2. QUANTIFICATION AND IMMUNOLOCALIZATION OF CYTOCHROMES P450c(1A1) AND P450d(1A2) IN THE LIVER. A Tritscher, G Clark, Z McCoy, C Portier, W Greenlee, J Goldstein, and G Lucier. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

TCDD and its structural analogs produce a broad spectrum of biochemical and toxic effects in animals and humans. The mechanisms responsible for these effects involve interactions with the Ah receptor but many of the steps necessary for biological response remain unknown. One of the troublesome knowledge gaps that causes uncertainty in risk assessments for TCDD is the lack of adequate dose-response relationships following chronic exposure to TCDD. One of the most sensitive responses to TCDD and its structural analogs is the induction of specific isozymes of cytochrome P450 (CYP1A1 and CYP1A2). CYP1A1 is induced in many tissues whereas CYP1A2 is induced only in liver. We have employed a two-stage model for hepatocarcinogenesis in female Sprague-Dawley rats to evaluate dose-response relationships for CYP1A1 and CYP1A2. A single dose of diethylnitrosamine was used as the initiating agent followed by biweekly gavage of TCDD at doses equivalent to 3.5, 10, 35 and 125 ng/kg/day for 30 weeks. CYP1A1 and CYP1A2 were quantified in liver microsomes from control and treated rats by immunoassay. Data revealed a maximum induction of CYP1A2 of 10-fold and induction was nearly 3-fold at the 3.5 ng/kg/day dose. The no detectable effect for 1A2 induction was estimated to be 0.1 to 0.3 TCDD ng/kg/day. A chronic dosing experiment is in progress to determine if this is an accurate estimate of the no detectable effect. Interestingly, TCDD-mediated induction of 1A2 appeared to occur at lower doses in DEN-initiated rats compared to non-initiated rats. Also, CYP1A2 induction appeared to be a slightly more sensitive marker of TCDD exposure than CYP1A1 in our rat liver tumor promotion model. We also analyzed liver TCDD concentrations by GC-MS. These data revealed a linear relationship between administered dose and TCDD liver concentrations throughout the entire dose range of our study. Therefore, induction of 1A2 does not enhance TCDD retention in liver, a hypothesis that had been proposed because 1A2 is a binding protein for TCDD. We also used immunocytochemical techniques to analyze the pattern of CYP1A1 and CYP1A2 distribution in livers of control and TCDD-treated rats. 1A2 was localized primarily in the centrolobular region with small amounts in the midzonal and periportal regions. Induction by TCDD increases the number of cells containing detectable amounts of 1A2 but not the intensity of staining of cells constitutively expressing this cytochrome. Localization patterns, in induced rats, were similar for 1A1 and 1A2. Taken together, these studies are characterizing dose response relationships for CYP1A1 and CYP1A2 that represent characteristic Ah receptor dependent responses to TCDD exposure. (Funding for TCDD analyses provided by the American Paper Institute.

DOSE RESPONSE RELATIONSHIPS FOR CHRONIC EXPOSURE TO 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD) IN A RAT LIVER TUMOR PROMOTION MODEL: 1. RELATIONSHIPS OF TCDD TISSUE CONCENTRATIONS TO SERUM CLINICAL CHEMISTRY, CELL PROLIFERATION, AND PRENEOPLASTIC FOCI. G Clark, A Tritscher, Z McCoy, C Portier, M Thompson, R Wilson, J Foley, R Maronpot, [1]T Goldsworthy, W Greenlee, and G Lucier. National Institute of Environmental Health Sciences, Research Triangle Park, NC and [1]Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

One of the important issues in a risk assessment for exposure to dioxins is the pharmacokinetic distribution of TCDD in a long term chronic exposure regimen and the biological responses associated with a potential carcinogenic outcome. A specific cytoplasmic binding protein, the Ah receptor, is generally thought to mediate most of the biological responses to TCDD including its action as a tumor promoter. We have used a rat liver tumor promotion model to investigate biochemical responses that may be associated with promotion of carcinogenesis. In previous studies we have found that alterations of hepatic cell proliferation and the appearance of enzyme altered foci (γ-glutamyl transpeptidase and glutathione S-transferase-positive foci) correlate with liver tumor formation but that the ovaries are necessary for the expression of these effects. In the current study we are investigating dose response relationships in female Sprague-Dawley rats with an initiating dose of 175 mg/kg DEN and biweekly exposure to TCDD for 30 weeks to give doses equivalent to 3.5, 10.7, 35.7, and 125 ng/kg/day TCDD. A linear distribution of TCDD in livers of exposed animals was found. The mean liver concentration of TCDD was 19.9 ppb at 125 ng/kg/day and the mean liver concentration was 0.5 ppb at 3.5 ng/kg/day. In serum samples from the rats exposed to 125 ng/kg/day the TCDD concentration was 23.9 ppt while the concentration at the lowest dose was 8 ppt. Several serum clinical chemistry parameters were measured including alkaline phosphatase, glucose, alanine transaminase, total cholesterol, triglycerides, sorbitol dehydrogenase, 5' nucleotidase, and total bile acids. A significant dose effect for TCDD exposure was determined for serum alkaline phosphatase, 5' nucleotidase activities and on the levels of serum cholesterol. We are in the process of analyzing cell proliferation in livers from these animals by incorporation of bromodeoxyuridine into newly-formed cells and immunohistochemical analysis. We are also quantifying γ-glutamyl transpeptidase and placental glutathione S-transferase-positive foci as indicators of preneoplastic lesions. These parameters will be correlated with the applied dose, the tissue specific dose, and the levels of occupied Ah receptors. We hope to determine a) what is the most sensitive biochemical response to TCDD exposure and b) which parameter correlates with carcinogenicity. These data will be useful in the development of mechanistic models for dioxin risk assessment. (Funding for TCDD analyses provided by the American Paper Institute).

19. Xu,Y.-H., Campbell,H.A., Sattler,G.L., Hendrich,S., Maronpot,R., Sato,K. and Pitot,H.C. (1990) Quantitative stereological analysis of the effects of age and sex on multistage hepatocarcinogenesis in the rat by use of four cytochemical markers. *Cancer Res.*, **50**, 472–479.
20. Campbell,H.A., Xu,Y.-H., Hanigan,M.H. and Pitot,H.C. (1986) Application of quantitative stereology to the evaluation of phenotypically heterogeneous enzyme-altered foci in the rat liver. *J. Natl. Cancer Inst.*, **76**, 751–767.
21. Steel,R.G.D. and Torrie,J.H. (1980) Enumeration data II: contingency tables, some uses of χ-square. In *Principles and Procedures of Statistics, a Biometrical Approach.* McGraw-Hill Book Company, New York, pp. 469–520.
22. Pitot,H.C., Goldsworthy,T.L., Moran,S., Kennan,W., Glauert,H.P., Maronpot,R.R. and Campbell,H.A. (1987) A method to quantitate the relative initiating and promoting potencies of hepatocarcinogenic agents in their dose–response relationships to altered hepatic foci. *Carcinogenesis*, **8**, 1491–1499.
23. Safe,S. (1983) Polychlorinated biphenyls (PCBs) and polybrominated biphenyls: biochemistry, toxicology and mechanisms. *CRC Rev. Toxicol.*, **13**, 319–325.
24. Silberhorn,E.M., Glauert,H.P. and Robertson,L.W. (1990) Carcinogenicity of polyhalogenated biphenyls: PCBs and PBBs. *Crit. Rev. Toxicol.*, **20**, 439–496.
25. Eriksson,L., Ahluwalia,M., Spiewak,J., Lee,G., Sarma,D.S.R., Roomi,M.J. and Farber,E. (1983) Distinctive biochemical pattern associated with resistance to hepatocytes in hepatocyte nodules during liver carcinogenesis. *Environ. Health Perspect.*, **49**, 171–174.
26. Dragan,Y.P., Xu,Y.-H., Hully,J.R., Bawa,N., Rizvi,T., Campbell,H.A., Maronpot,R.R. and Pitot,H.C. (19??) An initiation-promotion assay in rat liver as a potential complement to the two-year carcinogenesis bioassay. *Fund. Appl. Toxicol.*, in press.
27. Schulte-Hermann,R., Roome,N., Timmermann-Trosiener,I. and Schuppler,J. (1984) Immunocytochemical demonstration of a phenobarbital-induced cytochrome P450 in putative preneoplastic foci of rat liver. *Carcinogenesis*, **5**, 149–153.
28. Schwarz,M., Peres,G., Buchmann,A., Friedberg,T., Waxman,D.J. and Kunz,W. (1987) Phenobarbital induction of cytochrome P450 in normal and preneoplastic rat liver: comparison of enzyme and mRNA expression as detected by immunohistochemistry and *in situ* hybridization. *Carcinogenesis*, **8**, 1355–1357.
29. Forgue,S.T., Preston,B.D., Hargraves,W.A., Reich,I.L. and Allen,J.R. (1979) Direct evidence that an aerene oxide is a metabolic intermediate of 2,5,2′,5′-tetrachlorobiphenyl. *Biochem. Biophys. Res. Commun.*, **91**, 475–483.
30. Forgue,S.T. and Allen,J.R. (1982) Identification of an aerene oxide metabolite of 2,5,2′,5′-tetrachlorobiphenyl by gas chromatography–mass spectroscopy. *Chem.-Biol. Interactions*, **40**, 233–245.
31. Stadnicki,S.S., Francis,S.D.L. and Allen,J.R. (1979) DNA strand breaks caused by 2,5,2′,5′-tetrachlorobiphenyl and its metabolites. *Res. Commun. Chem. Pathol. Pharmacol.*, **24**, 313–325.
32. Preston,B.D., Miller,J.A. and Miller,E.C. (1984) Reactions of 2,2′,5,5′-tetrachlorobiphenyl 3,4-oxide with methionine, cysteine and glutathione in relation to the formation of methylthio-metabolites of 2,2′,5,5′-tetrachlorobiphenyl in the rat and mouse. *Chem.-Biol. Interactions*, **50**, 289–312.
33. Sargent,L.M., Roloff,B.D. and Meisner,L.F. (1989) *In vitro* chromosome damage due to PCB interactions. *Mutat. Res.*, **224**, 79–88.
34. Wyndhman,C., Devenish,J. and Safe.S. (1978) The *in vitro* metabolism, macromolecular binding and bacterial mutagenicity of 4-chlorobiphenyl, a model PCB substrate. *Res. Commun. Chem. Pathol. Pharmacol.*, **15**, 563–570.
35. Kawabata,T.T. and White,K.L., Jr (1989) Benzo[*a*]pyrene metabolism by murine spleen microsomes. *Cancer Res.*, **49**, 5816–5822.
36. Buchmann,A., Kunz,W., Wolf,C.R., Oesch,F. and Robertson,L.W. (1986) Polychlorinated biphenyls, classified as either phenobarbital- or 3-methylcholanthrene-type inducers of cytochrome P450, are both hepatic tumor promoters in diethylnitrosamine-initiated rats. *Cancer Lett.*, **32**, 243–253.
37. Roomi,M.W., Ho,R.K., Sarma,D.S.R. and Farber,E. (1985) A common biochemical pattern in preneoplastic hepatocyte nodules generated in four different models in the rat. *Cancer Res.*, **45**, 564–571.
38. Ghoshal,A., Gurtoo,H.L., Faletto,M.B., Koo,P., Nagi,M. and Farber,E. (1990) Molecular basis for the constitutive decrease in cytochromes P450 in putative preneoplastic hepatocytes. *Proc. Am. Assoc. Cancer Res.*, **31**, 136.
39. Goldstein,J.A., Hickman,P., Bergman,H., McKinney,J.D. and Walker, M.P.(1977) Separation of pure polychlorinated biphenyl isomers into two types of inducers on the basis of induction of P450 or P448. *Chem.-Biol. Interactions*, **17**, 69–87.
40. Cordle,F., Corneliussen,P., Jelinek,C., Hackley,B., Lehman,R., McLaughlin,J., Rhoden,R. and Shapiro,R. (1978) Human exposure to polychlorinated biphenyls and polybrominated biphenyls. *Environ. Health Perspect.*, **24**, 157–172.
41. Sherer,E., Feringa,A.W. and Emmelot,P.(1984) Initiation–promotion–initiation induction of neoplastic foci within islands of precancerous liver cells in the rat. In Börzxönyi,M., Lapi,K., Day,N. and Yamasaki,H. (eds), *Models Mechanisms and Etiology of Tumour Promotion.* IARC Scient. Pub. 56, Lyon, pp. 57–66.
42. Pitot,H.C. (1989) Progression: the terminal stages in carcinogenesis. *Jpn. J. Cancer Res.*, **80**, 599–607.
43. Schauer,A. and Kunze,E. (1976) Tumours of the liver. In Turusov,V.S. (ed.), *Pathology of Tumours in Laboratory Animals. Vol. 1. Tumours of the Rat, Part 2.* IARC, Lyon, pp. 41–72.
44. Squire,R.A. and Levitt,M.H. (1975) Report of a workshop on classification of specific hepatocellular lesions in rats. *Cancer Res.*, **35**, 3214–3223.
45. National Research Council (1980) Histologic typing of liver tumors in the rat. *J. Natl. Cancer Inst.*, **64**, 179–206.

Received on August 20, 1990; revised on January 17, 1991; accepted on January 25, 1991

detoxify the reactive intermediate (37). When PB administration followed AAF treatment, however, the level of P450 b/e was induced in AHF that had previously been negative for the enzyme (38). Thus, as a result of the alteration of drug-metabolizing enzymes, cells of AHF may have a selective advantage in a toxic environment. Since the growth of normal cells is suppressed by the cytotoxic effects of these treatments, the preneoplastic cells have an additional proliferative advantage.

The centrilobular to midzonal staining for P450 b/e that was evident in the livers of rats treated with DEN + PB or DEN + both TCBs indicates that enzyme induction occurred in response to these compounds in hepatocytes in these zones. Centrilobular staining with P450 c/d after treatment with DEN + 3,4,3',4'-TCB or DEN + both TCBs indicates that induction of this isozyme also occurred. The dose of 3,4,3',4'-TCB was 0.3% of the 6-day chronic dose used for maximal induction by Clevenger (14), and 0.003% of the acute dose used by Parkinson (6). The dose of 2,5,2',5'-TCB utilized in our studies was 33% of the maximal chronic dose and 3% of the maximal acute dose used in other studies (13,23,24).

The greater than additive effect of the mixture of 3,4,3',4'-TCB and 2,5,2',5'-TCB reported in this study may be the result of one or more of three possible mechanisms: (i) Ah receptor gene expression (1,4,5); (ii) the PB-type of cytochrome P450 response (24,39); (iii) the metabolic activation of PCBs to epoxides (29,30). Glutathione conjugation is the major phase II detoxification pathway for the 3,4-oxide of 2,5,2'-TCB. Several different mechanisms can contribute to the toxic effects of 2,5,2',5'-TCB. Although the mechanism of glutathione depletion may be different in hepatocytes and lymphocytes, continuous exposure to the TCB combination may have resulted in depletion of the glutathione levels in both cell types. Depletion of glutathione would prevent a major part of the detoxification of the 3,4-oxide of 2,5,2',5'-TCB (32).

Our results demonstrate an interaction of low doses of two PCBs *in vivo* in the two major target organs of PCB toxicity, the liver and the immune system, at doses that are relevant to human exposure levels (40). The observation of immune depression and promotion of AHF with very low PCB concentrations suggests that the biological effects of a complex Aroclor mixture in two different target cell populations of PCB toxicity may not be owing simply to the summed effects of each of the constituent chemicals or to the individual concentrations of the most toxic congeners, but rather largely to the effects of only a few constituents interacting at low concentrations.

This study also represents the first report of the appearance of an abnormal population of CD-4 lymphocytes in the peripheral blood after PCB exposure. This may be an important finding not only for rodent exposure, but also for human exposure, because this same PCB combination was very genotoxic to cultured human lymphocytes. The abnormal population of CD-4 cells in the peripheral blood may be the result of a genetic change that occurred in these cells. The aneuploidy of many hepatocytes (L.M.Sargent, G.Sattler, C.A.Sattler, B.Roloff, Y.Xu and H.C.Pitot, in preparation) and numerous large neoplastic nodules exhibiting cellular atypia in the liver are indications that the combination of 3,4,3',4'-TCB and 2,5,2',5'-TCB induces the stage of progression of hepatocarcinogenesis (41,42). Confirmation of this hypothesis will require further testing because the percentage of animals with hepatocellular carcinoma was not elevated after 1 year of treatment in this experiment. The numerous large neoplastic nodules with cellular atypia probably represent rapidly growing populations of abnormal cells. If this protocol had been allowed to continue further, it is possible that there would have been an increase in the frequency of hepatocellular carcinoma in the livers of rats receiving the combination compared with those administered each TCB alone.

Acknowledgements

We would like to thank Dr Colin Jefcoate for supplying the P450 antibodies. We would like to extend our gratitude to Dr James A.Miller for the gift of 2,5,2',5'-TCB. We also thank Dr David Auerbach and the State Laboratory of Hygiene for their help in performing the flow cytometry. The expert histotechnology of Ms Jane Weeks and Mrs Jennifer Potter is also gratefully acknowledged, as well as the expert technical typing of Mrs Mary Jo Markham. The authors are grateful to Dr Ilse Riegel for technical editing and comments on the manuscript. The experiments described in this document were funded in part by grants from the National Cancer Institute (CA-07175, CA-2284 and CA-45700) and by a training grant from the National Institute of Environmental Health Sciences (ES-07015).

References

1. Safe,S. (1989) Polychlorinated biphenyls (PCBs): mutagenicity and carcinogenicity. *Mutat. Res.*, **220**, 31–47.
2. Passivirta,J. and Linko,R. (1980) Environmental toxins in Finnish wildlife. A study of trends of residue contents in fish during 1973–1978. *Chemosphere*, **9**, 643.
3. Jacobs,L.W., Chou,S.F. and Tiedje,J.M. (1978) Field concentrations and persistence of polybrominated biphenyls in soils and solubility of polybrominated biphenyls in natural waters. *Environ. Health Perspect.*, **23**, 1.
4. Safe,S., Bandiera,S., Sawyer,T., Robertson,L.W., Safe,L., Parkinson,A., Thomas,P.E., Ryan,D.E., Reik,L.M., Levin,W., Denomme,M.A. and Fujita,T. (1985) PCBs: structure–function relationships and mechanisms of action. *Environ. Health Perspect.*, **60**, 47–56.
5. Poland,A. and Knutson,J.C. (1982) 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin and related halogenated aromatic hydrocarbons: examination of the mechanism of toxicity. *Annu. Rev. Pharmacol. Toxicol.*, **22**, 517–554.
6. Parkinson,A., Robertson,L., Safe,L. and Safe,S. (1981) Polychlorinated biphenyls as inducers of hepatic microsomal enzymes: structure–activity rules. *Chem.-Biol. Interactions*, **35**, 1–2.
7. McKinney,J.D. and Singh,P. (1981) Structure–activity relationships in halogenated biphenyls: unifying hypothesis for structural specificity. *Chem.-Biol. Interactions*, **333**, 271–283.
8. Yoshimura,H., Yoshihara,S., Ozawa,N. and Miki,M. (1979) Possible correlation between induction modes of hepatic enzymes by PCBs and their toxicity in rats. *Ann. NY Acad. Sci.*, **320**, 179–192.
9. Silkworth,J.B. and Grabstein,E.M. (1982) Polychlorinated biphenyl immunotoxicity: dependence on isomer planarity and the *Ah* gene complex. *Toxicol. Appl. Pharmacol.*, **65**, 109–119.
10. Greenlee,W.F. and Irons,R.E. (1981) Modulation of benzene-induced lymphocytopenia in the rat by 2,4,5,2',4',5'-hexachlorobiphenyl and 3,4,4',5'-tetrachlorobiphenyl. *Chem.-Biol. Interactions*, **33**, 345–360.
11. Wölfle,D., Münzel,P., Fischer,G. and Bock,K.-W. (1988) Altered growth control of rat hepatocytes after treatment with 3,4,3',4'-tetrachlorobiphenyl *in vivo* and *in vitro*. *Carcinogenesis*, **9**, 919–924.
12. Osterele,D. and Deml,E. (1981) Promotion effect of various PCBs and DDT on enzyme altered islands in rat liver. *Nauyn-Schmiedberg's Arch. Pharmacol. Suppl. R*, **16**, 316.
13. Preston,B.D., Miller,E.C. and Miller,J.A. (1985) The activities of 2,2',5,5'-tetrachlorobiphenyl, its 3,4-oxide metabolite and 2,2',5,5'-tetrachlorobiphenyl in tumor induction and promotion assays. *Carcinogenesis*, **6**, 451–453.
14. Clevenger,M.A., Roberts,S.M., Sattin,D.L., Harbison,R.D. and James,R.C. (1989) The pharmacokinetics of 2,2',5,5'-tetrachlorobiphenyl and 3,3',4,4'-tetrachlorobiphenyl and its relationship to toxicity. *Toxicol. Appl. Pharmacol.*, **100**, 315–327.
15. Pitot,H.C., Campbell,H.A., Maronpot,R., Nimrat,B., Rizvi,T.A., Xu,Y.-H., Sargent,L.M., Dragan,Y. and Pyron,M. (1989) Critical parameters in the quantitation of the stages of initiation, promotion, and progression in one model of hepatocarcinogenesis in the rat. *Toxicol. Pathol.*, **17**, 594–612.
16. Pitot,H.C., Barsness,L., Goldsworthy,T. and Kitagawa,T. (1978) Biochemical characterization of stages of hepatocarcinogenesis after a single dose of diethylnitrosamine. *Nature*, **271**, 456–458.
17. Yam,L.T., Li,C. and CrosbyW.H. (1971) Cytochemical identification of monocytes and granulocytes. *Am. J. Clin. Pathol.*, **55**, 283–290.
18. Braylan,R.C. (1983) Attributes and applications of flow cytometry. *Ann. Clin. Lab. Sci.*, **13**, 379–384.

Table II. AHF-positive P450 b/e expression after 1 year of treatment (%)

Groups	Foci positive for P450 b/e (%)
4	10 ± 7
10	68 ± 10
8	60 ± 5
12	65 ± 5
11	–[a]
3	–[a]
5	–[a]
9	40 ± 6

[a]Too few AHF to report significant data.

Table III. Promoting agents and promotion index

Promoting agents	Promotion index[a]
PB	100
3,4,3′,4′-TCB (0.1 p.p.m.)	1.5×10^4
2,5,2′,5′-TCB (10 p.p.m.)	200
2,5,2′,5′-TCB (100 p.p.m.)	250
2,5,2′,5′-TCB (10 p.p.m.) and 3,4,3′,4′-TCB (0.1 p.p.m.)	8×10^5
2,3,7,8-TCDD[b]	2.8×10^7

[a]See text for details of calculations. Promotion indices were determined in animals that had been initiated with DEN (10 mg/kg) following a 70% partial hepatectomy (see text for details).
[b]Ref. 22.

in comparison with PB from this experiment and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) from an earlier study (22). By contrast, a 10-fold higher dose of 2,5,2′,5′-TCB did not cause a significant increase in either the promotion index or the number of hepatic preneoplastic foci (Figure 9). The promotion index of 2,5,2′,5′-TCB was also considerably less than that of 3,4,3′,4′-TCB. The combination of the two congeners caused a dramatic increase in the number (Figure 9) and volume fraction (Figure 10) of preneoplastic foci. Indeed, the promotion index of the TCB combination is almost within one order of magnitude of that of TCDD, which has the highest known promotion potency of any compound (Table III). The number of animals treated with both TCBs that had numerous large neoplastic nodules exhibiting cellular atypia was also greater than that seen in either group treated with a single TCB.

The two TCB congeners differ in toxicity and binding affinity for the Ah receptor (8,23,24); however, the systemic clearance and volume of distribution of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB are essentially the same (15). When single PCB congeners were examined by others, the promotion potency could be correlated with the affinity for the Ah receptor (23). Our results also demonstrated that the strong Ah receptor ligand, 3,4,3′,4′-TCB, was a strong promoter of AHF, but the non-planar congener was a weak promoter relative to 3,4,3′,4′-TCB and TCDD. Furthermore, previous results have shown that TCDD, which has a 500-fold greater affinity for the Ah receptor than TCBs, was a stronger promoter than 3,4,3′,4′-TCB (24). The non-planar congeners, 2,4,5,2′,4′,5′-TCB (23), 2,4,2′,4′-TCB and 2,5,2′,5′-TCB, have been reported to exhibit promoting activity for hepatic preneoplastic foci (14). The presence of chlorine substitution in the *para* position correlated with an enhancement of promoting potency, but all the non-planar congeners were less potent than the planar 3,4,3′,4′-TCB.

An enhancement of the amount of P450 b/e enzymes was seen in preneoplastic hepatic foci (AHF) of rats receiving 10 p.p.m. 2,5,2′,5′-TCB or 100 p.p.m. 2,5,2′,5′-TCB and to an even greater extent in the DEN + both TCBs group. This same enhancement of the P450 b/e enzymes was observed in AHF of the DEN + PB treatment group. Many of the changes in gene expression seen in AHF may occur as a result of the selection of a population of altered cells that are resistant to the specific treatment utilized (25) or are selectively stimulated to grow by the particular promoting agent (26). Enhancement of the expression of this detoxification enzyme in cells of AHF is also exemplified by an increase of P450 b/e following promotion with PB as well as hexachlorocyclohexane (27,28).

The greater than additive toxicity of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB that was seen *in vivo* in hepatocytes and lymphocytes may have been owing to the metabolic activation of the 2,5,2′,5′-TCB congener to an epoxide intermediate (14, 29,30). This epoxide intermediate is more toxic and more chromosome damaging than the parent compound (31) and has been shown to bind to DNA (29,32). PCB congeners that have both the *meta* and *para* sites available for oxidation can be metabolized through an epoxide intermediate. These intermediates can bind to DNA and have been found to be mutagenic (25,31). Examination of the dose–response curves of previous *in vitro* studies of chromosome damage in human lymphocytes (33) caused by 3,4,3′,4′-TCB and a combination of 3,4,3′,4′-TCB + 2,5,2′,5′-TCB demonstrated that the two dose–response curves are parallel. This would suggest that the two events occurred by a common mechanism. Lymphocytes express the Ah receptor and have been shown to respond to the Ah receptor ligands by an increase in P450 c/d. Metabolic changes resulting from the combined induction of P450 c/d and P450 b/e can result in the metabolic activation of 4-chlorobiphenyl (34). Inhibition of P450 c/d metabolism of 2,5,2′,5′-TCB results in greater formation of the 3,4-diol and the 4-OH form, indicating that more 3,4-oxide occurs following P450 c/d induction. The induction of P450 b/e enzymes results in detoxification of the 2,5,2′,5′-TCB congener by direct *meta*-hydroxylation (32). The absence of the detoxification pathway (P450 b/e) and the presence of the activation pathway (c/d induction) may explain the greater sensitivity of the lymphocytes to 2,5,2′,5′-TCB observed in the *in vivo* studies (35). The enhancement of the P450 b/e expression in preneoplastic foci resulting from treatment with both TCBs and with DEN + 2,5,2′,5′-TCB as well as with DEN + PB may result in a selective reduced toxicity to 2,5,2′,5′-TCB conferred to these cells by this gene expression.

Although centrilobular to midzonal staining for P450 b/e was observed by Buchman *et al.* (36) after DEN initiation and promotion with 3,4,5,3′,4′,5′-hexachlorobiphenyl (HCB) or with 2,4,5,2′,4′,5′-HCB, no increased staining for the P450 b/e isozyme occurred in AHF with this protocol. The 2,4,5,2′,4′,5′-HCB congener is an inducer of the P450 b/e isozyme; however, this congener is not known to be metabolized by this form or any other form of P450. Increased expression of a detoxification enzyme in cells of AHF has been observed as an increase of P450 b/e after promotion with PB as well as with hexachlorocyclohexane (36). Cells of AHF resulting from *N*-hydroxy ethylnitrosamine treatment exhibit reduced levels of P450 b/e and P450 c/d forms and an increase in glutathione S-transferase and expoxide hydrolase (23). Chronic treatment of rats with 2-acetylaminofluorene, which is metabolized by multiple forms of P450 (36), causes the proliferation of focal areas of preneoplastic hepatocytes; this may significantly lower the expression of many P450 genes as well as increase the conjugating enzymes that

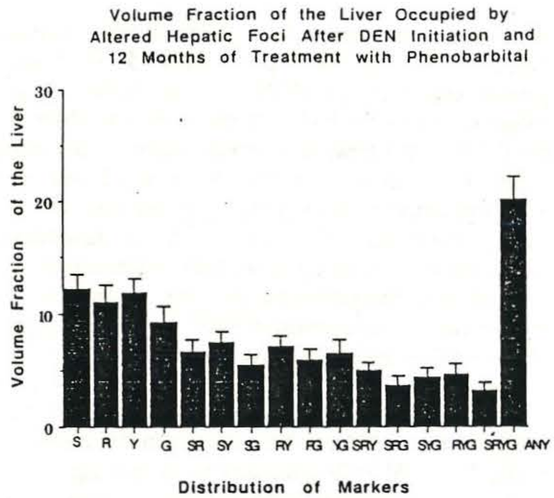


Fig. 7. Distribution of the volume fraction of AHF scored by multiple markers for AHF following initiation with 10 mg DEN/kg and 1 year of exposure to 0.1 p.p.m. 3,4,3',4'-TCB and 10 p.p.m. 2,5,2',5'-TCB (group 8, Figure 1). Abbreviations: S, glutathione S-transferase-positive volume fraction; R, GGT-positive volume. Y, ATPase-negative volume; G, G6Pase-negative volume; SR, S and R combined; SY, S and Y combined. SG, S and G combined; RY, R and Y combined; RG, R and G combined; YG, Y and G combined; SYG, S and Y and G combined; SRY, S and R and Y combined. See ref. 19 for further details.

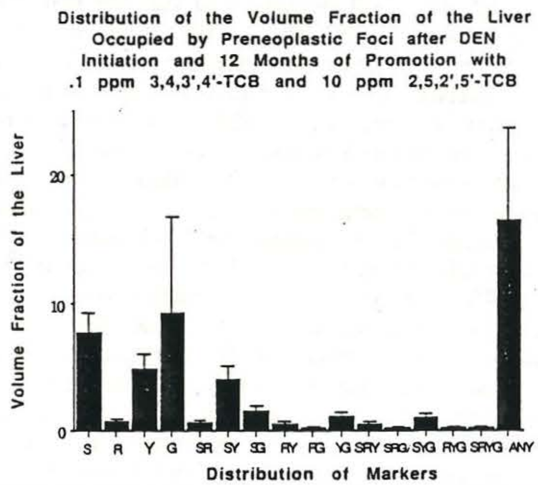


Fig. 8. Histogram of the distribution of the volume fraction of AHF scored by multiple markers for AHF following initiation with 10 mg DEN/kg and 1 year of exposure to 0.05% PB (group 12, Figure 1). See legend to Figure 7 for marker designation.

light-staining CD-4 cells was not a monocyte population, but was a new population of CD-4 cells exhibiting an abnormal surface membrane configuration.

The results from this research also demonstrated that the planar congener had more potent effects in liver cells than the non-planar TCB. The low dose of 3,4,3',4'-TCB chosen for this study produced a moderate increase in the volume of preneoplastic foci as well as an increase in chromosome damage (L.Sargent and H.C.Pitot, unpublished observations). The relative potency of promoting agents has been expressed by the following relationship:

$$\text{promotion index} = V_f/V_c \times 1/\text{mmol per week}$$

where V_f is the total volume fraction (%) occupied by AHF in the livers of rats treated with the promoting agent, V_c is the total

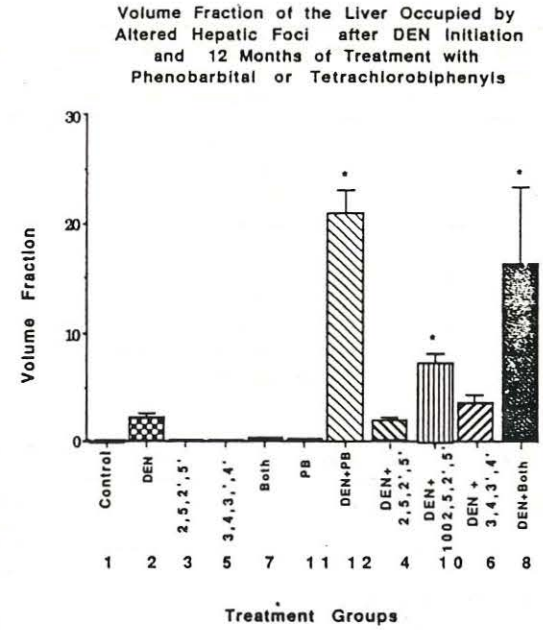


Fig. 9. Number of AHF per liver after initiation with 10 mg DEN/kg and/or 1 year of exposure to 0.1 p.p.m. 3,4,3',4'-TCB (groups 6 and 5), 10 p.p.m. 2,5,2',5'-TCB (groups 4 and 3), 0.1 p.p.m. 3,4,3',4'-TCB + 10 p.p.m. 2,5,2',5'-TCB (groups 8 and 7) or to 0.05% PB in the diet for 1 year (groups 12 and 11). Eleven animals per group were killed after each treatment. The bars above the columns indicate the standard error of the mean from 11 animals. See Figure 1 for details of each group designated by number under the columns. $*P < 0.001$ by Student's t-test.

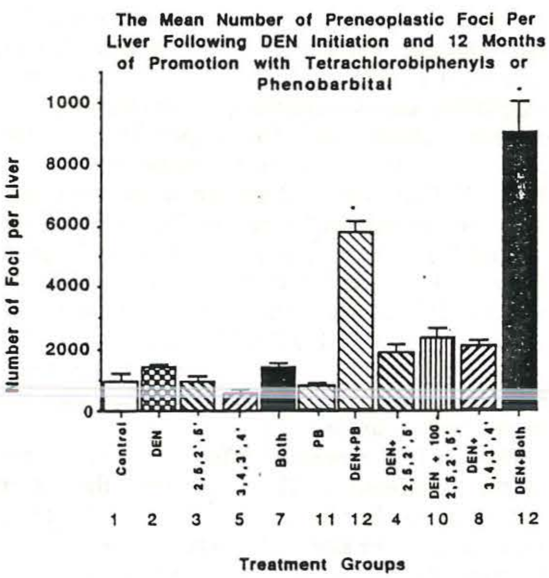


Fig. 10. Volume fraction (%) of AHF following initiation with 10 mg DEN/kg and/or 1 year of exposure to 0.1 p.p.m. 3,4,3',4'-TCB (groups 6 and 5), 10 p.p.m. 2,5,2',5'-TCB (groups 4 and 3), 0.1 p.p.m. 3,4,3',4'-TCB + 10 p.p.m. 2,5,2',5'-TCB (groups 8 and 7) or to 0.05% PB (groups 12 and 11) in the diet for 1 year. Each group had 11 animals. See legend to Figure 9 for further details.

volume of AHF in control animals that have only been initiated and not treated with the promoting agent, and mmol is the number of millimoles of the promoting agent.

The promotion index (22) is based on the total number of altered cells within all AHF, thus giving a measure of tumor promotion. Table III shows the relative promotion indices of 3,4,3',4'-TCB and 2,5,2',5'-TCB as well as their combination

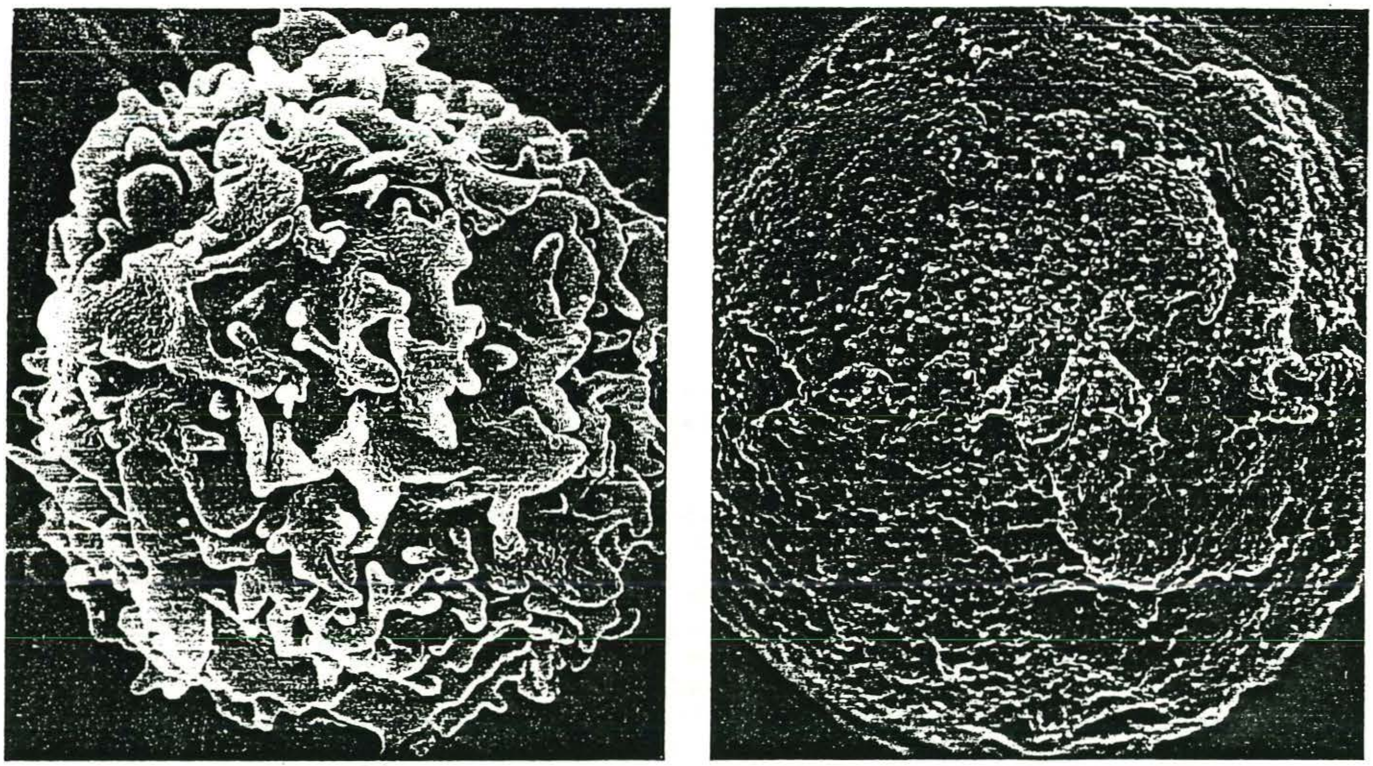


Fig. 5. Scanning electron micrograph of a normal T-helper cell (**left**) and an abnormal T-helper cell (**right**) isolated from the peripheral blood of an animal fed 0.1 p.p.m. 3,4,3',4'-TCB + 10 p.p.m. 2,5,2',5'-TCB for 1 year (×5000). See text for details.

cytochrome P450 marker in the DEN + 100 p.p.m. 2,5,2'.5'-TCB group. A larger number of positive foci was found in the group treated with DEN + both TCBs (60 ± 5%) than would be expected on the basis of the result seen with 10 p.p.m. 2,5,2',5'-TCB alone. The number of P450 b/e positive foci found in the DEN + PB group was as large as that of the group given DEN + both TCBs (65 ± 5%) (Table II).

The expression of P450 c/d was localized to the centrolobular and midzonal region of the regenerated liver in the DEN + 3,4,3',4'-TCB group, the DEN + both TCBs group, and the TCBs group (groups 6, 8 and 9). Centrilobular to midzonal staining was also seen with P450 b/e in the DEN + 10 p.p.m. 2,5,2',5'-TCB, the DEN + 100 p.p.m. 2,5,2',5'-TCB, the DEN + both TCBs and the DEN + PB groups. This degree of staining indicates that P450 c/d was induced by these regimens. In addition, P450 b/e was examined; in the DEN + PB group (group 12 in Figure 1), 76% of the PGST and 32% of the ATP-deficient foci were positive for this enzyme. In the DEN + 100 p.p.m. 2,5,2',5'-TCB group, 22% of the PGST-positive AHF and 41% of the ATP-negative AHF were positive for P450 b/e. When both TCBs were administered, 40% of the PGST and 40% of the ATP-deficient foci were positive for P450 b/e.

The combination of both TCBs also caused a superadditive increase in the number of animals with neoplastic nodules exhibiting cellular atypia ($P < 0.05$, Table I); however, only two of the animals treated with DEN + both TCBs developed hepatocellular carcinoma (HCC). Treatment with DEN + PB for 1 year caused 80% of the animals to develop HCC.

Discussion

The planar congener, 3,4,3',4'-TCB, and its non-planar isomer, 2,5,2',5'-TCB, which are found in the major Aroclor mixtures 1254, 1242 and 1248, induced a greater than additive toxicity in the two major target cell types of PCB toxicity, hepatocytes and lymphocytes, in the studies described here. Our results demonstrated that low doses of the planar 3,4,3',4'-TCB were more toxic to lymphocytes than a 100-fold higher dose of the non-planar 2,5,2',5'-TCB congener. The 3,4,3',4'-TCB congener caused a reduction in the number of B-cells. A similar reduction of B-cells has been noted after acute exposure to 3,4,3',4'-TCB (10). The combination of the two TCBs caused a greater than additive decrease in the number of circulating B-cells as well as the appearance of an abnormal subpopulation of T-helper cells. The esterase test verified that this abnormal population of

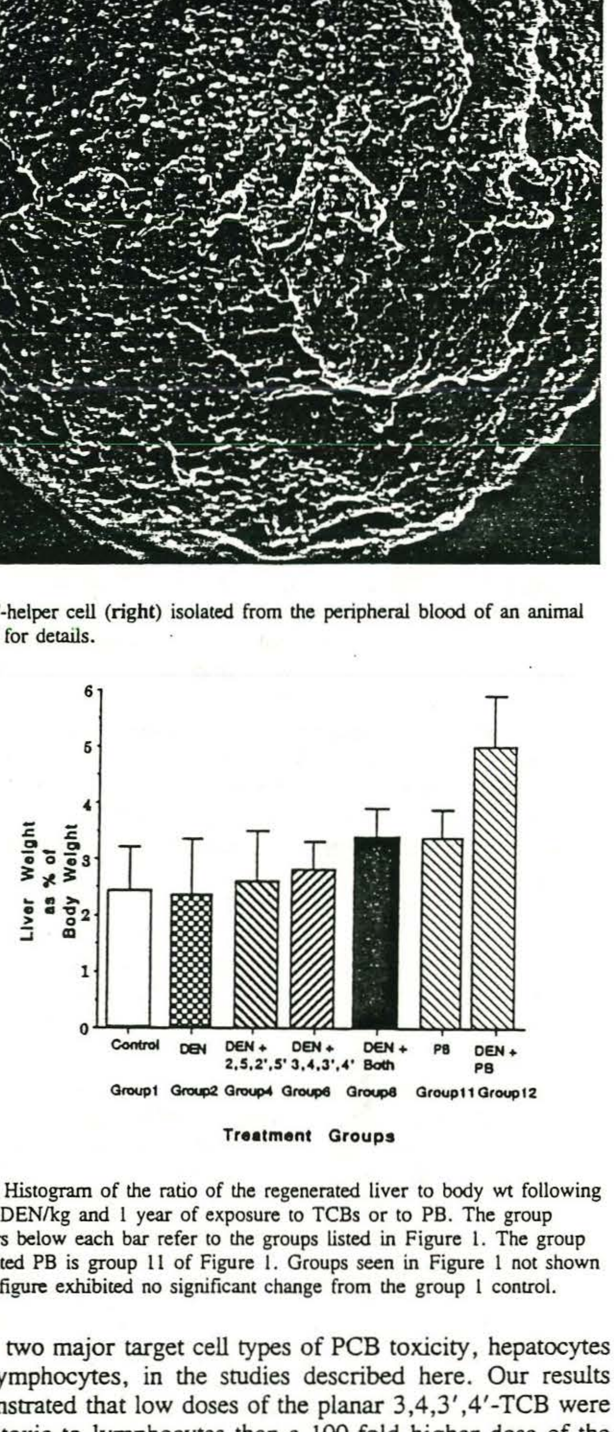


Fig. 6. Histogram of the ratio of the regenerated liver to body wt following 10 mg DEN/kg and 1 year of exposure to TCBs or to PB. The group numbers below each bar refer to the groups listed in Figure 1. The group designated PB is group 11 of Figure 1. Groups seen in Figure 1 not shown in this figure exhibited no significant change from the group 1 control.

Table I. Histopathologic changes in livers of rats on protocols depicted in Figure 1[a]

Group no.	Treatment	Portal damage[b]	Bile duct proliferation	Neoplastic nodules/rat	Cellular atypia/ neoplastic nodule/rat[c]	HCC/rat
1	Control	–	2/8	–	–	1/8
2	DEN	0/8	2/8	1/8	1/8	1/8
3	2,5,2′,5′-TCB (10 p.p.m.)	0/14	2/14	2/14	0/14	0/14
4	DEN + 10 p.p.m. 2,5,2′,5′-TCB	2/12	1/12	4/12	1/12	1/12
5	3,4,3′,4′-TCB (0.1 p.p.m.)	0/14	5/14	3/14	0/14	0/14
6	DEN + 0.1 p.p.m. 3,4,3′,4′-TCB	0/12	4/12	4/12	0/12	0/12
7	3,4,3′,4′-TCB + 2,5,2′,5′-TCB	9/12	9/12	1/12	1/12	0/12
8	DEN + 3,4,3′,4′-TCB + 2,5,2′,5′-TCB	9/11	11/11	11/11	9/11	2/11
10	DEN + 100 p.p.m. 2,5,2′,5′-TCB	3/5	2/5			
12	DEN + PB	2/11	11/11	11/11	11/11	9/11

[a]Data are presented as the number of rats exhibiting the pathologic process/total number of rats examined.
[b]Includes fibrosis, chronic inflammation and/or hydopic change of periportal hepatocytes. Control animals receiving control diets showed only occasional minimal portal damage and bile duct proliferation. The histopathology of livers of rats in groups 9, 11 and 13 (Figure 1) was no different from that seen in groups 1, 3 and 5.
[c]Cellular atypia is defined as morphological and cytological changes, usually focal, seen in neoplastic nodules, such changes being histologically compatible with one or more patterns of well-differentiated hepatocellular carcinomas (43–45).

total number of AHF or the volume fraction of the regenerated liver occupied by AHF.

Treatment with TCBs caused a predominance of AHF that were scored by the presence of PGST ($PGST^+$) and ATP deficiency as preneoplastic markers (Figure 7), whereas $PGST^+$, ATP deficiency and GGT^+ markers were equally distributed in AHF after DEN + PB (Figure 8). TCB treatment alone did not elevate the number of AHF when compared with the control livers; however, treatment with both TCBs increased the number of AHF to a level that was greater than that of the untreated control and statistically the same as the DEN control (groups 2, 3 and 5 in Figure 1; see also Figure 9). The numbers of preneoplastic foci per liver in the DEN + 10 p.p.m. 2,5,2′,5′-TCB group (group 4) or the DEN + 0.1 p.p.m. 3,4,3′,4′-TCB group (group 6 in Figure 1) were not significantly different from the DEN group (group 2, Figure 1). When rats were treated with DEN followed by both TCBs, the number of AHF was dramatically greater than additive (Figure 9) ($P < 0.001$). Treatment with DEN + 100 p.p.m. 2,5,2′,5′-TCB (group 10) did not cause a significant increase in the number of AHF when compared with DEN (Figure 9). Rats treated with the standard DEN + PB protocol had a significant increase in the number of AHF ($P < 0.001$, Figure 9).

Volume fraction of preneoplastic foci. When the volume fraction of AHF was analyzed, rats inititated with DEN and fed 10 p.p.m. 2,5,2′,5′-TCB (group 4) exhibited statistically the same volume percentage AHF as the DEN group (group 2 in Figure 10); however, the volume of AHF in the DEN + 3,4,3′,4′-TCB group (group 6) was slightly increased over that in the regenerated livers of animals receiving DEN only (group 2, Figure 10). The combination of DEN + both TCBs (group 8 in Figure 1) greatly increased the volume of the residual liver occupied by preneoplastic foci to a level that was much greater than would be expected by an additive model ($P < 0.001$; Figure 10). The group given a 10-fold greater level of 2,5,2′,5′-TCB (group 10) exhibited a significant increase in the volume of the regenerated liver occupied by AHF to 7% of the liver (Figure 10). This level was statistically greater than that of rats given DEN alone but not as great as the DEN plus both TCBs group. When the livers of rats given DEN followed by 0.05% PB in the diet were examined, there was a significant increase in the volume fraction of preneoplastic foci to 20% of the total regenerated liver (group 12 in Figure 1; see Figure 10).

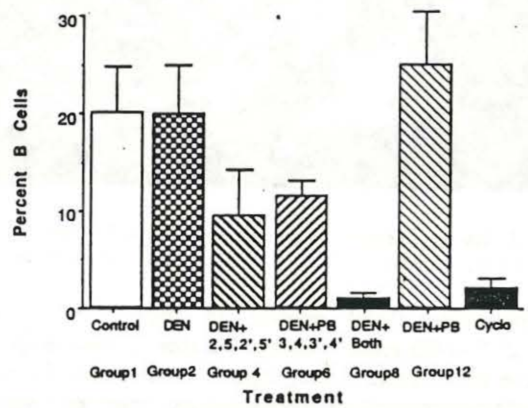


Fig. 3. Percentage of B-cells in the peripheral blood after 10 mg DEN/kg and 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB, 10 p.p.m. 2,5,2′,5′-TCB, or a combination of 3,4,3′,4′-TCB + 2,5,2′,5′-TCB or to cyclophosphamide. See text and legend to Figure 2 for details and statistical conclusions. Steel and Torrie's χ-square test for additivity was used to assess significance. $P < 0.05$.

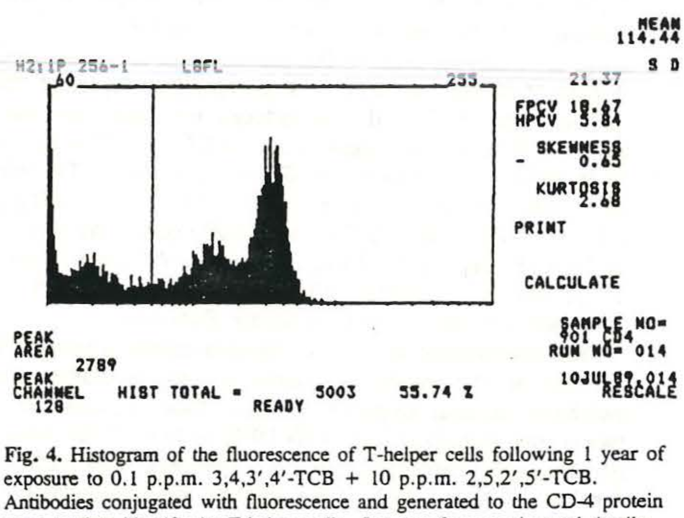


Fig. 4. Histogram of the fluorescence of T-helper cells following 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB. Antibodies conjugated with fluorescence and generated to the CD-4 protein were used to identify the T-helper cells. See text for experimental details.

Cytochrome P450 b/e was found in 10 ± 7% of the preneoplastic foci marked by PGST or ATP of the DEN + 10 p.p.m. 2,5,2′,5′-TCB, but 68 ± 10% of the AHF expressed the

10 mg DEN in trioctanoin/kg. After 1 week, the animals were randomly assigned to the treatment groups outlined in Figure 1. TCBs were dissolved in methylene chloride, added to the powdered chow, and mixed thoroughly in plastic bags. The solvent was evaporated in the hood for 24 h. Randomly selected rats were then placed on a control diet or control diet with one of the following additions: 0.1 p.p.m. 3,4,3',4'-TCB only, 10 p.p.m. 2,5,2',5'-TCB only, 0.1 p.p.m. 3,4,3',4'-TCB and 10 p.p.m. 2,5,2',5'-TCB, or 100 p.p.m. 2,5,2',5'-TCB. Another group was fed phenobarbital (PB) at a level of 0.05% in the diet as a positive control (15,16).

Analysis of lymphocytes

Rats were treated with 100 mg cyclophosphamide/kg and anesthetized with ether; blood was drawn by cardiac puncture 48 h later. The red blood cells were lysed with 2 ml hypotonic buffer (1000 ml of deionized water, 8.29 g NH_4Cl, 1.0 g KH_2CO_3, 0.372 g disodium EDTA, pH 7.4) and washed with phosphate-buffered saline. Washed lymphocytes were then mixed with fluorescein-conjugated antibodies generated against the CD-4 protein, the CD-8 protein, the 1.1 Thy protein and a general B-cell protein (17). The stained cells were then analyzed on the flow cytometer by standard methods (18). Lymphocytes of abnormal morphology were examined by scanning electron microscopy according to standard methods. Sections of the spleen were frozen on solid CO_2 and fixed in 10% buffered formalin.

Analysis of preneoplastic foci (altered hepatic foci, AHF)

The liver was removed, weighed, and sections from each liver lobe were immediately frozen on solid CO_2. Five 10-μ-thick serial sections were stained for γ-glutamyl transpeptidase (GGT), the placental form of glutathione S-transferase (PGST), canalicular ATPase (ATP), cytochrome P450 b/e, P450 c/d and glucose-6-phosphatase (G6P), according to the methods for staining outlined by Xu *et al.* (19). AHF were then quantitated by the procedure of Campbell *et al.* (20). Additional slices of tissue were stored in 10% formalin for histopathological analysis.

Statistics

Non-parametric Wilcoxon statistics were used to compare groups. For the determination of additivity, Steel and Torrie's χ-square test for additivity (21) was used.

Results

Lymphocyte analysis

The total number of circulating antibody-producing cells (B-cells) was reduced in the peripheral blood prepared from animals treated with 3,4,3',4'-TCB, but not from those treated with 2,5,2',5'-TCB (groups 3 and 5, Figure 2) when compared with untreated controls. The number of circulating B-cells isolated from animals treated with both TCBs was reduced by a greater than additive level ($P < 0.001$, group 7) when analyzed by flow cytometry. When DEN was included in the treatment protocol (Figure 3), the level of circulating B-cells was reduced in the 2,5,2',5'-TCB group as well as the 3,4,3',4'-TCB group ($P < 0.05$, groups 4 and 6). The level of B-cells in the group with DEN plus both TCBs (group 8) was reduced to 1%. A reduction to this level was greater than would be expected by an additive model when analyzed by the χ-square test for additivity.

There was no statistical reduction in the number of CD-4, CD-8 or Thy 1.1 cells. Although the total number of cells was the same, a population of light-staining CD-4 cells was observed by flow cytometry (Figure 4). Of the CD-4 cells, 50 ± 8% from group 7 (both TCBs) and 95 ± 5% of the samples from group 8 (DEN + both TCBs) had an abnormal population of light-staining CD-4 cells. The forward scatter of these cells was the same as that of the normal CD-4 cells, but the side scatter was different (Figure 4). A difference in the side scatter would indicate a difference in size or morphology. When these light-staining CD-4 cells were separated and examined by scanning electron microscopy, the surface morphology of all of the cells examined was distinctly different from the normal population (Figure 5). By standard methods (17), these abnormal cells were further examined for esterase activity and were determined to be negative and therefore not monocytes.

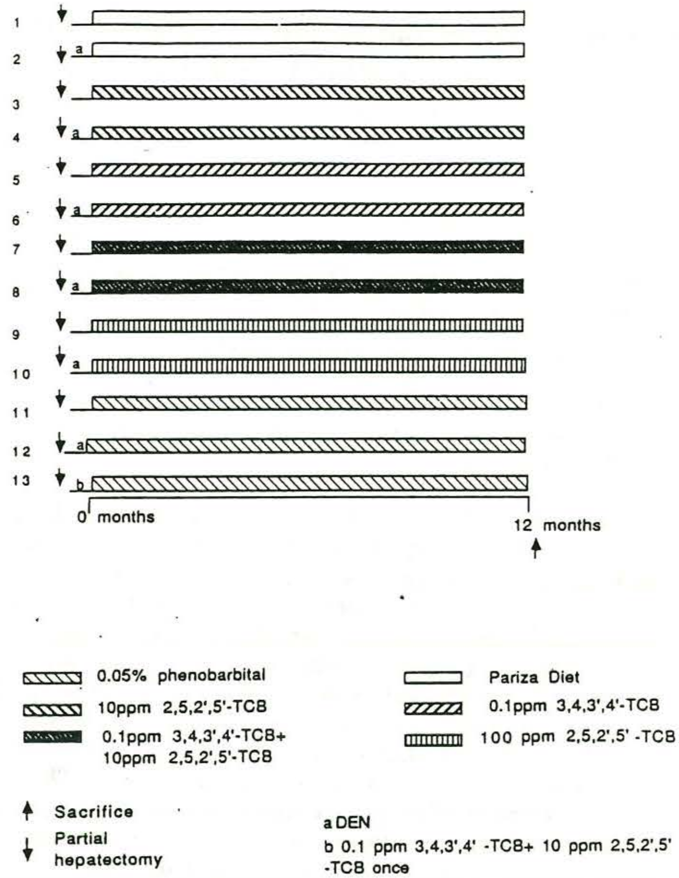


Fig. 1. Format of the protocol used for the initiation and promotion of AHF in female Sprague–Dawley rats.

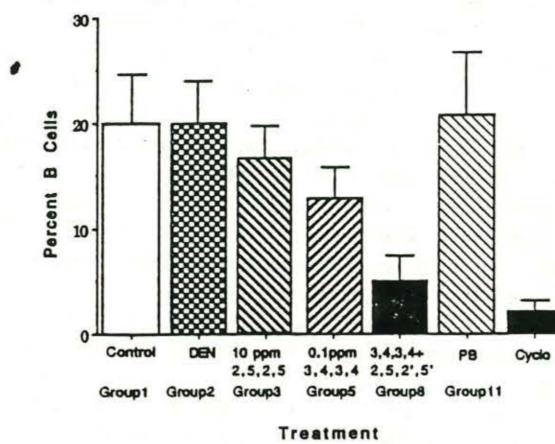


Fig. 2. Percentage of B-cells in the peripheral blood after chronic exposure to DEN alone or followed by 0.05% PB, 3,4,3',4'-TCB, 2,5,2',5'-TCB, or a combination of 3,4,3',4'-TCB + 2,5,2',5'-TCB or to cyclophosphamide. See text for details. Steel and Torrie's χ-square test for additivity (21) was used to examine an additive or greater than additive result. The conclusions of this test are given in the text. The bars above the columns indicate the standard error of the mean for analysis (1/rat in duplicate). The numbers of rats/group may be obtained from Table I.

Liver analysis

Number of preneoplastic foci. There was no statistical increase in the ratio of residual liver wt to body wt with any of the TCB treatments, but there was a significant increase in the PB and DEN + PB groups (Figure 6). A single dose of 0.1 p.p.m. 3,4,3',4'-TCB and 10 p.p.m. 2,5,2',5'-TCB did not increase the

Carcinogenesis vol.12 no.5 pp.793–800, 1991

Attachment 5

Study of the separate and combined effects of the non-planar 2,5,2′,5′- and the planar 3,4,3′,4′-tetrachlorobiphenyl in liver and lymphocytes *in vivo*

Linda Sargent[1], Yvonne P.Dragan, Chris Erickson, Chris J.Laufer and Henry C.Pitot[2]

McArdle Laboratory for Cancer Research, Department of Oncology and the Center for Environmental Toxicology, The Medical School, University of Wisconsin, Madison, WI 53706, USA

[1]Present address: Chemical Industry Institute of Toxicology, 6 Davis Drive, Research Triangle Park, NC 27709, USA
[2]To whom reprint requests should be sent

Polychlorinated biphenyls (PCBs) are a group of industrial chemicals that are widely distributed in the environment. Because these compounds occur as mixtures, studies of their possible interactive effects are essential for an understanding of the mechanism of the toxicity of these mixtures. For the determination of a possible interaction of the effects *in vivo* of 2,5,2′,5′-tetrachlorobiphenyl (TCB) and 3,4,3′,4′-TCB, rats were exposed to a single dose of diethylnitrosamine (DEN) and subsequently to 0.1 p.p.m. 3,4,3′,4′-TCB and/or 10 p.p.m. 2,5,2′,5′-TCB in the feed for 1 year. The two major targets of PCB toxicity, the liver and the peripheral blood, were examined after these treatments. TCB treatment after DEN exposure caused a predominance of increased placental glutathione S-transferase (PGST) and deficiencies of ATPase as preneoplastic markers in focal hepatic lesions. When 0.05% phenobarbital (PB) was administered after DEN exposure, the distribution of markers in altered hepatic foci (AHF) was essentially equal for increased PGST and γ-glutamyltranspeptidase (GGT) and for ATPase deficiency. Many of these AHF also exhibited increased P450 b/e expression. Our results demonstrated that the two PCB congeners interacted *in vivo* to produce an increase in AHF that were PGST positive and ATPase negative. PGST-positive and ATPase-negative AHF correlated best with focal areas of P450 b/e expression. The combination of the two PCBs caused a greater than additive decrease in the total number of lymphocytes and antibody-producing B-cells. Also the thymocyte-dependent T-helper cells isolated from the animals receiving the combination of TCBs demonstrated a morphologically abnormal subpopulation. The results indicate that the interaction of 2,5,2′,5′-TCB and 3,4,3′,4′-TCB *in vivo* induced much greater toxicity and mutagenicity in peripheral lympyhocytes and hepatocytes than treatment with either congener alone.

Introduction

Polychlorinated biphenyls (PCBs*) are a group of industrial chemicals that, in the past, had diverse uses owing to their chemical stability and their miscibility in organic solvents. These properties resulted in the use of PCBs as hydraulic fluids, plasticizers, adhesives, heat transfer fluids, wax extenders, dedusting agents, organic diluents, lubricants, flame retardants and as dielectric fluids in capacitors and transformers (1). The advantages that made PCBs such a versatile industrial chemical proved to be the source of their problem in the environment. Traces of PCBs have been found in environmental samples world-wide (2,3). Analyses of human breast milk, blood and adipose tissue have demonstrated that most individuals have been exposed to PCBs (2,3). The primary route of human exposure is through oral ingestion of contaminated products.

Technical mixtures of PCBs contain a combination of planar and non-planar congeners. The planar congeners bind to the Ah receptor, induce cytochrome P450 c and P450 d (4–7), and cause a cascade of events primarily in the liver and immune cells, including weight loss, thymic atrophy, decreased spleen weights (8), reduction of circulating lymphocytes of both the bursae and thymic cell populations (9–11), hepatomegaly, and subcapsular and midzonal hepatic necrosis. They are also potent promoters of the growth of preneoplastic hepatic foci (12). The non-planar congeners are less toxic, have a low affinity for the Ah receptor, and induce P450 b/e. The non-planar congeners cause hepatic enlargement and are relatively weak promoting agents in hepatocarcinogenesis (12,13). They do not cause thymic atrophy or reduction in immune function (5,6,14).

Planar and non-planar congeners occur as mixtures, yet there are few studies which have examined the potency of specific combinations of PCB congeners. The planar 3,4,3′,4′-tetrachlorobiphenyl (TCB) and the non-planar 2,5,2′,5′-TCB are found in the Aroclor mixtures 1254, 1248 and 1242. The ratio of the concentration of these two congeners in the major Aroclors was used to determine the concentration ratio for this study. In addition, we chose to use low-level, environmentally relevant doses of these TCBs in order to assess the potency of the combination for the determination of doses in this experiment. The sample of Aroclor that was used as a standard contained 0.002 μg of 3,4,3′,4′-TCB/ml and 0.2 μg of 2,5,2′,5′-TCB/ml. Hepatocytes and lymphocytes were chosen as target cells to study a possible superadditive toxicity and promotion potency of the combination of the planar and the non-planar TCBs, since these two target cell types are among the most sensitive to PCB toxicity.

Materials and methods

Chemicals

The Pariza purified diet was purchased from Teklad (Madison, WI). Diethylnitrosamine (DEN) was obtained from the Eastman Kodak Co. (Rochester, NY). 3,4,3′,4′-TCB was purchased from Ultra Scientific (Hope, RI) and 2,5,2′,5′-TCB was a gift from Dr James Miller (McArdle Laboratory, Madison, WI). All of the antibodies used for immunohistochemistry were obtained from Bioproducts for Science Inc. (Indianapolis, IN).

Animals and treatment protocol

Female Sprague–Dawley rats (Harlan Sprague Dawley, Madison, WI) weighing an average of 90 g were housed in wire mesh cages and fed the Pariza diet (30% casein, 5% corn oil, 10% partially hydrogenated corn oil, 40% sucrose, 15% cornstarch) and water *ad libitum*. A 70% partial hepatectomy was performed under ether anesthesia and 24 h later 50% of the animals were intubated with

*Abbreviations: PCBs, polychlorinated biphenyls; TCB, tetrachlorobiphenyl; DEN, diethylnitrosamine; PB, phenobarbital; AHF, altered hepatic foci; GGT, γ-glutamyl transpeptidase; PGST, placental form of glutathione S-transferase; ATP, canalicular ATPase; G6P, glucose-6-phosphatase; HCC, hepatocellular carcinoma; TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin; HCB, hexachlorobiphenyl.

Attachment 6

CANCER MORTALITY IN WORKERS EXPOSED TO 2,3,7,8-TETRACHLORODIBENZO-*p*-DIOXIN

Marilyn A. Fingerhut, Ph.D., William E. Halperin, M.D., David A. Marlow, B.S., Laurie A. Piacitelli, M.S., Patricia A. Honchar, Ph.D., Marie H. Sweeney, Ph.D., Alice L. Greife, Ph.D., Patricia A. Dill, A.B., Kyle Steenland, Ph.D., and Anthony J. Suruda, M.D.

Abstract *Background.* In both animal and epidemiologic studies, exposure to dioxin (2,3,7,8-tetrachlorodibenzo-*p*-dioxin, or TCDD) has been associated with an increased risk of cancer.

Methods. We conducted a retrospective cohort study of mortality among the 5172 workers at 12 plants in the United States that produced chemicals contaminated with TCDD. Occupational exposure was documented by reviewing job descriptions and by measuring TCDD in serum from a sample of 253 workers. Causes of death were taken from death certificates.

Results. Mortality from several cancers previously associated with TCDD (stomach, liver, and nasal cancers, Hodgkin's disease, and non-Hodgkin's lymphoma) was not significantly elevated in this cohort. Mortality from soft-tissue sarcoma was increased, but not significantly (4 deaths; standardized mortality ratio [SMR], 338; 95 percent confidence interval, 92 to 865). In the subcohort of 1520 workers with ≥1 year of exposure and ≥20 years of latency, however, mortality was significantly increased for soft-tissue sarcoma (3 deaths; SMR, 922; 95 percent confidence interval, 190 to 2695) and for cancers of the respiratory system (SMR, 142; 95 percent confidence interval, 103 to 192). Mortality from all cancers combined was slightly but significantly elevated in the overall cohort (SMR, 115; 95 percent confidence interval, 102 to 130) and was higher in the subcohort with ≥1 year of exposure and ≥20 years of latency (SMR, 146; 95 percent confidence interval, 121 to 176).

Conclusions. This study of mortality among workers with occupational exposure to TCDD does not confirm the high relative risks reported for many cancers in previous studies. Conclusions about an increase in the risk of soft-tissue sarcoma are limited by small numbers and misclassification on death certificates. Excess mortality from all cancers combined, cancers of the respiratory tract, and soft-tissue sarcoma may result from exposure to TCDD, although we cannot exclude the possible contribution of factors such as smoking and occupational exposure to other chemicals. (N Engl J Med 1991; 324:212-8.)

SEVERAL epidemiologic and toxicologic studies have suggested an association between 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), or the chemicals it contaminates, and soft-tissue sarcoma,[1-4] Hodgkin's disease,[5] non-Hodgkin's lymphoma,[6-8] stomach cancer,[9,10] nasal cancer,[11] and cancer of the liver.[12,13] In other studies of these cancers, no significant associations with TCDD exposure were found.[14-19] The carcinogenicity of TCDD has been demonstrated in studies of rats, mice, and hamsters; histiocytic lymphomas, fibrosarcomas, and tumors of liver, skin, lung, thyroid, tongue, hard palate, and nasal turbinates have been found.[12,13,20] TCDD acts as a promoter[21,22] and may also initiate carcinogenesis.[12,13,20] To evaluate the effect of occupational exposure to TCDD, particularly with respect to the cancers listed above, we conducted a retrospective cohort study of mortality among U.S. chemical workers assigned to the production of substances contaminated with TCDD.

Methods

Identification of Companies

In 1978 the National Institute for Occupational Safety and Health began an effort that would eventually identify the exposed workers at all U.S. chemical companies that had made TCDD-contaminated products between 1942 and 1984. TCDD was generated as a contaminant in the production of 2,4,5-trichlorophenol and was carried into subsequent production processes.[23] One derivative, 2,4,5-trichlorophenoxyacetic acid, was widely used in the United States to kill brush and was a constituent of defoliants such as Agent Orange. Other derivatives included the herbicides 2-(2,4,5-trichlorophenoxy)propionic acid (Silvex) and 2-(2,4,5-trichlorophenoxy)-ethyl 2,2-dichloropropionate (Erbon), the insecticide *O,O*-dimethyl *O*-(2,4,5-trichlorophenyl)phosphorothioate (Ronnel), and the bactericide 2,2′-methylene-bis[3,4,6-trichlorophenol] (hexachlorophene).

Identification of Exposed Workers

Workers from 12 companies were included in the study cohort if a personnel or payroll record documented that they had been assigned to a production or maintenance job in a process involving TCDD contamination (n = 5000), or if they had been identified in a previously published study on the basis of exposure to TCDD (n = 172).[24] Personnel records for 202 workers did not reveal the duration of their assignment to processes involving TCDD contamination; they were therefore included in the analysis of overall mortality but excluded from analyses according to duration of exposure. Sixty-seven women are not included in this report; there were 10 deaths among them, including a single death from cancer (lung cancer).

At each plant, we made a thorough review of operating conditions, job duties, and records of TCDD levels in industrial-hygiene samples, intermediate reactants, products, and wastes. This review provided clear evidence of potential daily exposure to TCDD. The production of TCDD-contaminated substances at the various plants involved similar raw materials, processes, and job duties.[25] However, there were differences between jobs and between plants in the extent of TCDD exposures. Occupational exposure to substances contaminated with TCDD was confirmed by measuring serum TCDD levels, as adjusted for lipids, in 253 surviving members of the study cohort from two plants who were also participants in a related cross-sectional medical study.[26]

Life-Table Analysis

Vital status was determined as of December 31, 1987, from records of the Social Security Administration or Internal Revenue Service, or from the National Death Index. All death certificates

From the Industrywide Studies Branch, Division of Surveillance, Hazard Evaluations, and Field Studies, National Institute for Occupational Safety and Health, Centers for Disease Control, 4676 Columbia Pky., Cincinnati, OH 45226, where reprint requests should be addressed to Dr. Fingerhut.

Supported in part by the Agency for Toxic Substances and Disease Registry.

were independently classified by two nosologists according to the rules of the revision of the *International Classification of Diseases* (ICD) in effect at the date of death.[27]

Life-table analysis was used to evaluate mortality in the cohort.[28] At each plant, the number of person-years at risk was calculated as the interval between the first systematically documented assignment to a process involving TCDD contamination and the date of death or December 31, 1987, whichever occurred first. Those whose vital status was unknown were assumed to be alive at the end of the study. Standardized mortality ratios (SMRs) were computed by dividing the observed number of deaths by the expected number and multiplying by 100, after stratification to adjust for the confounding effects of age, race, and year of death. Two-sided 95 percent confidence intervals were computed for each cause-specific SMR, with use of the Byar approximation for eight deaths or more and Fisher's exact method for fewer than eight deaths.[29] The U.S. population was used as the reference group, because the 12 plants were located in 11 states throughout the country.

Analyses According to Duration of Exposure and Employment

Duration of exposure was defined as the number of years the worker was employed in processes involving TCDD contamination and was calculated with data from personnel records. We used duration of exposure as a surrogate for cumulative exposure to TCDD on the basis of the high correlation of the logarithm of serum TCDD levels with the logarithm of the number of years assigned to processes involving TCDD contamination in our sample of 253 workers (Pearson's product-moment coefficient $r = 0.72$) (Fig. 1), and on the assumption that the production processes were similar in the 12 plants.[25]

Because of the concentration of person-years in the short-duration categories, duration of exposure was stratified before analysis into categories of <1, 1 to <5, 5 to <15, and ≥15 years (Table 1). Mortality was also examined according to time since first exposure (latency) in periods of 0 to <10, 10 to <20, and ≥20 years since first exposure. To examine mortality in a subgroup with substantial exposure and adequate time for cancer to develop, we identified a group of workers who had 1 year or more of exposure to processes involving TCDD contamination and at least 20 years of latency. One year was chosen as a cutoff point for this high-exposure subcohort because in the sample of workers whose serum TCDD levels were measured, 100 percent of those exposed for more than one year had serum TCDD levels higher than the mean level in the unexposed reference group (7 pg per gram of lipid). For this subcohort, the number of person-years at risk was calculated from the date the person attained both 20 years of latency and 1 year of exposure.

Most of the 12 plants were large U.S. chemical manufacturing sites that produced thousands of chemicals. Complete documentation of each worker's exposures was impossible. A separate measure called "duration of employment," defined as the total time that each worker was employed at a study plant, was therefore used. Because of the long total employment at the plants, analyses according to duration of employment were stratified into periods of <5, 5 to <10, 10 to <15, 15 to <20, 20 to <25, 25 to <30, and ≥30 years (Table 1). For these analyses, latency was defined as time since first employment.

When the SMRs showed an apparent trend associated with duration of exposure or employment and when the observed numbers of deaths were sufficiently large, we conducted internal comparisons using directly standardized rate ratios and tests for trend.[30] For the standardized rate ratios, the cause-specific mortality rate in each of the categories of longer duration was compared with the rate in the category of shortest duration, after stratification of the rates for the potential confounding effects of age, race, and calendar time.

Results

The cohort of 5172 male workers from 12 plants had 116,748 person-years of observation. Table 1 describes the vital status, race, latency, and duration of exposure and employment of the workers. Overall mortality for all causes of death was similar to national rates in the United States (1052 deaths; SMR, 99; 95 percent confidence interval, 93 to 105). Mortality from heart disease was also similar to national rates

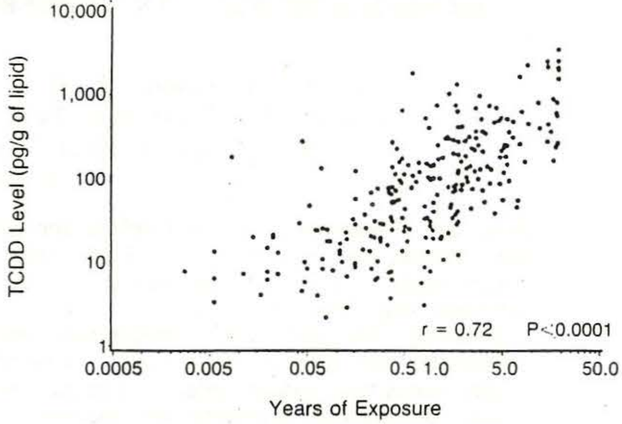


Figure 1. Serum Levels of TCDD, as Adjusted for Lipids, in 253 Workers, According to Years of Exposure.

Table 1. Vital Status and Demographic and Employment Characteristics of the Study Cohort.

Variable	Number (Percent)
Vital status*	
Alive	4043 (78)
Dead	1052 (20)
Unknown	77 (2)
Total	5172 (100)
Deaths*	
White men	985 (94)
Nonwhite men	67 (6)
Total	1052 (100)
Death certificates obtained	1037 (99)
Race	
White	4590 (89)
Nonwhite	385 (7)
Unknown	197 (4)
Total	5172 (100)
Duration of exposure (yr)†	
<1	2697 (54)
1 to <5	1427 (29)
5 to <15	639 (13)
≥15	207 (4)
Total	4970 (100)
Duration of employment (yr)†	
<5	2125 (43)
5 to <10	501 (10)
10 to <15	605 (12)
15 to <20	403 (8)
20 to <25	391 (8)
25 to <30	415 (8)
≥30	530 (11)
Total	4970 (100)
Years since first exposure (latency)†	
<10	271 (5)
10 to <20	1663 (33)
≥20	3036 (61)
Total	4970 (100)
Years since last exposure†	
<10	453 (9)
10 to <20	1789 (36)
≥20	2728 (55)
Total	4970 (100)

*As of December 31, 1987.

†Excludes 202 workers for whom duration of assignment to processes involving TCDD contamination was not available from work records.

(393 deaths; SMR, 96; 95 percent confidence interval, 87 to 106). There were significant reductions in the mortality rates for diseases of the circulatory system (67 deaths; SMR, 77; 95 percent confidence interval, 60 to 98), primarily because of fewer deaths from stroke, and for diseases of the digestive system (38 deaths; SMR, 70; 95 percent confidence interval, 49 to 96), primarily because of fewer deaths from cirrhosis. There were also significantly fewer deaths from alcoholism and personality disorders (2 deaths; SMR, 23; 95 percent confidence interval, 3 to 87). The low mortality from circulatory disease may be a reflection of the "healthy worker" effect — cohorts of workers die at lower rates than the general population, particularly of causes other than cancer.[31] The reduced number of deaths from cirrhosis and alcoholism implies that this cohort consumed less alcohol than the general population. Reduction may also have occurred simply by chance, since numerous comparisons were made between the cohort and the U.S. population. Fatal injuries were significantly more frequent in the cohort (106 deaths; SMR, 128; 95 percent confidence interval, 104 to 154), but they did not appear to be associated particularly with exposure to TCDD. Mortality from all cancers combined (265 deaths; SMR, 115; 95 percent confidence interval, 102 to 130) was significantly elevated in the cohort.

Cancers of a Priori Interest

The term "soft-tissue sarcoma" describes the group of rare malignant neoplasms arising from supporting tissue other than bone.[32] We restricted our analysis of mortality due to soft-tissue sarcoma to cases of soft-tissue sarcoma listed as the underlying cause of death

Table 2. Cancer Mortality in the Entire Cohort and in Workers with More Than 20 Years of Latency.

Site of Cancer	ICD Code*	Entire Cohort (N = 5172)†			Subcohort with ≥20 Yr of Latency (N = 3036)‡					
					<1 yr of exposure (N = 1516)§			≥1 yr of exposure (N = 1520)¶		
		deaths observed	deaths expected	SMR‖	deaths observed	deaths expected	SMR‖	deaths observed	deaths expected	SMR‖
All cancers	140–208	265	229.9	115 (102–130)**	48	46.8	102 (76–136)	114	78.0	146 (121–176)**
Buccal and pharynx	140–149	5	7.0	70 (23–166)	2	1.4	145 (18–524)	2	2.2	90 (11–325)
Pharynx	146–149	3	3.4	88 (18–259)	2	0.7	298 (36–1080)	0	1.2	0 (—)
Other parts	142–145	2	1.9	105 (13–379)	0	0.4	0 (—)	2	0.6	329 (40–1190)
Digestive organs	150–159	67	59.7	112 (87–143)	13	11.8	111 (59–189)	28	20.1	140 (93–202)
Esophagus	150	9	5.9	152 (70–290)	2	1.2	165 (20–602)	4	2.0	200 (55–513)
Stomach	151	10	9.7	103 (50–190)	3	1.7	178 (37–521)	4	2.9	138 (38–353)
Small intestine and colon	152–153	25	20.4	122 (79–181)	5	4.3	117 (38–274)	13	7.3	178 (95–304)
Rectum	154	5	5.6	89 (29–209)	1	1.0	100 (3–557)	2	1.7	115 (14–415)
Liver and biliary	155, 156	6	5.2	116 (42–252)	1	1.0	100 (3–557)	1	1.7	59 (1–327)
Pancreas	157	10	11.9	84 (40–155)	1	2.4	41 (1–232)	4	4.0	100 (27–253)
Peritoneum and unspecified	158, 159	2	1.1	184 (22–666)	0	0.2	0 (—)	0	0.4	0 (—)
Respiratory system	160–165	96	84.5	113 (92–139)	19	18.4	103 (62–161)	43	30.2	142 (103–192)
Larynx	161	7	3.3	211 (84–434)	2	0.7	297 (36–1074)	3	1.1	268 (55–783)
Trachea, bronchus, and lung	162	89	80.1	111 (89–137)	17	17.5	96 (56–155)	40	28.8	139 (99–189)
Male genital organs	185–187	17	15.3	111 (65–177)	2	3.2	63 (8–229)	9	6.0	149 (68–283)
Prostate	185	17	13.9	122 (71–195)	2	3.0	67 (8–237)	9	5.9	152 (70–290)
Urinary organs	188–189	17	11.4	148 (86–238)	3	2.4	128 (26–373)	6	4.0	149 (55–324)
Kidney	189.0–189.2	8	5.7	140 (60–275)	3	1.2	253 (52–742)	2	1.9	106 (13–384)
Bladder and other	188, 189.3–189.9	9	5.7	157 (72–298)	0	1.2	0 (—)	4	2.2	186 (51–476)
Lymphatic and hematopoietic tissue	200–208	24	22.1	109 (70–162)	4	3.9	102 (28–260)	8	6.4	125 (54–247)
Hodgkin's disease	201	3	2.5	119 (25–349)	0	0.2	0 (—)	1	0.4	276 (7–1534)
Non-Hodgkin's lymphoma††	200, 202	10	7.3	137 (66–254)	2	1.5	135 (16–488)	2	2.1	93 (11–337)
Lymphosarcoma and reticulosarcoma††	200	5	3.5	142 (46–332)	0	0.6	0 (—)	1	0.9	107 (3–594)
Other lymphatic††	202	5	3.7	133 (43–313)	2	0.9	215 (26–779)	1	1.4	71 (2–385)
Multiple myeloma††	203	5	3.0	164 (53–385)	0	0.6	0 (—)	3	1.1	262 (54–766)
Leukemia and aleukemia	204–208	6	8.9	67 (24–146)	2	1.6	126 (15–457)	2	2.6	77 (9–277)
Other sites	170–173, 190–199	39	29.6	131 (94–180)	5	5.8	87 (28–202)	18	9.0	201 (118–316)**
Skin	172, 173	4	4.9	82 (22–211)	0	0.9	0 (—)	2	1.3	155 (19–559)
Brain and nervous system	191, 192	5	7.3	68 (22–160)	0	1.3	0 (—)	2	1.9	106 (13–384)
Bone	170	2	0.9	227 (27–819)	0	0.1	0 (—)	1	0.2	521 (13–2903)
Connective tissue and soft tissue	171	4	1.2	338 (92–865)	0	0.2	0 (—)	3	0.3	922 (190–2695)**
Other and unspecified	194–199	24	14.8	162 (104–241)**	5	3.1	159 (52–372)	10	5.1	196 (94–361)

*From the *International Classification of Diseases*, 9th revision.

†Mean number of years exposed, 2.7; mean number of years employed, 12.6.

‡Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records.

§Mean number of years exposed, 0.3; mean number of years employed, 10.7; 12,299 person-years at risk.

¶Mean number of years exposed, 6.8; mean number of years employed, 19.2; 15,136 person-years at risk.

‖SMR equals deaths observed divided by deaths expected and multiplied by 100. Slight differences are due to rounding. Values in parentheses are 95 percent confidence intervals.

**$P<0.05$.

††Person-years at risk and observed deaths are computed from 1960; no deaths occurred before that year.

on death certificates and assigned to the ICD category "malignant neoplasms of connective and other soft tissue." In the cohort, mortality from soft-tissue sarcoma was nonsignificantly higher than in the reference population (four deaths; SMR, 338; 95 percent confidence interval, 92 to 865) (Table 2). The deaths occurred at 2 of the 12 plants, with a significant increase at 1 plant (two deaths; SMR, 1512; 95 percent confidence interval, 183 to 5462). A review of tissue specimens from the four men whose deaths were attributed to soft-tissue sarcoma showed that only two were in fact soft-tissue sarcomas (Cases 1 and 4, Table 3).[33] Mortality from soft-tissue sarcomas was increased significantly in the subcohort of 1520 workers with 1 year or more of exposure and at least 20 years of latency (the high-exposure subcohort) (three deaths; SMR, 922; 95 percent confidence interval, 190 to 2695). Two other deaths in the cohort (Cases 5 and 6) were attributed to soft-tissue sarcoma according to hospital records, and one of them (Case 5) was confirmed by review of a tissue specimen. These two deaths did not contribute to mortality due to soft-tissue sarcoma in our life-table analysis, because the deaths were assigned other ICD codes. We are aware of a seventh death from soft-tissue sarcoma, which occurred in a group of 139 workers with chloracne who were excluded from the cohort because they did not meet the entry criteria.

In the cohort, the SMRs for the other cancers of a priori interest were nonsignificantly increased (Table 2). There were no deaths from nasal cancer, although approximately one was expected. In the high-exposure subcohort, the SMRs were nonsignificantly higher for Hodgkin's disease and stomach cancer and lower for non-Hodgkin's lymphoma and cancer of the liver, biliary passages, and gallbladder (Table 2).

A Posteriori Findings

A small but significant increase in mortality due to all cancers combined was observed in the entire cohort (SMR, 115; 95 percent confidence interval, 102 to 130). In the high-exposure subcohort the SMR was 146 (95 percent confidence interval, 121 to 176) (Table 2). At 9 of the 12 plants, mortality from all cancers combined was increased; at one of these plants the increase was statistically significant. Mortality was significantly higher than expected in the category of cancers of unspecified sites, which included those of rare sites not included in a category of the life-table analysis and those for which no primary site was listed on the death certificate. Hospital records, which were obtained for 96 percent of these cancers, revealed no particular clustering according to site.

The cohort had a nonsignificant increase in mortality from cancers of the trachea, bronchus, and lung (ICD code 162; SMR, 111; 95 percent confidence interval, 89 to 137). Mortality from cancers of the respiratory system (ICD codes 160 to 165) was significantly higher than expected in the high-exposure subcohort (SMR, 142; 95 percent confidence interval, 103 to 192) (Table 2). To estimate the effect of smoking on the increase in lung cancer, the expected number of lung cancers was adjusted according to the smoking prevalence found in lifetime histories obtained in 1987 by interviewing 223 workers from two plants.[25] This adjustment increased the expected number of lung cancers in the overall cohort by 5 percent and in the high-exposure subcohort by 1 percent, which reduced the SMR in the full cohort to 105 (95 percent confidence interval, 85 to 130) and in the high-exposure subcohort to 137 (95 percent confidence interval, 98 to 187).

Analyses According to Duration of Exposure and Employment

The study cohort worked a mean of 2.7 years in processes involving TCDD contamination and 12.6 years at the plants. The high-exposure subcohort worked a mean of 6.8 years in processes involving TCDD contamination and a mean of 19.2 years in total employment at the plants.

The numbers of deaths due to the rare cancers of

Table 3. Deaths from Soft-Tissue Sarcoma among Workers in the Cohort.*

Case No.	Years Employed	Type of Exposure	Year First Exposed	Years Exposed	Year of Death	Latency (yr)†	Cause of Death: Death Certificate	Cause of Death: Hospital Records	Cause of Death: Tissue Review‡
1	1946–1978	TCP and 2,4,5-T	1950	8.8	1978	28	MFH	MFH	MFH
2	1946–1972	TCP and 2,4,5-T	1948	7.1	1972	24	Liposarcoma	Liposarcoma	Carcinoma, poorly differentiated§
3	1950–1975	TCP	1963	1.2	1975	12	Fibrosarcoma	Fibrosarcoma	Renal carcinoma§
4	1951–1982	TCP	1951	14.9	1983	32	MFH	MFH	MFH
5¶	1943–1975	TCP or 2,4,5-T	Intermittent	Unknown	1980	Unknown	Carcinomatosis§	Myxoid neurogenic sarcoma	Leiomyosarcoma
6¶	1941–1964	TCP	1949	Unknown	1965	16	Metastatic osteosarcoma§	Fibrosarcoma	Not available

*Cases 1 through 5 have been previously described.[33] For other previously described cases, records of exposure to TCDD were not available, and the cases were not included in this cohort study. Some information differs slightly from that reported earlier, since additional records were reviewed. Few details about exposure were available for Cases 5 and 6. TCP denotes 2,4,5-trichlorophenol; 2,4,5-T, 2,4,5-trichlorophenoxyacetic acid; and MFH, malignant fibrous histiocytoma.

†Time from first exposure to death.

‡Conducted at the Armed Forces Institute of Pathology.

§Not a soft-tissue sarcoma.

¶Death was not attributed to soft-tissue sarcoma in the life-table analysis.

Table 4. Mortality from All Cancers and from Cancers of the Trachea, Bronchus, and Lung, According to Latency Period and Duration of Exposure to Processes Involving TCDD Contamination.*

Cause/Latency Period	Duration of Exposure (yr)										Test for Trend
	<1		1 to <5		5 to <15		≥15		Overall		
	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	
All cancers											
<10 Yr	10	68	8	71	3	71	0	0	21	70	
10 to <20 Yr	28	109	16	87	18	122	7	340†	69	113	
≥20 Yr	48	102	59	165‡	37	138	18	115	162	129‡	
Total	86	98	83	127†	58	126	25	141	252	116†	
SRR		100		127		123		129			0.3
Trachea, bronchus, and lung											
<10 Yr	3	77	3	95	1	79	0	0	7	84	
10 to <20 Yr	6	69	5	79	9	180	1	137	21	101	
≥20 Yr	17	96	17	126	14	146	9	156	57	123	
Total	26	86	25	109	24	151	10	154	85	112	
SRR		100		109		166		136			0.2

*Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records. The number of observed deaths and the SMRs therefore differ slightly from those in Table 2. SRR denotes standardized rate ratio.

†P<0.05. ‡P<0.01.

a priori interest were too small to permit meaningful analyses according to duration. For all cancers combined and for cancers of the trachea, bronchus, and lung, Table 4 shows the distribution of mortality with increasing duration of exposure to products contaminated with TCDD. The standardized rate ratios were increased in the strata of longer duration for both these categories, but significant linear trends were not found. Mortality increased with increasing latency for both these categories of cancer. Table 5 shows the distribution of mortality for the same categories with increasing duration of employment. Significant linear trends were not observed for either category with increasing length of employment, although standardized rate ratios were higher than expected in several strata of employment ≥20 years. Mortality increased with increasing latency for both categories of cancer.

Serum Levels of TCDD

The mean serum TCDD level, as adjusted for lipids, in the sample of 253 workers from two plants was 233 pg per gram of lipid (range, 2 to 3400) (Fig. 1). A mean level of 7 pg per gram was found in the comparison group of 79 unexposed persons, all of whose levels were under 20, a range found in other unexposed populations.[34] The mean for 119 workers with one year or more of exposure was 418 pg per gram. All the workers had received their last occupational exposures 15 to 37 years earlier.

Discussion

TCDD, widely known as dioxin, has acquired the reputation of a potent carcinogen. Our study, although limited in its ability to detect increased numbers of rare cancers, found little increase in mortality from the cancers associated with TCDD in previous studies in humans. The exception was an increase in soft-tissue sarcoma. The difficulties of evaluating soft-tissue sarcomas in a cohort study of mortality have been described.[33] These include variability in pathological diagnosis and misclassification on death certificates. Consequently, the interpretation of the increased mortality from soft-tissue sarcoma in our study is limited by the small number of cases and the fact that the cause of death was sometimes misclassified on the death certificates of the workers (Table 3) and in the U.S. comparison population.[35]

Several case–control studies have found significant fourfold increases in non-Hodgkin's lymphoma in persons reporting exposure to phenoxy herbicides or chlorophenols, some of which contained TCDD.[6,8] The magnitude of the increase in mortality in the cohort described here (SMR, 137; 95 percent confidence interval, 66 to 254) suggests a smaller increase in this risk, or no increase at all. Mortality was not significantly higher than expected for other cancers of a priori interest — liver and stomach cancers and Hodgkin's disease. No deaths from nasal cancer were observed. The inconsistency between the results reported here and those of earlier epidemiologic studies is accentuated by the longer and probably greater exposure of this cohort to phenoxy herbicides and chlorophenols contaminated with TCDD.

Mortality from cancers of the trachea, bronchus, and lung was nonsignificantly higher in the cohort. Among the workers with 20 years or more of latency, mortality from respiratory cancer was significantly increased in the high-exposure subcohort, which had 1 year or more of exposure (SMR, 142; 95 percent confidence interval, 103 to 192) but not in the subcohort with less than 1 year of exposure (SMR, 103; 95 percent confidence interval, 62 to 161) (Table 2). SMRs for lung cancer are known to be somewhat higher in blue-collar groups than in the general U.S. population because of more cigarette smoking in the blue-collar groups.[36] However, the increased number of lung cancers in the high-exposure subcohort was probably not due to confounding by smoking, for several reasons. First, other diseases related to smoking were not more common than expected in this subco-

Table 5. Mortality from All Cancers and from Cancers of the Trachea, Bronchus, and Lung, According to Latency Period and Duration of Employment at the Study Plants.*

Cause/Latency Period	Duration of Employment (yr) <5 deaths observed	<5 SMR	5 to <10 deaths observed	5 to <10 SMR	10 to <15 deaths observed	10 to <15 SMR	15 to <20 deaths observed	15 to <20 SMR	20 to <25 deaths observed	20 to <25 SMR	25 to <30 deaths observed	25 to <30 SMR	≥30 deaths observed	≥30 SMR	Overall deaths observed	Overall SMR	Test for Trend
All cancers																	
<10 Yr	10	85	1	18	0	0	0	0	0	0	0	0	0	0	11	64	
10 to <20 Yr	21	114	5	126	12	103	8	80	0	0	0	0	0	0	46	105	
≥20 Yr	40	138	15	140	6	70	15	98	34	134	31	116	54	135†	195	125‡	
Total	71	120	21	104	18	89	23	91	34	134	31	116	54	135†	252	116	
SRR		100		99		61		76		128		84		115			0.9
Trachea, bronchus, and lung																	
<10 Yr	3	103	1	74	0	0	0	0	0	0	0	0	0	0	4	94	
10 to <20 Yr	5	82	0	0	5	139	4	122	0	0	0	0	0	0	14	98	
≥20 Yr	11	102	2	51	2	65	3	55	12	133	18	180†	19	126	67	117	
Total	19	96	3	46	7	105	7	81	12	133	18	180†	19	126	85	112	
SRR		100		65		91		89		171		147		98			0.6

*Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records. SRR denotes standardized rate ratio.

†P<0.05. ‡P<0.01.

hort; mortality from nonmalignant respiratory disease (ICD codes 470 to 478 and 490 to 519), which is often associated with smoking, was lower than expected (15 deaths; SMR, 96; 95 percent confidence interval, 54 to 158). Second, in the exposed population with 20 years of latency, whose members presumably shared similar smoking habits, the increase was confined to the high-exposure subcohort. Third, on the basis of empirical evidence from other studies, Siemiatycki et al.[36] have shown that between a blue-collar population and the general U.S. population, confounding by smoking is unlikely to account for an excess risk of more than 10 to 20 percent. Finally, a limited adjustment in the risk of lung cancer,[37,38] based on the smoking prevalence of surviving workers at only two plants, did not substantially change our results.[25] Although confounding by smoking is unlikely to explain the higher rate of respiratory cancer in the high-exposure subcohort, it remains possible that the increase was due to confounding by occupational exposures other than TCDD. For example, asbestos may have contributed to mortality from lung cancer in the cohort, since two deaths were due to mesotheliomas.

An unexpected finding was the small but significant increase in mortality from all cancers combined. The observed increase is consistent with a carcinogenic effect of TCDD. For all cancers combined, mortality was significantly higher than expected in the entire cohort, more pronounced in the high-exposure subcohort, and increased at 9 of 12 plants. With mortality from cancers of the trachea, bronchus, and lung excluded, mortality from all remaining cancers combined was still higher than expected in the overall cohort (SMR, 117; 95 percent confidence interval, 100 to 136) and in the high-exposure subcohort (SMR, 150; 95 percent confidence interval, 118 to 189). Consequently, the increased risk for all cancers combined is not explained by smoking or by increased mortality due to cancer of the trachea, bronchus, and lung. The generation of tumors in a number of organs in animals exposed to TCDD[12,13] and the demonstration that TCDD promoted tumors in two organs[21,22] make it biologically plausible that TCDD may produce tumors in more than one organ in humans. Moreover, a significantly increased SMR for all cancers combined is unusual in occupational studies of chemical workers. Results similar to ours were observed in a study of German workers exposed to TCDD after a 2,4,5-trichlorophenol reactor accident in 1953. A subgroup of workers with chloracne (used as a surrogate for exposure) and at least 20 years of latency had an SMR of 201 (90 percent confidence interval, 122 to 315) for all cancers combined, based on 14 deaths.[39] This is the only other industrial cohort with both substantial exposure to TCDD and a long period of latency during which mortality was examined. Workers from U.S. production cohorts described in previous studies were included in the current study if they met our entry criteria.[40-42]

Two observations argue against a carcinogenic effect of TCDD. First, there was not a significant linear trend of increasing mortality with increasing duration of exposure to products contaminated with TCDD (Table 4). However, our use of duration of exposure may have misclassified the cumulative dose of some workers. In addition, a dose–response relation is generally viewed as strong evidence for an association when it is present, but as fairly weak evidence against an association when it is absent.[43] Second, our study did not directly assess the effect of exposure to TCDD alone. The workers were exposed concurrently to the chlorophenols and phenoxy herbicides that were contaminated with TCDD. In addition, they may have been exposed to numerous other chemicals while employed at the plants.

Because the exposure of our cohort was substantially higher than that of most nonoccupational populations, the estimates of effect in this study may provide an upper level of risk to be anticipated in humans. For several types of cancer previously associated with

TCDD, we found no increases above expected levels. Soft-tissue sarcoma was an exception; a ninefold increase was found among workers who were exposed for 1 year or more and who had at least 20 years of latency. Interpretation of the increased SMR is limited, however, by the small number of cases and because this cause of death was sometimes misclassified on the death certificates of the workers and in the national comparison population. Continued surveillance of the cohort may provide a firmer estimate of risk.

Mortality from all cancers combined was 15 percent higher than expected in the overall cohort. The subcohort with 1 year or more of exposure and 20 years or more of latency had a 46 percent increase in all cancers combined and a 42 percent increase in cancers of the respiratory tract. Although the study could not completely exclude the possible contribution of other occupational carcinogens or smoking, the increased mortality, especially in the subcohort with one year or more of exposure, is consistent with the status of TCDD as a carcinogen.

We are indebted to the National Institute for Occupational Safety and Health statistical clerks, Steve Green, Joyce Godfrey, and others, for their technical contributions; to representatives of the companies and unions for assistance in gathering the data for the study; to our colleagues at the Center for Environmental Health and Injury Control, Centers for Disease Control, for analysis of the serum samples; and to Lawrence Fine, David Brown, and the members of our blue-ribbon review panel for their helpful advice.

References

1. Hardell L, Sandstrom A. Case-control study; soft-tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. Br J Cancer 1979; 39:711-7.
2. Eriksson M, Hardell L, Adami HO. Exposure to dioxins as a risk factor for soft tissue sarcoma: a population-based case-control study. J Natl Cancer Inst 1990; 82:486-90.
3. Eriksson M, Hardell L, Berg N, Moller T, Axelson O. Soft-tissue sarcomas and exposure to chemical substances: a case-referent study. Br J Ind Med 1981; 38:27-33.
4. Hardell L, Eriksson M. The association between soft tissue sarcomas and exposure to phenoxyacetic acids: a new case-referent study. Cancer 1988; 62:652-6.
5. Hardell L, Bengtsson NO. Epidemiologic study of socioeconomic factors and clinical findings in Hodgkin's disease, and reanalysis of previous data regarding chemical exposure. Br J Cancer 1983; 48:217-25.
6. Hardell L, Eriksson M, Lenner P, Lundgren E. Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols and phenoxy acids: a case-control study. Br J Cancer 1981; 43:169-76.
7. Woods JS, Polissar L, Severson RK, Heuser LS, Kulander BG. Soft tissue sarcoma and non-Hodgkin's lymphoma in relation to phenoxyherbicide and chlorinated phenol exposure in western Washington. J Natl Cancer Inst 1987; 78:899-910.
8. Persson B, Dahlander A, Fredriksson M, Brage HN, Ohlson CG, Axelson O. Malignant lymphomas and occupational exposures. Br J Ind Med 1989; 46:516-20.
9. Axelson O, Sundell L, Andersson K, Edling C, Hogstedt C, Kling H. Herbicide exposure and tumor mortality: an updated epidemiologic investigation on Swedish railroad car workers. Scand J Work Environ Health 1980; 6:73-9.
10. Thiess AM, Frentzel-Beyme R, Link R. Mortality study of persons exposed to dioxin in a trichlorophenol-process accident that occurred in the BASF AG on November 17, 1953. Am J Ind Med 1982; 3:179-89.
11. Hardell L, Johansson B, Axelson O. Epidemiological study of nasal and nasopharyngeal cancer and their relation to phenoxy acid or chlorophenol exposure. Am J Ind Med 1982; 3:247-57.
12. Kociba R, Keyes D, Beyer J, et al. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. Toxicol Appl Pharmacol 1978; 46:279-303.
13. National Toxicology Program (NTP). Carcinogenesis bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin (CAS No. 1746-01-6) in Osborne-Mendel rats and B6C3F1 mice (gavage study) 1982. Washington, D.C.: Government Printing Office, 1982. (DHHS publication no. (NIH) 82-1765.)
14. Smith AH, Pearce NE, Fisher DO, Giles HJ, Teague CA, Howard JK. Soft tissue sarcoma and exposure to phenoxyherbicides and chlorophenols in New Zealand. J Natl Cancer Inst 1984; 73:1111-7.
15. Wiklund K, Holm L. Soft tissue sarcoma risk in Swedish agricultural and forestry workers. J Natl Cancer Inst 1986; 76:229-34.
16. Pearce NE, Sheppard RA, Smith AH, Teague CA. Non-Hodgkin's lymphoma and farming: an expanded case-control study. Int J Cancer 1987; 39:155-61.
17. Wiklund K, Dich J, Holm LE. Risk of malignant lymphoma in Swedish pesticide appliers. Br J Cancer 1987; 56:505-8.
18. Olsen JH, Jensen OM. Nasal cancer and chlorophenols. Lancet 1984; 2:47-8.
19. Hardell L, Bengtsson N, Jonsson V, Ericksson S, Larsson L. Aetiological aspects on primary liver cancer with special regard to alcohol, organic solvents and acute intermittent porphyria — an epidemiological investigation. Br J Cancer 1984; 50:389-97.
20. Rao MS, Subbarao V, Prasad JD, Scarpelli DG. Carcinogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the Syrian golden hamster. Carcinogenesis 1988; 9:1677-9.
21. Poland A, Palen D, Glover E. Tumour promotion by TCDD in skin of HRS/J hairless mice. Nature 1982; 300:271-3.
22. Pitot HC, Goldsworthy T, Campbell HA, Poland A. Quantitative evaluation of the promotion by 2,3,7,8-tetrachlorodibenzo-p-dioxin of hepatocarcinogenesis from diethylnitrosamine. Cancer Res 1980; 40:3616-20.
23. Esposito M, Tiernan T, Dryden F. Dioxins. 1980. Cincinnati: Industrial Environmental Research Laboratory, 1980. (EPA publication 600/2-80-197.)
24. Suskind RR, Hertzberg VS. Human health effects of 2,4,5-T and its toxic contaminants. JAMA 1984; 251:2372-80.
25. Fingerhut M, Halperin W, Marlow D, et al. Mortality among U.S. workers employed in the production of chemicals contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). NIOSH Final Report PB91125971. Springfield, Va.: National Technical Information Service, 1990.
26. Sweeney MH, Fingerhut MA, Connally LB, et al. Progress of the NIOSH cross-sectional medical study of workers occupationally exposed to chemicals contaminated with 2,3,7,8-TCDD. Chemosphere 1989; 19:973-7.
27. World Health Organization. International classification of diseases: manual of the international statistical classification of diseases, injuries, and causes of death. Geneva: World Health Organization, 1977.
28. Steenland K, Beaumont J, Spaeth S, et al. New developments in the NIOSH lifetable analysis system. J Occup Med 1990; 32:1091-8.
29. Rothman K, Boice J. Epidemiologic analysis with a programmable calculator. Washington, D.C.: Government Printing Office, 1979:30-1. (DHEW publication no. (NIH) 79-1649.)
30. Rothman KJ. Modern epidemiology. Boston: Little, Brown, 1986:229, 338-9.
31. Fox AJ, Collier PF. Low mortality rates in industrial cohort studies due to selection for work and survival in the industry. Br J Prev Soc Med 1976; 30:225-30.
32. Suit HD. Sarcoma of soft tissue. CA 1978; 28:284-95.
33. Fingerhut MA, Halperin WE, Honchar PA, Smith AB, Groth DH, Russell WO. An evaluation of reports of dioxin exposure and soft tissue sarcoma pathology among chemical workers in the United States. Scand J Work Environ Health 1984; 10:299-303.
34. Patterson DG Jr, Fingerhut MA, Roberts DR, et al. Levels of polychlorinated dibenzo-p-dioxins and dibenzofurans in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Am J Ind Med 1989; 16:135-46.
35. Percy C, Stanek E III, Gloekler L. Accuracy of cancer death certificates and its effect on cancer mortality statistics. Am J Public Health 1981; 71:242-50.
36. Siemiatycki J, Wacholder S, Dewar R, Cardis E, Greenwood C, Richardson L. Degree of confounding bias related to smoking, ethnic group, and socioeconomic status in estimates of the association between occupation and cancer. J Occup Med 1988; 30:617-25.
37. Axelson O. Aspects on confounding in occupational health epidemiology. Scand J Work Environ Health 1978; 4:98-102.
38. Steenland K, Beaumont J, Halperin W. Methods of control for smoking in occupational cohort mortality studies. Scand J Work Environ Health 1984; 10:143-9.
39. Zober A, Messerer P, Huber P. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. Int Arch Occup Environ Health 1990; 62:139-57.
40. Zack JA, Suskind R. The mortality experience of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident. J Occup Med 1980; 22:11-4.
41. Zack JA, Gaffey WR. A mortality study of workers employed at the Monsanto Company plant in Nitro, West Virginia. Environ Sci Res 1983; 26:575-91.
42. Ott MG, Olson RA, Cook RR, Bond GG. Cohort mortality study of chemical workers with potential exposure to the higher chlorinated dioxins. J Occup Med 1987; 29:422-9.
43. Monson RA. Occupational epidemiology. Boca Raton, Fla.: CRC Press, 1990:100.

750 30# 1012082 ATTACHMENT 7
02/10 09:22

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE 4 February 1987

SUBJECT 2,3,7,8-TCDD in Aquatic Environments

FROM Philip M. Cook, Ph.D. PMC
Chief, Hazardous Waste Research Branch, ERL-Duluth

TO Jim Cummings
Office of the Assistant Administrator
for Solid Waste and Emergency Response

This memorandum is provided in response to your request for an update on the state of knowledge concerning 2,3,7,8-TCDD in aquatic environments. A considerable amount of new information is being generated and much will be reported during 1987. Most of the information I can provide results from our own research. I believe you have already received reprints for research results already published.

I reported bioconcentration factor (BCF) determinations for 2,3,7,8-TCDD, 1,2,3,4-TCDD, 1,3,6,8-TCDD and 1,3,7,9-TCDD at the Society for Environmental Toxicology and Chemistry meeting last November. A journal publication is in preparation. The EPA Water Quality Criteria Document presently uses a value of 5000 for the 2,3,7,8-TCDD BCF. We determined a value of 66,000 for carp and 97,000 and 159,000 for fathead minnows at two different exposure concentrations. Our BCF data for the four TCDD isomers is summarized in the attached table. We concluded from this study that ---

1. BCFs for different TCDD isomers vary greatly as expected from field monitoring data.

2. TCDD isomers other than 2,3,7,8-TCDD have lower BCFs than predicted on the basis of structure or log Kow due to more rapid rates of elimination.

3. Differences in rates of metabolism probably explain differences in TCDD rates of elimination and thus BCFs.

4. The gill uptake efficiencies for the four TCDD isomers studied appear to be similar despite structural differences and different uptake rate measurements attributed to large differences in elimination rates.

5. Approximately 90% of the TCDD in the fish exposure water was associated with particulate and dissolved organic matter. Thus, BCFs calculated on the basis of organic carbon free TCDD in the water would be ten times greater.

6. The Water Quality Criteria Document BCF value for 2,3,7,8-TCDD is very low because previously reported BCF determinations were made on the basis of very short exposure periods, inadequate depuration data, static exposure conditions, overestimates of water exposure concentrations, and other factors which lower the estimate of equilibrium fish concentrations with respect to actual water concentrations.

7. 2,3,7,8-TCDD is so toxic to fish that BCF determinations have not yet been made over long exposure periods without toxic effects and mortality occurring. No-effect levels are likely to be less than 10 ppq total 2,3,7,8-TCDD in water and possibly less than 1 ppq if only "dissolved" 2,3,7,8-TCDD is considered in the bioaccumulatable and toxic component.

8. 2,3,7,8-TCDD was lethal to carp at an accumulated dose of 2 ug/Kg. Rainbow trout appear to be a little more sensitive. This toxicity is comparable to the 1 ug/Kg LD50 found for the guinea pig, the most sensitive mammalian species known. Fathead minnows appear to be at least five times less sensitive than carp or rainbow trout.

It is likely that fish bioaccumulation of PCDDs and PCDFs is greatly influenced by food chain links to contaminated sediments and contact time of fish with sediment. Field monitoring data generally supports this premise. For example, fish collected from field surveys when analyzed for all TCDD isomers generally only have detectable amounts of 2,3,7,8-TCDD despite the presence of greater amounts of other TCDD isomers in contaminated sediments. Many of the TCDD isomers have relatively low bioaccumulation potential as seen from our BCF measurements for 1,2,3,4-TCDD and 1,3,7,9-TCDD and thus are not likely to be detected. 1,3,6,8-TCDD, however, would be expected in the fish in detectable levels if uptake from water was the major route for bioaccumulation. The lack of 1,3,6,8-TCDD in the fish is consistent with a kinetic effect involving decreasing amounts of 1,3,6,8-TCDD with respect to 2,3,7,8-TCDD in each step along the food chain to a fish and the absence of significant uptake from water.

For higher chlorinated PCDD and PCDF congeners, differences in elimination rates from fish and their food chain organisms create similar preferential bioaccumulation of 2,3,7,8-substituted planar molecules which are likely to be metabolized at a slower rate. In addition, as molecular weight and size increase with increasing degree of chlorination, it is apparent that the rate uptake from water across the gills decreases. Absorption efficiency from ingested material is also probably less for higher chlorinated congeners.

The net result of the above considerations is that many PCDDs and PCDFs found in sediments are not detectable in fish. The attached table on "Congener Dependent Bioavailability of PCDDs and PCDFs" .

demonstrates how this same effect occurs for laboratory exposure of fish to municipal incinerator fly ash. The effect is more extreme when the "food chain chromatography" effect is present and longer exposure times are involved (much longer time required to reach steady state) as with the fish exposed to sediment in a reservoir. The compounds included in the table are all members of the "biosignificant fraction of PCDDs and PCDFs in that they do appear to bioaccumulate, are all 2,3,7,8-substituted and thus all have significant toxic potential. We developed a simple expression called the "bioavailability index" (BI) for comparing relative bioaccumulation tendencies for different chemicals associated with different solid wastes on sediments. The BI is simply the ratio of chemicals accumulated per gram of fish lipid to the amount present per gram of organic carbon in the solid material the fish are exposed to. The BI can be normalized to a value of 1.0 for 2,3,7,8-TCDD in order to make comparison of the other PCDD and PCDF congener's BIs easier. Although the magnitudes of the fly ash and sediment BIs cannot be directly compared due to great differences in the fish exposures, the normalized BIs for both fly ash and sediment show the same trends. For both PCDDs and PCDFs the normalized BIs decrease as the degree of chlorination increases. There also appears to be a tendency for 2,3,7,8-TCDF to be less bioaccumulable than 2,3,7,8-TCDD. The penta-CDD and -CDF results for the sediment seem divergent and will be rechecked before this data is published in this form. We will soon have much more of this kind of data when results are obtained for Lake Ontario sediments and paper mill sludges.

EPA is frequently faced with the question of what fish TCDD contamination levels will result from known or projected environmental contamination levels. The use of a BCF value, no matter how accurate, for predicting fish residues has a major limitation in that environmental TCDD water concentrations can never be detected even with the most sensitive techniques. Even if water measurements could be made, it would be difficult to determine what fraction of TCDD in water is not associated with dissolved or particulate organic carbon so that a laboratory derived BCF could be applied. An alternative approach is to use expected equilibrium partitioning relationships for sediment and fish to predict maximum levels of fish contamination and rely on site-specific sediment to fish TCDD ratios to determine more realistic "approach to steady-state" relationships likely to exist between sediments and fish. This should be done on the basis of partitioning between organic carbon in sediment and lipid in fish. In theory there should be a simple 1:1 equilibrium relationship between sediment organic carbon and lipid concentrations for very hydrophobic organic compounds such as 2,3,7,8-TCDD which are very slowly metabolized and eliminated from the organism. There are data for compounds such as PCBs which indicate approximately a four-fold preference of these compounds for lipids over organic carbon in sediment. Our 2,3,7,8-TCDD BI value of .27 for sediment is 4X less than the theoretical partitioning value of 1.0 and 16 ~~8X~~ less than the lipid preference value of 4.0 at least in part because steady-state conditions were not reached when the fish were exposed to the sediment.

In many environmental situations expected steady-state relationships between fish bioaccumulation levels and sediment contamination levels will

4

not be reached. Kinetic models and appropriate rate constants are needed to accurately predict fish bioaccumulation levels. When an aquatic ecosystem has a constant input of TCDD so that surface sediment concentrations are relatively constant, fish concentrations will approach a steady-state level dependent on rates of uptake from water, food and contact with sediment. For Lake Ontario we are investigating sediment to fish TCDD ratios under present conditions so that remedial actions for Superfund sites and other sources of TCDD can be evaluated with respect to changes in fish residues which will result in the future. That is, if sediment TCDD levels are decreased or increased in the future through man's activities, we should be able to predict eventual changes in fish contamination levels when a new "approach to steady-state" system results. In Lake Ontario our preliminary data indicates that fish lipids have only about 5% of the TCDD concentration found in the organic carbon fraction of the surface sediments. An extensive survey of sediment and fish TCDD levels throughout Lake Ontario is scheduled for this summer.

CONGENER DEPENDENT BIOAVAILABILITY OF PCDDs AND PCDFs IN FLY ASH AND SEDIMENT

Compound	Fly Ash PG/G Carbon	Fish PG/G Lipid	BI	Normalized BI	Sediment PG/G Carbon	Fish PG/G Lipid	BI	Normalized BI
2,3,7,8-TCDD	1.3×10^5	93	7.4×10^{-4}	1.00	5450	1500	.27	1.00
2,3,4,8-TCDF	1.7×10^5	95	5.7×10^{-4}	.77	5870	300	.06	.22
1,2,3,7,8-PeCDD	1.2×10^6	540	4.3×10^{-4}	.58	1000	60	.06	.22
2,3,4,7,8-PeCDF	7.3×10^5	180	2.5×10^{-4}	.34	190	55	.28	1.04
1,2,3,6,7,8-; 1,2,3,4,7,8-H_xCDD	5.0×10^6	1300	2.6×10^{-4}	.35	5800	200	.04	.13
1,2,3,6,7,8-H_xCDF	8.2×10^5	290	3.5×10^{-4}	.47	560	~~200~~ 12	.04	.14
1,2,3,4,6,7,8-H_pCDD	1.6×10^7	1300	7.8×10^{-5}	.11	71000	340	.005	.018
1,2,3,4,6,7,8-H_pCDF	3.7×10^6	340	9.2×10^{-5}	.12	9400	31	.003	.012

Attachment 8

Environmental Toxicology and Chemistry, Vol. 7, pp. 47–62, 1988
Printed in the USA. Pergamon Journals Ltd.

555

TOXICITY AND BIOCONCENTRATION OF 2,3,7,8-TETRACHLORODIBENZODIOXIN AND 2,3,7,8-TETRACHLORODIBENZOFURAN IN RAINBOW TROUT

PAUL M. MEHRLE,* DENNY R. BUCKLER, EDWARD E. LITTLE, LARRY M. SMITH, JIM D. PETTY, PAUL H. PETERMAN and DAVID L. STALLING
National Fisheries Contaminant Research Center, U.S. Fish and Wildlife Service, Columbia, Missouri 65201

G. M. DE GRAEVE and JAMES J. COYLE
Battelle Laboratories—Columbus, Columbus, Ohio 43201

WILLIAM J. ADAMS
Monsanto, St. Louis, Missouri 63167

(*Received* 25 *March* 1987; *Accepted* 14 *July* 1987)

Abstract—Among the most toxic isomers of polychlorinated dibenzodioxins and polychlorinated dibenzofurans, two groups of toxic aromatic compounds, are 2,3,7,8-tetrachlorodibenzodioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF). We examined the chronic toxicity of these compounds to rainbow trout (*Salmo gairdneri*). The fish (0.38 ± 0.09 g) were continuously exposed in an intermittent-flow proportional diluter for 28 d to 0, 38, 79, 176, 382, and 789 pg TCDD/L (parts per quadrillion) or to 0, 0.41, 0.90, 1.79, 3.93, and 8.78 ng TCDF/L (parts per trillion); exposures to each chemical were followed by a 28-d depuration phase. TCDD had significant effects on survival, growth, and behavior during the exposure and depuration phases. The no observed effect concentration was lower than the lowest exposure concentration of 38 pg/L. The average measured BCF at 28 days was 26,707. The estimated bioconcentration factor at steady-state equilibrium was 39,000 in the lowest exposure concentration where fish were least affected. TCDF, like TCDD, induced similar effects on survival, growth and behavior. The no observed effect concentration, based on survival, was 1.79 ng/L; that based on growth was 0.41 ng/L. The measured bioconcentration factor was 6,049 in fish exposed to 0.41 ng/L, and 2,455 in fish exposed to 3.93 ng/L for 28 d.

Keywords—Dioxin Furan 2,3,7,8-tetrachlorodibenzodioxin (TCDD) Rainbow trout 2,3,7,8-tetrachlorodibenzofuran (TCDF)

INTRODUCTION

Polychlorinated dibenzofurans (PCDFs) and polychlorinated dibenzo-*p*-dioxins (PCDDs) are two groups of toxic compounds composed of 135 and 75 individual isomers, respectively. Certain of these isomers are extremely toxic, particularly those with chlorine substituents in the 2,3,7,8-positions of the aromatic rings. PCDFs occur as trace contaminants in polychlorinated biphenyls (PCBs) and are sometimes formed in significant quantities from pyrolysis or incomplete combustion of PCBs [1]. Isomer specific PCDFs and PCDDs also occur as contaminants in the manufacture and pyrolysis of certain chlorinated phenols [2]. During combustion of these formulations, PCDDs are formed primarily from thermal dimerization and conversion of chlorinated phenoxyphenols, whereas PCDFs are formed from chlorinated diphenyl ethers. PCDDs and PCDFs have also been found in fly ash of municipal waste incinerators [3].

The isomers 2,3,7,8-tetrachlorodibenzodioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF) have been reported as contaminants in fish and sediment. Both have been detected in fish from the Great Lakes [4–6], and residues have been found in resident and migratory fish, crustaceans and sediment in the Chesapeake Bay area [7] and in industrialized and heavily populated areas of the northeastern United States [8]. The concentrations of these compounds in fish vary widely from low pg/g to ng/g quantities, and those of

*To whom correspondence may be addressed.

TCDF are usually higher than those of TCDD. In certain areas of the Great Lakes and the northeastern United States (Newark Bay, Passaic River), TCDD residues in fish and crustaceans exceed the U.S. Food and Drug Administration (FDA) "levels of concern" of 25 pg/g and 50 pg/g, respectively [8,9].

The chronic toxicity and bioconcentration of TCDD and TCDF in aquatic species have not been elucidated. Helder [10,11] reported that exposing fertilized eggs of rainbow trout (*Salmo gairdneri*) for 96 h to TCDD concentrations of 0.1 ng/L significantly decreased the growth of the resulting fry, and that exposing rainbow trout fry for 96 h to 10 and 100 ng/L TCDD retarded growth, caused histological changes in tissues and delayed mortality. Miller et al. [12] reported the toxicity and pathologic changes induced by short-term exposures of guppies (*Poecilia reticulata*) and coho salmon (*Oncorhyncus kisutch*) to TCDD. Coho salmon exposed to 56 pg/L and 1,000 ng/L for 24 h exhibited delayed mortality. Cooper et al. [13] observed delayed development and decreased survival in Japanese medaka (*Oryzias latipes*) exposed to TCDD concentrations of 6 to 500 ng/L. The oral toxicity and metabolism of TCDD in rainbow trout and yellow perch (*Perca flavescens*) were recently reported by Kleeman et al. [14,15]. In rainbow trout exposed for 6 h to 107 ng/L TCDD, followed by a 139-d depuration period, Branson et al. [16] estimated the bioconcentration factor (BCF) to be 9,270 and the elimination half-life to be 58 d. Significant delayed effects were similar to those reported by Miller et al. [12]. No similar studies have been conducted to characterize the toxicity and bioconcentration of TCDF in aquatic species.

Because of the lack of chronic toxicity data involving continuous low-level exposures of fish to TCDD and TCDF, we attempted to measure the chronic toxicity of these two compounds to rainbow trout. Their effects on survival, growth, and behavior were evaluated during a 28-d continuous exposure followed by a 28-d depuration phase. Uptake and depuration kinetics and BCFs for TCDD and TCDF were also evaluated.

METHODS

Test organisms

Eyed eggs of rainbow trout obtained from the Erwin (Tennessee) National Fish Hatchery came from two-year-old spawners of the "Fish Lake" strain; they were transferred to the National Fisheries Contaminant Research Center (NFCRC), Columbia, Missouri, where they hatched on 11 April 1985. About 2,000 swim-up fry produced from the eggs were shipped by air to Battelle Laboratories, Columbus, Ohio, on 2 May 1985. Mortality associated with shipping was less than 5%.

The fish were maintained in reconstituted water in 1,200-liter fiberglass tanks until the study was begun. The fish were held at a temperature of 11°C (±1°C), and were fed Tetramin floating flake food ad libitum. Analysis of the food showed no detectable quantities of TCDD (detection limit, less than 0.06 ng/g), TCDF (detection limit, less than 0.04 ng/g) or other organochlorine compounds.

Experimental approach

A flow-through diluter was used to continuously expose rainbow trout for 28 d to five duplicated concentrations each of [^{3}H]TCDD and TCDF plus duplicated controls. After the exposure period, toxicant input to the exposure chambers was terminated and the fish were held in laboratory water under flow-through conditions in the same test chambers during the 28-d depuration period. The fish were fed Tetramin floating flake food ad libitum throughout the study.

Fifty fish (0.38 ± 0.09 g each) were stocked in each aquarium. Samples of fish for residue analyses were taken on days 7, 14, 21, and 28 of the exposure phase and on day 28 of the depuration phase. To determine initial background concentrations of TCDD and TCDF, 30 fry with no previous TCDD and TCDF exposure history were weighed, measured, frozen, and analyzed for TCDD and TCDF. Fish collected for residue analyses were frozen until the time of analysis.

Daily survival records were maintained throughout the study. In addition, we recorded daily observations of swimming behavior, feeding behavior, location and position in the exposure tank, external lesions, and deformities.

Diluter and toxicant exposure system

The diluter system used in the study was constructed at NFCRC and installed in the West Jefferson Environmental Research Laboratory, Battelle Laboratories, Columbus, Ohio. The system consisted of two separate proportional flow-through diluters in a temperature-controlled waterbath. Both the diluter and waterbath were enclosed in a vented Plexiglas structure to reduce environmental exposures resulting from volatilization of the compounds. Each diluter delivered five concentrations (50% dilutions) of each compound (plus water for controls) into duplicate tanks containing

15 liters of water. Over the course of the study the diluter cycle rate varied between 2.4 and 3.0 cycles per hour; the replacement volume was 500 ml per replicate tank per cycle. The approximate water turnover rate in the exposure tanks was 2.4 times per day. The maximum fish loading in each test tank throughout the study was about 1.3 g/L and the maximum fish loading was 0.5 g/L of water passing through the tank in 24 h. Excess food and fecal matter were removed daily. Daily records of diluter operations were maintained throughout the studies. Nominal exposure concentrations (ng/L) were 0 (control), 0.115, 0.231, 0.463, 0.925, and 1.85 for TCDD; and 0 (control), 1.3, 2.7, 5.3, 10.6, and 21.3 for TCDF. Water temperature in the exposure tanks was maintained at 12 ± 1°C.

The combined effluents from the diluter system were recycled through two columns containing activated charcoal to remove TCDD and TCDF from solution. GC-MS and radiometric analyses were used to monitor the effluent for TCDD and TCDF.

Toxicants

Monsanto Company (St. Louis, MO) supplied the TCDD and TCDF used in the studies. The [^{3}H]TCDD (99+% pure; 22% unlabeled, 42% monotritiated and 36% ditritiated) used had a specific activity of 2.81 × 10^5 dpm/ng (0.128 μCi/ng) as determined by radiometric and GC-MS analyses. The TCDF provided by Monsanto was originally obtained from KOR, Inc. (Cambridge, MA), and was 98+% pure as determined by GC-MS.

Preparation of stock solutions

All glassware used to prepare stock solutions was rinsed several times with reagent-grade solvents. Carrier solvent for the compounds was acetone (Baker-analyzed). The [^{3}H]TCDD was diluted with acetone to a concentration of 36 ng/L. The stock solution was analyzed by GC-MS and by liquid scintillation radiometric analysis. Toxicants were delivered by an automatic pipetting system (Micromedic) that provided 0.05 ml/L or less of acetone to each exposure concentration. The TCDF was diluted with acetone to a measured concentration of 407 ng/L. This stock solution was used throughout the study and was delivered to exposure tanks by Micromedic pipetting systems. The acetone concentration delivered to each tank was 0.05 ml/L or less.

Water chemistry

In an effort to reduce the number of instruments coming in contact with the toxicants, we performed routine water chemistry only on the control chambers of both compounds, and only once during the exposure phase and once during the depuration phase. Alkalinity was measured by potentiometric titration with 0.02 N H_2SO_4 to pH 4.5, and hardness was titrated with EDTA according to standard methods [17]. We used an Orion

Table 1. Concentration of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in exposure water as measured by radiometric and GC-MS analyses

Day	Measurement	TCDD nominal concentration (pg/L)					
		0	115	231	463	925	1,850
1	pg/L (^{3}H)[a]	1.2	31	62	130	280	527
	pg/L (GC-MS)	—[b]					—[b]
7	pg/L (^{3}H)[a]	1.4	41	78	169	359	705
	pg/L (GC-MS)	<25[c]					840
14	pg/L (^{3}H)[a]	1.1	34	69	146	298	606
	pg/L (GC-MS)	<15[c]					730
21	dpg/L (^{3}H)[a]	0.7	41	87	200	466	970
	pg/L (GC-MS)	<15[c]					1,220
28	pg/L (^{3}H)[a]	1.3	44	99	234	507	1,135
	pg/L (GC-MS)	<20[c]					1,400
$\bar{x}$ pg/L (^{3}H) ± SD		1.1	38 ± 5	79 ± 15	176 ± 42	382 ± 101	789 ± 256
$\bar{x}$ pg/L (GC-MS) ± SD		<15[c]					1,048 ± 315

[a]Measured by radiometric analyses for [^{3}H]TCDD. Conversion of dpm/L to pg/L (^{3}H) based on specific activity of 2.81 × 10^5 dpm ^{3}H/ng TCDD.
[b]Not determined.
[c]None detected (less than minimal detectable limits).

digital pH meter to measure pH, a Sybron/Barnstead Model pM-70CB conductivity bridge to measure conductivity and a Varian Model 3700 gas chromatograph to measure ammonia. Water chemistry determinations were as follows: hardness, 153 ppm; alkalinity, 88 ppm; pH, 7.7; conductivity, 215 μohms; un-ionized ammonia, 0.0013 mg/L; and dissolved oxygen, 65 to 85% saturation.

Analyses of exposure water

During the exposure phase of the study, samples for GC-MS analysis were extracted from the TCDD control and highest exposure concentrations and from all TCDF exposure concentrations on days 0, 7, 14, 21, and 28. On each day immediately following the date of sample collection for GC-MS, we took samples for radiometric TCDD analyses from all exposure chambers. Radiometric analyses of all water extracts were conducted at Battelle Laboratories. Water from replicate *A* was sampled on days 0, 7 and 21, and water from replicate *B* on days 1, 14, and 28. On day 7 of the depuration period, the TCDD control and highest concentrations were measured radiometrically, and the TCDF control and highest concentrations were sampled for GC-MS analysis. On day 7 of the depuration phase, only 92 pg/L TCDD was measured in water from the highest TCDD exposure chamber, and 0.56 ng/L TCDF in the highest TCDF exposure chamber. The TCDD and TCDF exposure concentrations measured throughout the exposures are shown in Tables 1 and 2.

Water samples of a volume necessary to provide an adequate amount of analyte were collected from the diluter tanks with solvent-washed glassware and transferred directly to a glass separatory funnel. The water sample was then spiked with the appropriate internal standard solution containing $[^{13}C_{12}]$2,3,7,8-TCDD and $[^{13}C_{12}]$2,3,7,8-TCDF at 4.0 pg/μl in acetonitrile. The water sample was extracted three times with 50-ml portions of methylene chloride (CH_2Cl_2) and the extracts were passed through a column (about 2 × 6 cm) of anhydrous, granular sodium sulfate to break emulsions and remove suspended water. The extract was then rotary-evaporated to a low volume and transferred with three or four portions of CH_2Cl_2 to a glass ampoule, blown to dryness with nitrogen and flame-sealed.

The sample was removed from the opened ampoule with four 1.5-ml portions of 20% CH_2Cl_2 in hexane onto a dual column arrangement of 2 × 0.5 cm 40% H_2SO_4 on silica gel (SA-SG) in the first column and 15 mg Amoco PX-21 activated carbon dispersed in 150-mg glass fibers (CGF) [18]. The efficiency of transfer of $[^3H]$TCDD from these ampoules in the presence of solid residues was determined to exceed 99%. The SA-SG column was then discarded and the CGF column slightly pressurized to move the sample entirely onto the carbon adsorbent. We applied 15 ml CH_2Cl_2 to the CGF column at about 2 ml/min under pressure, and discarded the eluate.

The analyte, either $[^3H]$TCDD or TCDF, was recovered from the CGF by back-flushing with 15 ml toluene. The toluene was removed by rotary evaporation in a waterbath at 65 to 70°C under a 9.8-cm vacuum (sample taken just to dryness).

At this point, we added 2-(4-biphenyl)-6-phenylbenzoxazole (PBBO) to perform radiometric analyses on each sample or aliquots thereof containing $[^3H]$TCDD. The quench curve for counting efficiency was determined by the sealed tritium standard (HAV3612), corrected for decay, as the reference point, and replicate analyses of samples of $[^3H]$TCDD at various quench values. We used the equation, dpm = cpm/0.85 × S, where dpm is disintegrations per minute, cpm is counts per minute and S is the quench value.

Table 2. Concentration (ng/L) of 2,3,7,8-tetrachlorodibenzofuran (TCDF) as measured by GC-MS in exposure water during a 28-d chronic toxicity study with rainbow trout

	TCDF nominal concentration (ng/L)					
Day	0	1.3	2.7	5.3	10.6	21.3
1	0.02	0.38	0.70	1.40	3.20	6.60
7	<0.06	0.33	0.91	1.98	3.84	9.04
14	<0.029	0.44	0.86	1.56	3.82	7.97
21	<0.025	0.37	0.93	1.93	4.19	10.4
28	0.017	0.52	1.10	2.10	4.60	9.9
$\bar{x} \pm$ SD	<0.02	0.41 ± 0.07	0.90 ± 0.14	1.79 ± 0.30	3.93 ± 0.52	8.78 ± 1.53

We applied the sample to alumina (Bio-Rad AG4 acid alumina, 3.5 ml = 3.65 g activated at 190°C) packed in a 5-ml graduated pipet with solvent reservoir using multiple washings of hexane totaling 5.0 ml. The column was then washed with 10 ml 5% CH_2Cl_2 in hexane (discarded) and the analyte recovered with 10 ml 20% CH_2Cl_2/hexane. The sample was evaporated just to dryness by rotary evaporation and transferred with three 1-ml portions of CH_2Cl_2 to a conical vial. The solvent was gently removed under a stream of nitrogen. The sample was then dissolved in a minimum of 5 μl *o*-xylene in preparation for GC-MS analysis.

We carried out the GC-MS analysis on a Finnigan 4023 quadrupole mass spectrometer (EI mode at 35 eV), using a 30 m × 0.25 mm DB-5 (0.25 μm) column (J&W Scientific, Inc., Rancho Cordova, CA) and helium carrier gas at about 35 cm/s. The temperature program was 120°C, hold 1 min, increase 20°C/min to 210°C, 5°C/min to 270°C and 4.5°C/min to 300°C. Selected ions monitored were m/z 304, 306, and 308 summed for 2,3,7,8-TCDF; m/z 316, 318 and 320 summed for [$^{13}C_{12}$]2,3,7,8-TCDF; m/z 320, 322, 324 and 326 summed for [^{3}H]2,3,7,8-TCDD; and m/z 332, 334, and 336 summed for [$^{13}C_{12}$]2,3,7,8-TCDD. We calibrated the internal standard solutions by preparing calibration mixtures of these standards with quantitative standards of native 2,3,7,8-TCDD and 2,3,7,8-TCDF prepared at the NFCRC and 2,3,7,8-TCDD solution as a U.S. Environmental Protection Agency (EPA) quality assurance material (Ref. No. 20603; EPA, Las Vegas, NV). We assumed equal integrated GC-MS responses for the molecular ions of native and [^{3}H]2,3,7,8-TCDD. The level of tritiation of the [^{3}H]2,3,7,8-TCDD computed from the molecular ion abundances measured by GC-MS gave a mole fraction of tritium of 27.3% and a specific activity of 2.15×10^5 dpm/ng. We calculated the specific activity, using the GC-MS–determined concentration and measured activity, to be $2.81 \pm 0.07 \times 10^5$ dpm/ng (triplicate analyses).

Collection of fish for residue analyses

Fish for whole-body TCDD and TCDF residue analyses were collected during the exposure period on days 0 (prior to exposure), 7, 14, 21, and 28, and on day 56 (after 28 d of depuration). When we removed fish from the exposure tanks for residue analyses on day 7, we removed unequal numbers from different tanks to reduce the number of fish remaining in all tanks to 42, and thus reduce the biomass and avoid potential overloading in the exposure tanks.

Fish for residue analyses were collected randomly from the exposure tanks for each toxicant. Individual weights and lengths were measured for fish collected on day 7 of the exposure and on day 28 of the depuration phase. Fish collected on other sampling days were weighed but not measured for length. All fish were blotted dry before they were weighed and were then wrapped in hexane-rinsed aluminum foil, placed in labeled screw-topped glass vials and stored at −10°C until residue analyses were begun.

GC-MS determinations of TCDD and TCDF in fish

Analyses of fish samples were performed by the method of Smith et al. [19]. The GC-MS conditions and spiking procedures were as described above for the analysis of the water samples.

Sample extracts that required radiometric analysis for [^{3}H]TCDD were rotary-evaporated and brought to 10.0-ml volumes; an appropriate aliquot (usually 1.00 ml) was then taken for scintillation counting. The quench values for the aliquots of the fish extracts were uniformly near the minimum (*S* values of 0.65), as observed for analytical standards. Negative and positive control samples were routinely included in the radiometric determinations of [^{3}H]TCDD and established so that there was no procedural background contribution in these determinations.

The internal standard procedure for GC-MS determinations of both [^{3}H]TCDD and TCDF provided internal quality control for overall accuracy of quantitation. In all reported determinations of these analytes, the criteria attained were relative GC retention time (±1 scan number in 1,160 or ±0.001 relative retention units) and correct ion abundances of the three or four molecular ion cluster members (±10% of theoretical value). The limit of quantitation was five times the signal-to-noise ratio and the limit of detection was three times the signal-to-noise ratio. The molecular ion cluster for [^{3}H]TCDD was significantly distorted from that produced by the native populations of ^{35}Cl and ^{37}Cl. Relative ion abundances of m/z 320, 324, and 326 were 24, 75, 100 and 70%, respectively. This pattern remained constant throughout the study, indicating no significant exchange of hydrogen for tritium in TCDD during the exposure. This observation also demonstrated no significant background of native 2,3,7,8-TCDD in any of the samples, because the presence of

native dioxin would have had an easily discernible effect on this pattern. Procedural background controls showed no 2,3,7,8-TCDD (limit of quantitation, less than 0.006 ng/g) by radiometric analysis and no TCDF (limit of quantitation, less than 0.06 ng/g) by GC-MS. The limit of quantitation for [^{3}H]TCDD was also less than 0.06 ng/g by GC-MS.

Analyses of fish food were carried out by the same procedure used for fish samples, and analyses of [^{3}H]TCDD and TCDF stock solutions were performed by direct dilution before analysis.

We computed percent recoveries of [^{13}C]TCDD and [^{13}C]TCDF internal standards by the less precise external standard technique, using the responses of the [^{13}C]TCDD and [^{13}C]TCDF internal standards; the recoveries of [^{13}C]TCDF and [^{13}C]TCDD, respectively, are listed here according to the various matrices: stock solutions, 71 ± 30% and 71 ± 33%; exposure water, 134 ± 55% and 109 ± 52%; fish, 101 ± 37% and 117 ± 46%; all matrices combined, 112 ± 51% and 105 ± 47%.

Determination of total concentration of [^{3}H]TCDD species in fish by biological material oxidation procedure

Determinations of total body burden of [^{3}H]TCDD residues in fish, as opposed to extractable residue, were made on homogenate aliquots of individual fish by the method of total burn, followed by liquid scintillation radiometric analysis of the combustion products. A Harvey Biological Materials Oxidizer (Model OX-100, R. J. Harvey Instrument Corp., Hillsdale, NJ) and a Harvey tritium cocktail (lot No. DC02) were used in the procedure. The combustion/trapping efficiency was 84% with triplicate analyses of a [^{14}C]PCB standard. Cryogenic traps and dry ice and methanol were used to trap the tritiated water produced in the combustion. The combustion/trapping efficiency observed for a standard of [^{3}H]TCDD was 89 ± 3% for spiked fish tissue. The scintillation counting efficiency when the tritium cocktail was used was 37%, and radioactivity was calculated from scintillation analysis using the equation, dpm = cpm/0.64 × S, after subtraction of 50 cpm background.

Samples that had previously been weighed, wrapped in filter paper and aluminum foil and stored in the freezer were transferred along with the approximately 1-cm^2 pieces of filter paper to the quartz combustion boats. Before combustion of samples, we ran a series of blanks and spikes to ensure that performance was satisfactory. Each sample was combusted twice into the cryogenic trap, which contained about 0.5 ml residual methanol. The glass elbow connecting the trap and oxidation chamber was heated with a hot air gun during the procedure to prevent loss by condensation. The condensed residue was transferred from the trap to a scintillation vial with three 5-ml portions of the cocktail. We then washed the trap thoroughly three times with methanol, leaving about 0.5 ml to aid in the next trapping. Because previous tests had indicated that carryover between sample combustions was a potential problem, blank combustions were performed after each sample and control. Scintillation analysis of the blanks showed that carryover was negligible.

Observation of fish for behavioral responses

The behavioral responses of rainbow trout were assessed daily during the TCDD and TCDF exposures. A checklist of behavioral reactions modified from Drummond et al. [20] was used to systematically document and characterize abnormal responses. The responses included coloration, activity (hyperactive, lethargic), excitability by external stimuli (hyperactive, unresponsive), location in aquaria, mode of swimming (head-up, frequent sinking and rising, swimming on side, swimming on back, free swimming), feeding, and morphological observations (bent spine, fin erosion). Observations were made each day by the same observer at the time of feeding.

An aberrant behavioral reaction was recorded when at least one fish in a given treatment responded in a manner that obviously differed from that of controls. Although no attempt was made to quantify the number of fish responding abnormally, an overall measure of the onset, duration and sequence of behavioral changes was made from the systematic daily observations.

Statistical analyses

Daily mortality was analyzed by one-way analysis of variance on the arc-sin transformed values. Differences among means were determined using Fisher's least significant difference (LSD) procedure [21].

Growth as measured by weight or length was analyzed by analysis of variance, including the effects of treatment, replicate within treatment, day, treatment × day, and replicate (treatment × day). Since the replicates, not the individual fish, were the experimental unit, replicate within treatments was used as the error term for testing the effect of treatment, and replicate (treatment × day) was used as the error term for testing the effects of day and treatment × day. We deter-

mined differences among means by calculating a t statistic, using the standard error of the difference for a split-plot design. For growth of TCDD-exposed fish during the depuration phase, we tested the control and lowest exposure concentration groups for equal population means, using a two-sample t test adjusted for unequal variance where appropriate [21].

The cumulative number of days on which fish showed abnormal behavior, from the time of induction to the day of depuration, was analyzed by simple regression against concentration, to provide an estimate of the behavioral responses to chemical exposure.

The BIOFAC computer program [22] was used to estimate the bioconcentration kinetics for TCDD and TCDF. Data from only the exposure phase in each study were used to estimate the kinetics because the number of fish residue samples available during the depuration phase was not adequate. In addition, the fish were held in their original exposure test tanks during the depuration phase, which resulted in the presence of the toxicants in the water because they desorbed from the glass aquaria. Because water concentration measurements and sufficient fish to sample during the depuration phase were not available, we were unable to use data from the depuration phase to estimate rate constants for the toxicants.

To estimate the 56-d LC50 value for TCDD, we computed a multiple-regression model to determine the relationship between percent mortality (arc-sin transformation) to concentration and time of exposure. The linear statistical model contained the effects of linear concentration (CL), days of exposure linear (DL), concentration quadratic (CQ), and day of exposure quadratic (DQ): CL * DL, CL * DQ, CQ * DL and CQ * DQ [21]. We used a quadratic function relationship to estimate the concentration of TCDD at a constant mortality (50%) and period of exposure (56 d).

RESULTS AND DISCUSSION

Mortality

TCDD induced significant mortality in rainbow trout within 14 d of exposure in the highest exposure concentration (789 pg/L), and there was a trend toward increased mortality in fish exposed to 176 and 382 pg/L (Table 3). After 28 d of exposure, significant mortality was evident in the three highest exposure concentrations; the no observed effect concentration (NOEC) was 79 pg/L. Although no mortality was observed, fish in the 38 and 79 pg/L exposure groups were obviously stressed, as judged by reduced growth and behavioral responses. Only rainbow trout in the control group and the three lowest exposure concentrations were observed during the 28-d depuration phase of the study; fish in the two highest exposure concentrations were excluded because the survivors were few and obviously stressed. Significant mortality continued to occur throughout the depuration period in fish previously exposed to 38, 79, and 176 pg/L. There was no apparent recovery in the fish during the 28-d depuration period in clean

Table 3. Cumulative mortality (%) in rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzodioxin (TCDD) for 28 d followed by a 28-d depuration period

	Mean TCDD exposure concentration (pg/L)						
Phase and day	0	38	79	176	382	789	*F* value
Exposure							
7	5	0	1	4	6	10	1.79
14	5	1	1	13	17	33[a]	5.48[b]
21	5	3	9	36[a]	46[a]	74[a]	28.02[b]
28	5	6	18	50[a]	73[a]	85[a]	27.51[b]
Depuration							
7	5	12	64[a]	85[a]	—[c]	—[c]	9.33[b]
14	5	22	78[a]	95[a]	—	—	30.49[b]
21	7	33	83[a]	95[a]	—	—	28.63[b]
28	7	45[a]	83[a]	95	—	—	27.72[b]

[a]Significantly different from controls by least-significant-difference multiple means comparison test ($p < 0.05$).

[b]Significant treatment effect (one-way analysis of variance; $p < 0.05$).

[c]Exposure groups not part of depuration phase.

water. The NOEC of TCDD, based on mortality throughout the exposure and depuration phases, was less than the lowest exposure concentration of 38 pg/L (parts per quadrillion).

Further insight into the NOEC was inferred from the background concentration of 1.1 pg/L of TCDD detected by radiometric analyses in the control group throughout the study. This low background was probably due to volatilization of TCDD and translocation within the diluter system. Mortality in the control group was 5% during the exposure phase and most of the depuration phase. We suggest from these observations that the NOEC was between 1.1 and 38 pg/L. However, the minimal detectable limits for TCDD in water by GC-MS were not adequate to confirm the 1.1 pg/L detected by radiometric analyses.

A 56-d LC50 of 46 pg/L was calculated from the combined mortality data for the exposure and depuration phases. The surface response curve describing the relation among daily mortality, time and exposure concentrations is shown in Figure 1. The quadratic equation describing this relation was used to derive the 56-d LC50.

Significant mortality was induced by TCDF in rainbow trout within 14 d at exposure concentrations of 3.93 and 8.78 ng/L (Table 4). No additional significant mortality occurred throughout the 28-d exposure phase. During the depuration phase, additional mortality occurred only in fish exposed to 8.78 ng/L. The NOEC throughout the exposure and depuration phases was 1.79 ng/L.

Growth

Growth as measured by the weight of the fish was significantly decreased by all TCDD concentrations after 28 d of exposure (Table 5). There were trends of decreased growth within 14 d of exposure, but significant effects in all concentrations were not observed until 28 d of exposure. During the 28-d depuration phase, growth was measured in fish from only the control and the lowest exposure concentration because of the excessive mortality in the higher TCDD exposure concentrations. There was a significant decrease in growth in the fish exposed to 38 pg/L after the 28-d depuration phase. Fish exposed to 38 pg/L TCDD did not grow during the depuration phase, whereas the weight of fish in the control group exhibited an 80% increase. The NOEC of TCDD on growth during the exposure and depuration phases was less than the lowest exposure concentration of 38 pg/L.

TCDF exposure concentrations of 1.79, 3.93 and 8.78 ng/L significantly decreased the growth of rainbow trout within 28 d of exposure (Table 6). There were trends toward decreased growth

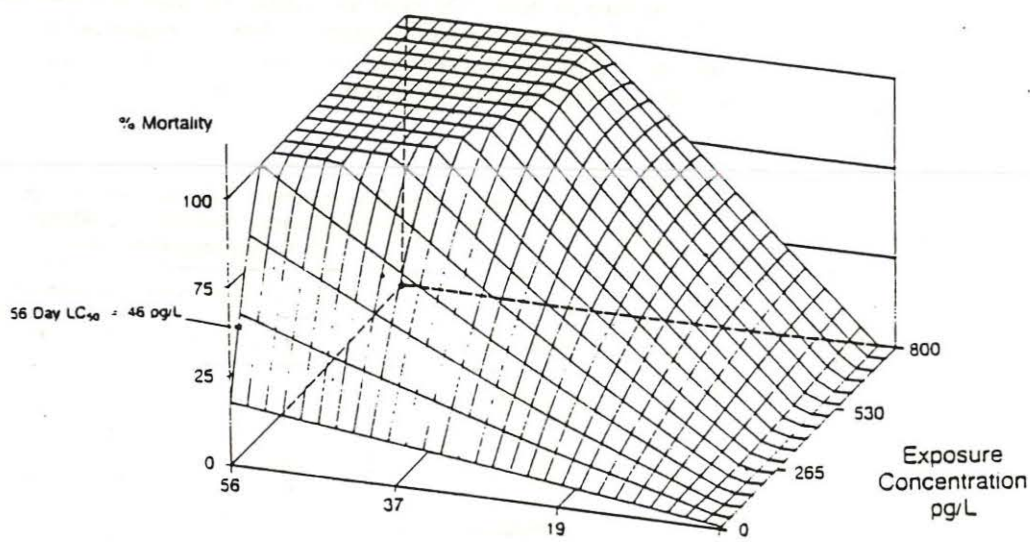


Fig. 1. Surface response describing the relation among daily mortality, time of exposure during the 28-d exposure and 28-d depuration phases, and TCDD exposure concentrations. The quadratic relation was used to derive a 56-d LC50 value of 46 pg/L TCDD for rainbow trout.

Table 4. Cumulative mortality (%) in rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d followed by a 28-d depuration period

Phase and day	Mean TCDF exposure concentration (ng/L) 0	0.41	0.90	1.79	3.93	8.78	F value
Exposure							
7	0	1	1	2	2	12	2.54
14	0	1	3	3	16[a]	22[a]	4.51[b]
21	0	2	5	3	18[a]	23[a]	3.73[b]
28	0	2	6	3	18[a]	28[a]	4.49[b]
Depuration							
7	0	2	6	3	20[a]	37[a]	6.53[b]
14	0	2	6	3	22[a]	46[a]	8.56[b]
21	0	2	6	3	22[a]	46[a]	8.56[b]
28	0	2	6	3	22[a]	46[a]	8.56[b]

[a]Significantly different from controls by least-significant-difference multiple means comparison test ($p < 0.05$).
[b]Significant treatment effect (one-way analysis of variance; $p < 0.05$).

Table 5. Weight (g) of rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzodioxin (TCDD) for 28 d followed by a 28-d depuration period

Phase and day	Mean TCDD exposure concentration (pg/L) 0	38	79	176	382	789
Exposure[a]						
7	0.37	0.36	0.38	0.33	0.36	0.33
14	0.41	0.39	0.42	0.33	0.35	0.40
21	0.48	0.35[b]	0.40	0.39	0.39	0.44
28	0.61	0.53[b]	0.47[b]	0.49[b]	0.45[b]	0.42[b]
Depuration[c]						
28	1.1	0.54[b]	—[d]	—[d]	—[d]	—[d]

Weights are expressed as the mean of 7 to 22 observations.
[a]Analysis of variance used for testing the effects of exposure concentration and time; $F = 2.43$ (time × exposure), $p < 0.03$.
[b]Significantly different from control group (t test; $p < 0.05$).
[c]Fish weight in depuration phase analyzed by t test adjusted for unequal variances.
[d]No measurements made.

after 21 d of exposure but the decrease observed was significant only in the group exposed to 3.93 ng/L. Decreased growth was evident in fish exposed to 0.90 ng/L or more after the 28-d depuration phase. The NOEC for TCDF based on growth during the exposure and depuration phases was 0.41 ng/L. This was the most sensitive response to TCDF.

Behavioral responses

Exposure to TCDD and TCDF induced behavioral impairments that became progressively worse over time and with increasing concentration. The two highest concentrations of TCDD caused behavioral changes within two weeks of exposure that included lethargic swimming, feeding inhibition, and lack of response to external stimuli, for example, waving of hand above aquaria (Fig. 2). Similar changes were evident in all groups exposed to TCDD by the end of the 28-d exposure, whereas the behavior of the controls remained normal. Although significant mortality did not occur in the two lowest exposure concentrations during 28 d of exposure, the fish were seriously stressed, as evidenced by an abnormal head-up swimming posture and confinement to the bottom of the aquar-

Table 6. Weight (g) of rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d followed by a 28-d depuration period

	Mean TCDF exposure concentration (ng/L)					
Phase and day	0	0.41	0.90	1.79	3.93	8.78
Exposure[a]						
7	0.33	0.35	0.37	0.36	0.35	0.32
14	0.39	0.40	0.43	0.42	0.31	0.41
21	0.55	0.47	0.45	0.50	0.39[b]	0.44
28	0.59	0.59	0.53	0.48[b]	0.50[b]	0.46[b]
Depuration[c]						
28	1.1	0.91	0.85[b]	0.80[b]	0.79[b]	0.71[b]

Weights represent the mean of 8 to 24 observations.
[a]Analysis of variance used for testing the effects of exposure concentration and time; $F = 4.37$ (time × exposure), $p < 0.05$.
[b]Significantly different from controls (t test; $p < 0.05$).
[c]Analysis of variance used for testing the effect of exposure concentration; $F = 5.73$ (exposure), $p < 0.03$.

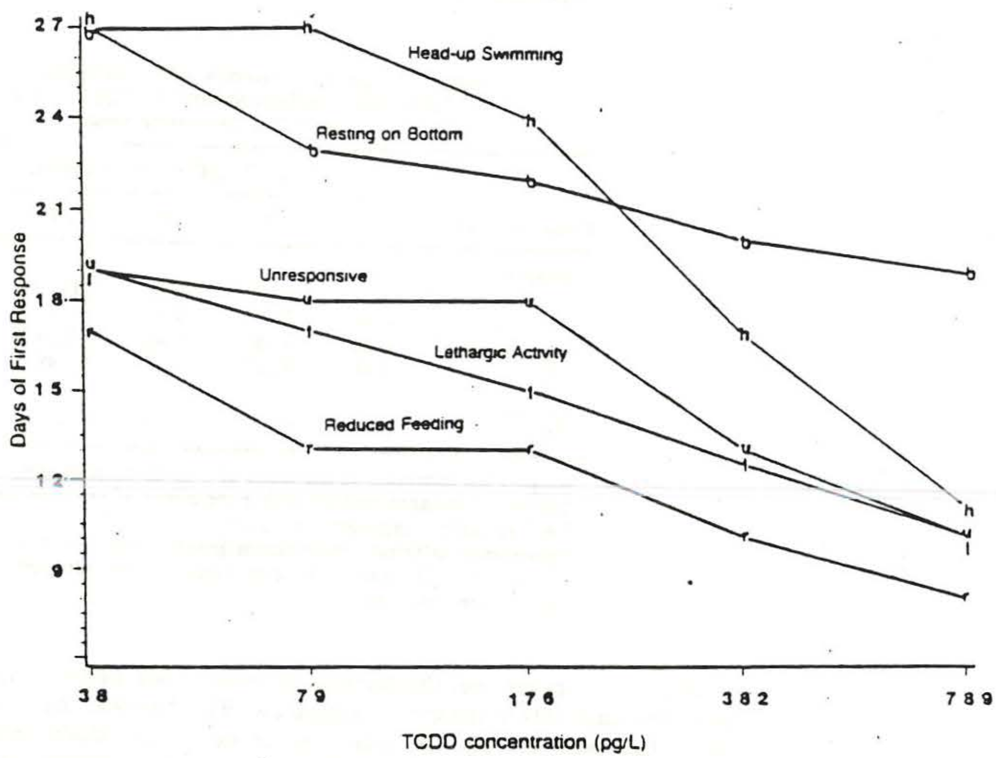


Fig. 2. Days of TCDD exposure required to induce behavioral changes in rainbow trout during a 28-d exposure.

ia. The feeding inhibition and other behavioral changes were not reversed during the 28-d depuration period.

Behavioral reactions similar to those observed in the TCDD exposure were observed in fish exposed to TCDF; however, the responses were of lesser magnitude (Fig. 3). Lethargy, unresponsiveness to external stimuli and diminished feeding

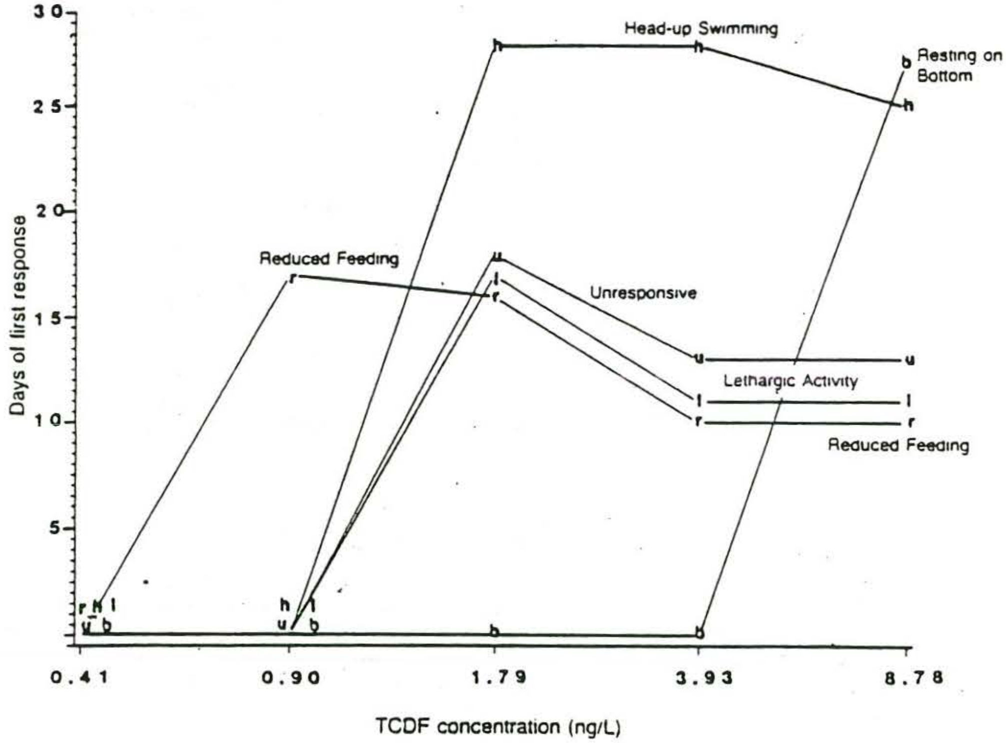


Fig. 3. Days of TCDF exposure required to induce behavioral changes in rainbow trout during a 28-d exposure.

reactions increased significantly in the three highest exposure groups. Recovery of behavioral function was evident in all but the two highest treatment groups by the end of the 28-d depuration period.

Neither TCDD nor TCDF induced observable responses in coloration or morphological characteristics such as scoliosis or lordosis; however, fin erosion was observed in fish in the lowest TCDD exposure concentration at the end of the depuration phase. In addition, exposure to both TCDD and TCDF induced observable, unique characteristics in fecal appearance. The two highest exposure concentrations of each toxicant induced long, stringy faces within the last several days of the 28-d exposure phase.

Bioconcentration

The BCFs for TCDD and TCDF differed greatly during the 28 d of continuous exposure. Whole-body residues throughout the exposure phase were in the low end of a 0.41 to 15.41 ng/g range for TCDD (Table 7). The greater the exposure concentration, the higher were the whole-body residues of TCDD during the 28-d exposures. The measured BCF for TCDD ranged from 8,558 to 28,664 during the exposure and did not appear to reach steady-state equilibrium in any of the exposure concentrations during the 28-d exposure (Table 8). The GC-MS analyses for whole-body TCDD levels agreed closely with the whole-body radiometric determinations for [^{3}H]TCDD. This similarity suggests that the ^{3}H label on the TCDD molecule was not being exchanged, and that the ^{3}H detected in the fish tissue was associated with the parent TCDD molecule. This similarity also indicates that organic extracted [^{3}H]TCDD was not being appreciably metabolized during the exposure and depuration phases. However, as judged by the results of total combustion of fish samples, it appears that about 30% of the ^{3}H label was associated with polar compounds that could have been TCDD metabolites.

Since it was apparent that a steady-state equilibrium for TCDD bioconcentration had not been reached after 28 d of exposure, we used the BIOFAC computer program [22] to estimate the bioconcentration kinetics for TCDD based only on data from the exposure phase. The estimated BCF at steady-state equilibrium was relatively consistent in fish from different exposure concentrations; the

Table 7. Whole-body residues of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout continuously exposed for 28 d followed by a 28-d depuration phase

	Mean TCDD exposure concentration (pg/L)				
Phase and day	0	38	176	382	789
Exposure					
0	[<0.02][a]				
7	0.012[a]	0.41[b] (0.05) [0.38]	1.68[b] (0.15)	3.44[b] (0.20)	6.75[b] (0.37) [6.78]
14	0.022[c]	0.77[b] (0.06) [0.71]	2.81[b] (0.18)	6.22[b] (0.67)	11.67[b] (0.68) [12.3]
21	0.023[d]	0.99[e] (0.03) [0.96]	3.87[b] (0.14)	10.10[e] (1.42) [11.3]	15.41[e] (0.86) [17.6]
28	0.027[a] [<0.02]	0.98[b] (0.05) [0.93]	4.52 (0.41)	10.95[b] (0.87) [10.8]	ND
Depuration					
28	0.22[a]	0.74[b] (0.11) [0.78]	ND	ND	ND

Values (ng/g) represent the mean (with standard deviation in parentheses) of individual fish analyzed radiometrically for [^{3}H]TCDD. Values in brackets represent GC-MS analyses performed on a pooled sample of fish, expressed as ng/g.
ND, not determined.
[a]One observation.
[b]Six observations.
[c]Two observations.
[d]Four observations.
[e]Eight observations.

Table 8. Measured bioconcentration factor (BCF)[a] for 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout exposed continuously for 28 d

	Measured TCDD exposure concentration (pg/L)			
Days of exposure	38	176	382	789
7	10,736	9,551	9,005	8,558
14	20,131	15,966	16,282	14,790
21	25,947	21,977	26,439	19,510
28	25,789	25,670	28,664	ND

[a]BCF = $(C_f/C_w) \times 1{,}000$. ND, not determined.

estimated BCF at 90% steady-state equilibrium ranged from about 37,000 to 86,000 (Table 9). Fish exposed to 382 pg/L showed somewhat different kinetics in that the estimated BCF, time to reach steady-state equilibrium and half-life were greater than in the other exposure concentrations. The relatively low K_2 value, compared with K_2 values from other exposure groups, suggested that metabolic effects may have been reducing the elimination of TCDD.

Ideally, the BCF should be estimated in fish not showing toxicity-induced responses. Inasmuch as the fish exposed to the lowest TCDD concentration of 38 pg/L showed the least toxic responses during the 28-d exposure, we suggest that the predicted BCF of 39,000 is probably the most reliable

Table 9. Estimated bioconcentration kinetics[a] of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout exposed to TCDD for 28 d

Kinetic parameter	TCDD exposure concentrations (pg/L) 38	176	382	702[b]
K_1, uptake rate constant (d^{-1})	1,852 (132)[c]	1,543 (69)	1,337 (61)	1,591 (53)
K_2, depuration rate constant (d^{-1})	0.047 (0.01)	0.041 (0.005)	0.015 (0.005)	0.043 (0.005)
BCF-K_B	39,000 (9,400)	37,560 (5,032)	86,000 (25,000)	36,637 (4,290)
Time to reach 90% steady state (d)	49 (11)	56 (7)	149 (43)	53 (6)
Elimination half-life, $t_{1/2}$ (d)	15 (3)	17 (2)	48 (13)	16 (2)

[a]Estimated kinetics using BIOFAC [22].
[b]Mean of TCDD measurements at days 1, 7, 14 and 21.
[c]Values in parentheses represent standard deviations.

estimate. The range in BCF we observed was substantially greater than the BCF of 7,000 to 9,270 previously reported in the literature [16,23,24]. Results from our study were perhaps better estimates of the equilibrium BCF because we used a continuous exposure in flowing water for a longer period at lower exposure concentrations. Based on the water solubility of 7.9 ng/L for TCDD [25], the predicted BCF would be about 467,000 if the regression equation, log BCF = 2.791 − 0.564 log *S* [26], were used; it would be about 1,000,000 if the regression equation, log BCF = 3.41 − 0.508 log *S* [27], were used.

We suggest from our experimental data that the overall bioconcentration from water to fish is probably much less than the theoretical estimation. The obvious toxicity-induced effects of TCDD, as well as potential influences on membrane transport and other metabolic functions, could account for the observed BCF being less than the theoretical predictions.

The estimated elimination half-life ($t_{1/2}$) from the BIOFAC ranged from 15 to 17 d among exposure concentrations, except for the estimated half-life of 48 d in fish exposed to 382 pg/L. Adams et al. [24] reported an elimination half-life of 15 d, and Branson et al. [16] reported a half-life of 58 d. In the fish exposed to 38 pg/L for 28 d and then held during the 28-d depuration phase, the whole-body residues did not decrease sufficiently to support an estimated half-life in the range of 15 to 17 d (Table 7). The whole-body residues decreased from 0.93 (±0.05) to 0.74 (±0.11) ng/g during the 28-d depuration phase. Excessive mortality in the other TCDD exposure concentrations precluded our obtaining experimental data on elimination in fish exposed to higher concentrations.

The uptake and depuration of TCDF were measured in fish exposed to 0.41 and 3.93 ng/L. In contrast to TCDD kinetics, TCDF uptake reached an apparent steady-state equilibrium after only 7 d of exposure (Table 10). Whole-body residues of TCDF did not increase after 7 d of exposure in fish exposed to 0.41 and 3.93 ng/L. In fish exposed for 28 d, the measured BCF was 6,049 at 0.41 ng/L and 2,455 at 3.93 ng/L (Table 11). The estimated bioconcentration kinetics of TCDF are shown in Table 12. Rainbow trout apparently were able to readily eliminate or metabolize TCDF. The whole-body residues in fish held during the 28-d depuration phase suggested a very short elimination half-life for this compound. Although TCDD and TCDF are structurally very similar, their bioconcentration kinetics and toxicities were found to be very different.

Table 10. Whole-body residues of 2,3,7,8-tetrachlorodibenzofuran (TCDF) in rainbow trout continuously exposed for 28 d followed by a 28-d depuration phase

Phase and day	Mean TCDF exposure concentration (ng/L) 0	0.41	3.93
Exposure			
0	<0.06		
7	0.17	1.63 (0.89)	11.9 (2.88)
14	0.12	1.80 (0.62)	9.30 (2.26)
21	0.19	1.05 (0.44)	10.7 (2.24)
28	0.22	2.48 (1.32)	9.65 (1.30)
Depuration			
28	<0.06	0.09 (0.06)	0.54 (0.08)

Values represent the mean (with standard deviation in parentheses) of four observations performed on individual fish, expressed as ng/g wet weight.

Table 11. Measured bioconcentration factors (BCF)[a] for 2,3,7,8-tetrachlorodibenzofuran (TCDF) in rainbow trout exposed continuously for 28 d

Days of exposure	TCDF exposure concentration (ng/L)	
	0.41	3.93
7	3,976	3,028
14	4,390	2,366
21	2,561	2,730
28	6,049	2,455

[a]BCF = $(C_t/C_w) \times 1{,}000$.

CONCLUSIONS

We conclude that TCDD and TCDF—especially TCDD—are extremely toxic to rainbow trout. A relative comparison of TCDD and TCDF chronic toxicities with those of several other organochlorine compounds demonstrated that TCDD is more than 10,000 times as toxic to fish as either endrin or toxaphene, and that TCDF is about 1,000 times more toxic than either of these insecticides (Table 13). Results from previous toxicity studies with fish by Helder [10,11], Miller et al. [12] and Adams et al. [24] demonstrated the toxicity of TCDD to be in the low ng/L range. However, we have shown that our lowest TCDD exposure concentration of 38 pg/L induced significant adverse effects on survival, growth, and behavioral responses. Results from our studies are perhaps more adequate estimates of TCDD toxicity because we used continuous exposure techniques for a longer time than had been used in previous studies. For similar reasons, we believe the BCF for TCDD derived from our studies is a more accurate estimate of the bioconcentration potential than are the estimates reported by Branson et al. [16] and Adams et al. [24]. Although we showed that TCDD was ex-

Table 12. Estimated bioconcentration kinetics[a] for TCDF in rainbow trout exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d

Kinetic parameter	TCDF exposure concentration (ng/L)	
	0.41	3.93
K_1 uptake rate constant (d^{-1})	1,228 (1,191)	6,852 (8,037)
K_2 depuration rate constant (d^{-1})	0.28 (0.30)	2.60 (3.04)
BCF-K_u	4,449 (6,481)	2,640 (4,379)
Time to reach 90% steady state (d)	8 (9)	0.90 (1.04)
Elimination half-life, $t_{1/2}$ (d)	3 (3)	0.27 (3.1)

Values in parentheses represent standard deviations.
[a]Estimated kinetics using BIOFAC [22].

Table 13. Chronic no effect concentrations (μg/L) for growth and survival of freshwater fish exposed to various organochlorine chemicals

Chemical and fish species	Days of exposure	Survival	Growth[a]	Source
Aroclor 1254, brook trout	118	9.0	9.0	[28]
Chlorodecone, fathead minnows	120	>0.31	>0.31	[29]
Pentachlorophenol (ultrapure), fathead minnows	90	>139	>139	[30]
Toxaphene, brook trout	90	>0.50	0.38	[31]
Toxaphene, channel catfish	90	0.096	0.20	[32]
Endrin, bluntnose minnows	30	0.1	0.1	[33]
TCDD, rainbow trout	56	<0.000038	<0.000038	This study
TCDF, rainbow trout	56	0.00179	0.00041	This study

[a]Change in weight of fish.

tremely toxic to rainbow trout, even our lowest exposure concentration was too high to derive a NOEC.

Acknowledgement – We are grateful to the many people from the Fish and Wildlife Service (FWS), Battelle and Monsanto who assisted in conducting these studies. We especially thank Mr. Dave Zumwalt for his efforts in designing the specialized diluter exposure system, and Mr. Zumwalt and Mr. George Holroyd for their outstanding efforts in constructing and calibrating the system. We appreciate the excellent advice and assistance of Dr. Mark Ellersieck and Ms. Linda Sappington in analyzing the data, and the technical assistance of Mr. Rick Archeski in analyzing the behavioral data. We give special thanks to Dr. Paul Eschmeyer, Editorial Section, Office of Information Transfer, FWS, Fort Collins, Colorado, for his review of the manuscript and for editorial advice.

REFERENCES

1. **Olie, K., M.v.d. Berg** and **O. Hutzinger.** 1983. Formation and fate of PCDD and PCDF from combustion processes. *Chemosphere* 12:627–636.
2. **Firestone, D.** 1972. Determination of polychlorodibenzo-*p*-dioxins and related compounds in commercial chlorophenols. *J. A.O.A.C.* 55:85–92.
3. **Ballschmiter, K., W. Zoller, C. Scholz** and **A. Nottrodt.** 1983. Occurrence and absence of polychlorodibenzofurans and polychlorodibenzodioxins in fly ash from municipal incinerators. *Chemosphere* 12: 585–594.
4. **Petty, J.D., D.L. Stalling, L.M. Smith** and **J.L. Johnson.** 1983. Occurrence and potential impact of PCDF's and PCDD's in aquatic ecosystems. In D.D. Hemphill, ed., *Trace Substances in Environmental Health* – XVII. University of Missouri Press, Columbia, MO, pp. 96–102.
5. **Crummett, W.B.** 1982. Environmental chlorinated dioxins from combustion: The trace chemistries of fire hypothesis. In O. Hutzinger, R.W. Frei, E. Merian and F. Pocchiari, eds., *Chlorinated Dioxins and Related Compounds Impact on the Environment.* Pergamon Press, Elmsford, NY, p. 261.
6. **Ryan, J.J., P.-Y. Lan, J.C. Pilon** and **D. Lewis.** 1983. 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and 2,3,7, 8-tetrachlorodibenzofuran residues in Great Lakes commercial and sport fish. In G. Choudhary, L.H. Keith and C. Rappe, eds., *Chlorinated Dioxins and Dibenzofurans in the Total Environment.* Butterworth, Boston, MA, pp. 87–97.
7. **Columbia National Fisheries Research Laboratory.** 1983. Impacts of contaminants on early life stages of striped bass. In P.M. Mehrle and J.L. Ludke, eds., *Progress Report.* U.S. Fish and Wildlife Service, Columbia, MO.
8. **Belton, T.J., R. Hazen, B.E. Ruppel, K. Lockwood, R. Mueller, E. Stevenson** and **J.J. Post.** 1985. A study of dioxin contamination in select finfish, crustaceans, and sediments of New Jersey Waterways. Office of Science and Research, New Jersey Department of Environmental Protection, Trenton, NJ.
9. **U.S. Food and Drug Administration.** 1981. Correspondence from FDA Commissioner Dr. Arthur Hall Hayes, Jr., to Governor Milliken of Michigan concerning the public health significance of TCDD contaminant "levels of concern" for finfish in Great Lakes. 26 August.
10. **Helder, T.** 1980. Effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on early life stages of the pike (*Esox lucius* L.). *Sci. Total Environ.* 14:255–264.
11. **Helder, T.** 1981. Effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on early life stages of rainbow trout (*Salmo gairdneri*, Richardson). *Toxicology* 19: 101–112.
12. **Miller, R.A., A.N. Logan** and **C.L. Hawkes.** 1979. Toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in aquatic organisms. *Environ. Health Perspect.* 5: 177–186.
13. **Cooper, K.R., J. Schell, P. Kahn** and **M. Gallo.** 1986. The effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on the development and survival of the Japanese medaka (*Oryzias latipes*). *Toxicologist* 6:27 (Abstract).
14. **Kleeman, J.M., J.R. Olson, S.M. Chen** and **R.E. Peterson.** 1986. Metabolism and disposition of 2,3, 7,8-tetrachlorodibenzodioxin in rainbow trout. *Toxicol. Appl. Pharmacol.* 83:391–401.
15. **Kleeman, J.M., J.R. Olson, S.M. Chen** and **R.E. Peterson.** 1986. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin metabolism and disposition in yellow perch. *Toxicol. Appl. Pharmacol.* 83:402–411.
16. **Branson, D.R., I.T. Takahashi, W.M. Parker** and **G.E. Blau.** 1985. Bioconcentration kinetics of 2,3,7, 8-tetrachlorodibenzo-*p*-dioxin in rainbow trout. *Environ. Toxicol. Chem.* 4:779–788.
17. **American Public Health Association, American Water Works Association** and **Water Pollution Control Federation.** 1980. *Standard Methods for the Examination of Water and Wastewater*, 15th ed. American Public Health Association, Washington, DC.
18. **Smith, L.M.** 1981. Carbon dispersed in glass fibers as an adsorbent for contaminant enrichment and fractionation. *Anal. Chem.* 53:2152–2154.
19. **Smith, L.M., D.L. Stalling** and **J.L. Johnson.** 1984. Determination of part-per-trillion levels of dibenzofurans and dioxins in environmental samples. *Anal. Chem.* 56:1830–1842.
20. **Drummond, R.A., C.L. Russom, D.L. Geiger** and **D.L. DeFoe.** 1986. Behavioral and morphological changes in fathead minnow, *Pimephales promelas*, as diagnostic endpoints for screening chemicals according to mode of action. In *Aquatic Toxicology and Hazard Assessment: Ninth Symposium.* American Society for Testing and Materials, Philadelphia, PA, pp. 415–435.
21. **Snedecor, G.W.** and **W.C. Cochran.** 1967. *Statistical Methods*, 6th ed. Iowa State University Press, Ames, IA.
22. **Blau, G.E., W.B. Neely** and **D.R. Branson.** 1975. Ecokinetics: A study of the fate and distribution of chemicals in laboratory ecosystems. *AIChE J.* 21: 854–861.

23. **Isensee, A.R.** 1978. Bioaccumulation of 2,3,7,8-tetrachlorodibenzo-para-dioxin. *Ecol. Bull.* 27:255–262.
24. **Adams, W.J., G.M. DeGraeve, T.D. Sabourin, J.D. Cooney** and **G.M. Mosher.** 1986. Toxicity and bio-concentration of 2,3,7,8-TCDD to fathead minnows (*Pimephales promelas*). *Chemosphere* 15:1503–1511.
25. **Adams, W.J.** and **K.M. Blaine.** 1986. A water solubility determination of 2,3,7,8-TCDD. *Chemosphere* 15:1397–1400.
26. **Kenaga, E.E.** and **C.A.I. Goring.** 1980. Relationship between water solubility, soil sorption, octanol-water partitioning, and concentration of chemicals in biota. In J.G. Eaton, P.R. Parrish and A.C. Hendricks, eds., *Aquatic Toxicology*. STP 707. American Society for Testing and Materials, Philadelphia, PA, pp. 78–115.
27. **Chiou, C.T., V.H. Freed, D.H. Schmedding** and **R.L. Kohnert.** 1977. Partition coefficients and bio-accumulation of selected organic chemicals. *Environ. Sci. Technol.* 11:475–478.
28. **Mauck, W.L., P.M. Mehrle** and **F.L. Mayer.** 1978. Effects of the polychlorinated biphenyl Aroclor 1254 on growth, survival, and bone development in brook trout (*Salvelinus fontinalis*). *J. Fish. Res. Board Can.* 35:1084–1088.
29. **Buckler, D.R., A. Witt, Jr., F.L. Mayer** and **J.N. Huckins.** 1981. Acute and chronic effects of Kepone and mirex on the fathead minnow. *Trans. Am. Fish. Soc.* 110:270–280.
30. **Cleveland, L., D.R. Buckler, F.L. Mayer** and **D.R. Branson.** 1982. Toxicity of three preparations of pentachlorophenol to fathead minnows: A comparative study. *Environ. Toxicol. Chem.* 1:205–212.
31. **Mayer, F.L., P.M. Mehrle** and **W.P. Dwyer.** 1975. Toxaphene effects on reproduction, growth, and mortality of brook trout. EPA-600/3-75-013. U.S. Environmental Protection Agency, Duluth, MN.
32. **Mayer, F.L., P.M. Mehrle** and **W.P. Dwyer.** 1977. Toxaphene: Chronic toxicity to fathead minnows and channel catfish, EPA-600/3-77-069. U.S. Environmental Protection Agency, Duluth, MN.
33. **Mount, D.I.** 1962. Chronic effects of endrin on bluntnose minnows and guppies. U.S. Fish and Wildlife Service Research Report No. 58, Washington, DC.

Attachment 9

ASSESSMENT OF THE HUMAN HEALTH RISKS RELATED TO THE PRESENCE OF DIOXINS IN COLUMBIA RIVER FISH

Prepared by:

Russell E. Keenan, Ph.D.
Alan H. Parsons, Ph.D.
Ellen S. Ebert
Pamela D. Boardman, M.P.H.
Steven L. Huntley
Mary M. Sauer, M.S.P.H.

ChemRisk™
A McLaren Company
1685 Congress Street
Stroudwater Crossing
Portland, ME 04102
(207) 774-0012
(207) 774-8263

January 8, 1990

ChemRisk
A McLaren Company

An exposure pathway consists of four necessary elements: a source and mechanism of chemical release into the environment, an environmental transport medium for the released chemical, a point of potential human contact with the environmental medium, and a human exposure route (eg., inhalation, dermal contact, ingestion) at the point contact. Each pathway describes a unique potential mechanism by which a population or an individual may be exposed to a chemical. For each exposure pathway, the environmental fate and persistence of the chemical from the point of discharge to the point of human contact is an important consideration. Many factors such as adsorption onto particulates, sedimentation, and solubility influence the degree of human exposure. These factors are highly variable in the environment. Consequently, a truly valid exposure assessment can only be conducted using site-specific data. To this purpose, a study of the levels of dioxin in the edible portions of Columbia River fish has been conducted. Additionally, the rates of consumption of locally caught fish were estimated.

Columbia River fish sampling

For the purpose of determining accurate species-specific concentrations of dioxin in edible fish fillets, a variety of species of fish were collected from six different sites along the Columbia River system by an independent laboratory and consultant. A total of 680 individual fish were sampled at the six sites. Species collected included top and bottom feeders as well as resident and anadromous populations. Migratory fish sampled included coho salmon, fall chinook salmon (upriver and tule) and summer steelhead trout. Resident species sampled included white sturgeon, largescale sucker, and carp. Results of sampling data are reported below[1].

Fillet TCDD Levels in Columbia River Fish (ppt)

	Sampling Site					
Species	1	2	3	4	5	6
Coho salmon	0.08	0.10	NS	NS	NS	NS
Fall chinook salmon (Upriver)	0.08	0.09	NS	NS	NS	NS
Fall chinook salmon (Tule)	0.31	0.18	NS	NS	NS	NS
Summer steelhead trout	0.07	0.07	NS	NS	NS	NS
White sturgeon	0.09	0.12	1.09	0.88	1.68	0.55
Largescale sucker	0.32	NS	0.39	0.19	0.22	0.26
Carp	0.79	NS	1.06	1.35	1.46	0.76

At Sites 1 and 2, located downstream of NWPPA pulp and paper mills, the geometric mean concentrations of TCDD in salmon ranged from 0.08 to 0.31 parts per trillion (ppt) and steelhead trout averaged 0.07 ppt. Sturgeon, sucker, and carp collected from sites 1, 2, 3, and 4 had fillet TCDD levels averaging

1 Note: 80% of the anadromous and 45% of all species sampled had nondetectable levels of TCDD. Nondetectable samples were assigned a value equal to one half the limit of detection per EPA protocol. This results in a more conservative estimation of tissue TCDD levels because actual values could equal zero.

DRAFT Attachment 10

ANALYSIS OF THE POTENTIAL POPULATIONS AT RISK FROM THE CONSUMPTION OF FRESHWATER FISH CAUGHT NEAR PAPER MILLS

Craig McCormack
Office of Policy Planning and Evaluation

David Cleverly 202-382-7891 (D.C)
Office of Research and Development

April 23, 1990

INTRODUCTION:

OTS, OSW, and OW have conducted a detailed human and ecological risk assessment of environmental loadings of dioxin from bleached pulp and paper mills. In that analysis only maximum lifetime cancer risk and average lifetime cancer risk to the hypothetically exposed individual was estimated for various exposure scenarios. No estimation of potential population risk, especially to sensitive subgroups, was provided in the analysis. Since draft publication of these results, we have identified populations of Asians, and tribal Native Americans that reside along the banks of the Columbia River in Oregon. The State government indicates that there are eight bleached pulp and paper mills that directly discharge to the Columbia River. The State also indicates that freshwater fish caught from the Columbia river are the main source of animal protein for these people. They consume an average of 100 to 150 grams of fish flesh each day over the course of the year. These individuals are much more likely to catch and consume fish that has been contaminated with dioxin from the effluent discharged from the mills than other populations in the area. The Native Americans number about 15,000, and the Asians number about 30,000 people.

In addition to these subpopulations exposed by diet to dioxin, we have estimated that approximately 610,000 people living in the vicinity of pulp and paper mills have family incomes at or below the poverty level. These individuals are also expected to derive a significant portion of animal protein from both subsistence and sports fishing in rivers near paper mills. Subsistence fishermen consume about 100 grams of fish per day/1, and sports fishermen consume about 69 grams fish per day/2.

For purposes of the assessment of potential cancer risk, we have employed monitoring data of dioxin contamination in fresh water fish caught in the vicinity of bleached pulp and paper mills. This was developed by the Environmental Research Laboratory in Duluth Minnesota as part of the National Bioaccumulation Study of freshwater fish in the U.S. The range of detected TCDD equivalent concentration in the edible fish fillet was from 0.1 ppt - 24 ppt. The weighted

average fillet concentration was 6.5 ppt (6.5 pg/gm). For purposes of estimating incremental lifetime cancer risk to the most exposed individual, a fillet concentration of 24 ppt was used. The weighted average dioxin concentration in the fillet of 6.5 ppt was used to derive the approximate average lifetime risk to subsistence and sports fishermen. The average exposure and average lifetime risk was used to estimate the annual cancer incidence in these sensitive subpopulations. In addition a human body weight of 70 kilograms was assumed to compute estimates of excess cancer risk.

CONCLUSIONS:

It is currently not possible to directly measure the association between the chronic dietary intake of dioxin contaminated freshwater fish, and the occurrence of specific forms of cancer in the exposed populations. The epidemiologic studies of these populations with a high dependency for subsistence fishing as a source of dietary animal protein have not been conducted. Therefore we have mathematically estimated lifetime excess cancer risk to the population residing near the Columbia River, as well as to low-income populations living in the vicinity of other mills in the U.S. This analysis is not intended to replace any previous risk assessments involving the human consumption of fish that has been contaminated with dioxin from the effluent discharged from paper mills, but is merely to illustrate that methodologies can be developed to estimate total populations at risk in the U.S.

The following are the results:

	Pop.	MIR(a)	AVG Risk(b)	Cancer Inc.(c)
Native Americans	15,000	8.6×10^{-3}	1.5×10^{-3}	0.33
Asian Americans	30,000	8.6×10^{-3}	1.5×10^{-3}	0.67
Total Risk	45,000	8.6×10^{-3}	1.5×10^{-3}	1.0
Low income families	**610,000**	5.4×10^{-3}	1.0×10^{-3}	9.3

(a) MIR is the maximum individual risk, and is associated with the highest fish consumption rate and the highest dioxin concentration in fish caught near paper mills.

(b) Average lifetime cancer risk is the excess cancer risk based on the average fish consumption rate for subsistence and sports fishermen, and the weighted average dioxin concentration in fish caught near paper mills.

(c)Cancer incidence is the estimated number of cancer cases per year within the

defined exposed population. This was computed using average lifetime risk.

1/ U.S. Environmental Protection Agency (1988). Risk Assessment for Dioxin Contamination Midland, Michigan. Region 5. EPA-905/4-88-005.

2/Estimated consumption by the U.S. Food and Drug Administration, assuming substitution of average U.S. population daily consumption of red meat with fish.

Calculations of Risk

1. Native Americans

Assumptions:

a. MEI consumes 150 gms fish/day.
b. Average consumption is 100 grms fish/day.
c. 70 kilogram person.
d. Lifetime exposure.
e. Max. dioxin concentration in fish fillet = 24 pg/gm.
f. Weighted average dioxin in fish fillet = 6.5 pg/gm.
g. Population of 15,000.
h. Risk Specific Dose of Dioxin = lifetime cancer risk of one in a million is: 0.006 pg/kg/day.

Max. Daily Dose= (150 gms/day X 24 pg/gm) / 70 kg person
= 51.43 pg dioxin/kg/day

MIR ={(51.43 pg/kg/day) / (0.006 pg/kg/day)} X 10^{-6}
MIR = 8.6 X 10^{-3}

Avg. Daily Dose= (100 gms/day X 6.5 pg/gm)/ 70 kg person
= 9.28 pg dioxin/kg/ day

Avg. lifetime risk = {(9.28 pg/day)/(0.006 pg/kg/day)} X 10-6
= 1.5 X 10^{-3}

Annual Cancer Incidence = (Avg risk * population)/ 70 year lifespan
= (1.5 X 10^{-3} * 15,000)/ 70 yrs
= 0.33

2. Asian Americans

Assumptions are the same as with Native Americans. The population size is

MEI = maximally exposed individual

30,000.

Max. Daily Dose = 51.43 pg dioxin/kg/day.
MIR = 8.6 X 10-3

Avg. Daily Dose = 9.28 pg dioxin/kg/day
Avg. lifetime risk = 1.5×10^{-3}

Annual Cancer Incidence = (1.5×10^{-3} * 30,000)/70 yr lifespan
= 0.67

3. <u>Low income families.</u>

Assumptions:

a. MEI consumes 100 gms fish/day.
b. Average consumption is 69grms fish/day.
c. 70 kilogram person.
d. Lifetime exposure.
e. Max. dioxin concentration in fish fillet = 24 pg/gm.
f. Weighted average dioxin in fish fillet = 6.5 pg/gm.
g. Population of 610,000.
h. Risk Specific Dose of Dioxin = lifetime cancer risk of one in a million is: 0.006 pg/kg/day.

Max Daily Dose = (100 gms/day) X (24 pg dioxin/gm)/ 70 kg person
= 34.28 pg dioxin/kg/day

MIR = {(34.28 pg/kg/dy)/(0.006 pg/kg/dy)} X 10^{-6}
= 5.7×10^{-3}

Avg. Daily Dose = (69 gms/day) X (6.5 pg/gm)/70 kg person
= 6.41 pg dioxin/kg/day

Avg. lifetime risk = { (6.41 pg/kg/dy)/(0.006 pg/kg/dy)} X 10-6
= 1.0×10^{-3}

Annual Cancer Incidence ={ (1.0×10^{-3}) * (610,000)}/ 70 year lifespan
=9.3

The Bottom Line:

• The "Forest through the trees" is that the environmental loadings of dioxin from the mills may result in high levels of risk to humans.

• The analysis of the regulatory options suggests that this particular industrial source category fits the mold for a regulatory pollution prevention initiative through use of the CWA, TSCA, and RCRA.

* could require substantial reduction in the overall use of chlorine
* BACT seems to be oxygen delignification

OREGON
INSIDER
A BIWEEKLY DIGEST OF ENVIRONMENTAL NEWS

Inside the Dioxin Standard: Is it Defensible?

CONTENTS

■ The Environmental Quality Commission (EQC) will decide Nov. 2 whether to hold public hearings on a complex proposal to update the state's water quality standards. The proposal covers an enormous number of topics including a new "anti-degradation standard" to protect pristine waterways, a new "wetlands" definition, and new standards for dissolved oxygen, bacteria, toxic pollutants, particulate matter and bacteria (see Issue 20).

Tucked somewhere in the middle of the package, the Department of Environmental Quality (DEQ) has proposed to keep unchanged the current and seemingly incomprehensible water quality standard for dioxin: 0.013 parts per quadrillion (ppq). In addition, the agency has for the first time proposed a standard limiting the amount of dioxin that can accumulate in fish tissue. Both proposals are sure to draw the attention of the pulp and paper industry and environmentalists.

Industry representatives have long questioned the scientific underpinnings of the dioxin standard. They have even challenged the assertion that dioxin poses any threat to human health or the environment, comparing it to broccoli in one study. On the other hand, environmentalists see a standard that leaves completely unregulated hundreds of closely related toxic organo-chlorine compounds that are discharged from bleach kraft pulp mills every day. Based only on protecting human populations from cancer, they also see a standard that ignores documented impacts on fish and wildlife and fails to address non-cancerous affects on human health such as reproductive interference and immune system suppression.

Each side contends that the standard for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) -- the only compound regulated by DEQ's dioxin standard -- should be changed in some way. For now, DEQ has decided to keep the standard as it is.

The standard "answers" a very narrow question for DEQ and the public: How much 2,3,7,8-TCDD can exist in the water column without creating more than a 1-in-a-million cancer risk?

The standard does not regulate the amount of dioxin in river bottom sediments, where a seemingly significant percentage of these insoluble compounds settle. It does not take into account the natural loss, or "attenuation," of dioxin through breakdown and binding with particles suspended in the water column. And, since compliance with the standard is measured down river at the edge of the "mixing zone," it isn't even used to directly regulate the amount of dioxin coming out of pulp mill discharge pipes.

There are significant gaps in the scientific understanding of this toxin and in the regulatory mechanism by which it is controlled. While it is impossible to resolve the many questions surrounding dioxin, it is not particularly difficult to understand the guts of the standard and how the federal government came up with the result of 0.013 parts per quadrillion.

An Understandable Formula

For all the rhetoric, battling experts, and discussions of "linearized multistage models," "LD_{50} values" and all the rest, the standard is surprisingly understandable. The Environmental Protection Agency developed the dioxin standard using a relatively simple formula that includes six factors:

$$\text{Dioxin Standard} = \frac{\text{RISK} \times \text{WT}}{[\text{WCR} + (\text{BCF} \times \text{FCR}) \times \text{CPF}]}$$

The Six Factors

RISK: The cancer risk society is willing to tolerate from dioxin.

WT: The weight of the average adult.

WCR: The amount of water ingested by the average person each day – called the water consumption rate.

BCF: The extent to which fish concentrate dioxin in their tissues by swimming in contaminated water – called the bio-concentration factor.

FCR: The amount of fish ingested by the average person each day – called the fish consumption rate.

CPF: The chemical's cancer potency, a measure of how harmful the toxin really is – called the cancer potency factor.

The Overall Debate

Agency officials, industry representatives and environmentalists seem to agree that the formula itself is scientifically defensible. The debate rages over what numbers go into the formula and to many broader issues surrounding dioxin regulation.

EPA/DEQ Numbers

Through laboratory tests and simple assumptions, EPA assigned values to each of these factors, plugged them into a formula, and came up with the dioxin standard. DEQ adopted all of EPA's recommended values. With estimates of potential compliance costs running in the hundreds of millions of dollars and predictions of disastrous human health and environmental impacts, there is a surprisingly high degree of "play" in the numbers used to calculate the final standard. As a result, experts on both sides have been free to tweak the

THE EPA/DEQ NUMBERS:

RISK	1-in-a-million
WT	70 kilograms*
WCR	2 liters/day
BCF	5,000
FCR	6.5 grams/day*
CPF	156,000

* 6.5 grams per day is about ¼ of an ounce of fish. 70 kgs is about 155 pounds.

OREGON INSIDER (ISSN 1043-7142) is published biweekly (twenty-four times a year) as a news service of the Oregon Environmental Foundation, 2637 SW Water Avenue, Portland, Oregon 97201 (503) 222-2252. The Foundation is a non-profit corporation dedicated to education and research. Executive Editor: Peter A. Ravella, OSB No. 86264. Staff Writers: Jeff Bernstein & Sarah McCoy. Business Manager: Greg Tozian. Advisory Board Members: Roy Hemmingway, Consultant; Margaret Kirkpatrick, Attorney, Stoel, Rives, Boley, Jones & Grey; Judy Roumpf, Publisher, Resource Recycling magazine; Connie Taylor, Associate, HartCrowser; Dan Saltzman, President, Environmental Management Solutions and Diane Dimon Snow, Assistant to Earl Blumenauer. Subscription Rates: $245 per year including first-class delivery, $135 for private, non-profit 501(c)(3) organizations. Multiple subscription rates available. Letters to the Editor and comments welcome at above address.

numbers to better fit their view of the relative risks and benefits of dioxin regulation.

Three of the six factors are generally accepted and attract little attention. These are the water consumption rate, body weight, and the acceptable risk (RISK) determination.

THE "ACCEPTED" NUMBERS

WCR - 2 liters/day

Water Consumption Rate (WCR). Because of how the formula works, this factor has virtually no affect on the final standard and consequently draws little attention. If DEQ were to eliminate drinking water as a route of dioxin exposure altogether -- and plug in a "0" for the WCF -- the final standard would not change.

WT - 70 kilograms

Body Weight Factor (WT). EPA used 70 kilograms for the body "weight" factor. At about 155 pounds, this seems to be a pretty good approximation of the average adult's weight. The dioxin standard would be stricter if the agency plugged in a smaller number for body weight. For example, had EPA used 50 kilograms -- about 110 pounds -- the final dioxin standard would be .009 PPQ instead of .013 PPQ.

All else being equal, people weighing less than 155 pounds, such as children and women would, on average, face a slightly greater risk of cancer than their heavier counterparts under the .013 PPQ standard.

RISK - 1-in-a-million

Acceptable Cancer Risk (RISK). There is no magic behind DEQ's decision to base the state's dioxin standard on a 1-in-a-million cancer risk. It is not mandated by federal or state law; it is a policy decision. According to Lydia Taylor, administrator of the Water Quality Division, all DEQ water quality standards have been based on this risk level since 1987.

1-in-10-million?

Reasonable people differ whether it would be appropriate to set environmental regulatory policy on a less demanding cancer risk limit. John Bonine, a professor of environmental law at the University of Oregon, questioned whether the general population should be subjected to any greater cancer risk for the sake of industry profits. "EPA has developed guidance for dioxin based on a 1-in-10-million cancer risk. Oregon is free to adopt it but hasn't," he said.

A standard based on a 1-in-10-million cancer risk would be ten times tougher than the current one, or .0013 PPQ.

1-in-10,000?

According to Doug Morrison, environmental counsel for the Northwest Pulp & Paper Association, using a 1-in-a-million cancer risk level can be overly protective. Morrison said it would be statistically sound to accept cancer risks as high as 1-in-100,000 or 1-in-10,000 for certain sub-populations -- such as Native Americans, Asians and recreational fisherman who eat more river fish -- because there are fewer than 1 million in the group. "You can allow a higher risk factor for these smaller groups and still not cause any additional cancers," he said.

Other States Vary

At least one other state has decided to accept greater risks. Maryland's dioxin standard is based on a 1-in-100,000 cancer risk and is 1.2 PPQ, about 100 times less stringent than Oregon's.

DEQ Uses 1-in-a-million

Because DEQ's Water Quality Division has uniformly set its standards based on a 1-in-a-million cancer risk, it seems unlikely that the state would follow Maryland's lead. The EQC has made it an agency-wide goal to apply a uniform risk level to all regulatory programs, but that level has not been defined, (see DEQ 1990 "Strategic Plan."

THE "CONTROVERSIAL" NUMBERS

The remaining three factors — fish consumption (FCR), cancer potency (CPF), and bio-concentration (BCF) — have attracted the most debate for a couple of reasons. Not only do these factors have the greatest impact on the final standard, but the information on them is less developed. The bio-concentration and cancer potency numbers are based on laboratory studies that remain open to interpretation in the scientific community. Definitive surveys on consumption of Columbia River fish have not been done.

FCR: Who Does the Standard Protect?

Fish Consumption Rate (FCR). The debate over this factor is not complicated. Because different people eat different amounts and kinds of fish, a simple question arises: What single number best represents the public's average fish consumption? The answer may be, "There isn't one."

EPA's Number

In adopting the dioxin standard, DEQ accepted EPA's estimate that the average person consumes 6½ grams of freshwater or estuarine fish per day. That's a little less than one-quarter of an ounce per day, or about 5 pounds of fish and shellfish per year. According to Gene Foster, DEQ's expert on the dioxin standard, EPA based its estimate on a limited nationwide market survey of consumer buying habits.

Complete Data is Unavailable

"Complete fish consumption data has not been compiled specifically for the Columbia River system — where the pulp mills discharge their effluent — or for the fish most commonly consumed," said Foster. With the help of the Columbia River Intertribal Fish Commission, EPA is studying the diets of Native Americans along the river. Results could be available by year's end.

Accounting for Sub-Groups

Foster said differences between identifiable sub-groups cannot be overlooked when compiling fish consumption data. Native Americans — particularly those living along the river — Asians, commercial and recreational fisherman, and low-income subsistence fisherman all eat more fish than the general population.

FCR Range: 6.5 to 150 g/day

According to a preliminary risk assessment done by EPA this Summer, members of some sub-groups along the Columbia consume as much as 100 to 150 grams or about 3½ to 5¼ ounces of fish per day. "These rates are not off the wall," added Foster.

Industry says 13 - 16 g/day

Even the Northwest Pulp and Paper Association (NWPPA) — an industry trade group — acknowledges that EPA's 6.5 g/day figure is too low. The NWPPA estimates that recreational fisherman and Native Americans eat a little more than 13 and 16 grams of fish per day, respectively.

Most Agree 6.5 g/day is Low

The table at right shows how the dioxin standard would change if higher fish consumption numbers were plugged into the formula. No one claims that the average fish consumption rate in the Northwest is less than the 6.5 g/day. While

HOW MUCH FISH DO YOU EAT?

Grams Per Day	No. of 6 oz. Meals / Wk.	New Standard*
6.5	.2	0.013
10	.4	0.089
25	1.0	0.0035
50	2.0	0.0017
75	3.0	0.0012
100	4.0	0.0009
150	6.0	0.0006

* This is how the standard would change if DEQ used a higher FCR.

individuals may consume as much as 150 g/day, the overall average for the population would be lower.

BCF: Inadequate Science

Bio-concentration Factor (BCF). Dioxin in the environment tends to concentrate in living organisms, but in different ways and in different amounts. This factor quantifies the amount of dioxin fish concentrate in their tissues by swimming in contaminated water. Surprisingly, it does not take into account dioxin entering the fish through the food chain, just absorption through the skin.

Simplistic Studies

Based on simplistic laboratory experiments, EPA concluded that some fish concentrate 5,000 times as much dioxin in their tissues as is found in the water column. As with all other factors, DEQ adopted EPA's conclusion rather than conduct its own experiments.

Food Chain Ignored

Environmentalists argue a BCF of 5,000 grossly underestimates the amount of dioxin in fish tissue and therefore, the amount ingested by humans. "This is a significant oversight in the standard," said Bonine. "Scientists have documented dioxin accumulation in fish through the food change — called "bio-accumulation" — and it is a more important route of exposure than absorption through the skin," he said.

BCF Could Go Higher

Agency officials, industry representatives, and environmentalists generally agree that the BCF should be higher. The debate is over how much higher. Studies conducted for the NW Pulp & Paper Association indicate the BCF for sturgeon ought to be 10,600, over twice as high as the number EPA plugged into the formula.

HOW MUCH DIOXIN DO FISH ACCUMULATE?

BCF Values	New Standard*
10,000	0.0069
25,000	0.0027
50,000	0.0013
75,000	0.0009
100,000	0.0006
150,000	0.0004

* This is how the standard would change if DEQ used a higher BCF.

BCF for Non-Resident Fish at Issue

"We acknowledge that our effluent is responsible for elevated dioxin levels in local, resident fish populations near our discharge pipes, said Llewellyn Matthews, executive director of the NWPPA. "We are not convinced that pulp mill effluent contributes to dioxin levels found in non-resident fish such as salmon. There are other sources of dioxin," she said.

BCF Range: 5,000 to 150,000

According to Bill Diamond, director of EPA's Water Quality Criteria and Standards Division, EPA studies suggest the bio-concentration factor could range as high as 159,000.

Environmentalists have even argued the BCF could be as high as 500,000 for some species, if contamination of the food chain is taken into account.

DEQ Leans to 50,000

DEQ seems to be leaning toward a moderate increase in the bio-concentration factor. "The conclusions on this factor are very crude at this point," said Foster. "My guess is it will settle in somewhere around 50,000 to 60,000." The table at right shows how the dioxin standard would change if a higher bio-concentration factors were used. According to Foster, DEQ is planning to conduct field studies to develop a more accurate BCF for Columbia River fish.

CPF: How Toxic is Dioxin?

Cancer Potency Factor. Most of the debate has focused on this factor, which indicates dioxin's human cancer-causing potential. All arguments by industry and the environmental community regarding dioxin's dangerousness are subsumed in this factor. A closer look at this factor reveals that even if the industry's lowest cancer potency number is plugged into the formula, the dioxin

standard is still less than 1 part per quadrillion.

EPA selected a CPF of 156,000 mg/kg/day. The higher the CPF, the more dangerous the chemical, and the lower the water quality standard.

The Kociba Study . . .

The federal agency based its CPF on a single, two-year rat liver study completed in 1978 by Dr. R.J. Kociba. Since then, industry representatives and some members of the scientific community have challenged the Kociba study. Critics point out that the model used to develop the CPF is too simplistic. They argue Dr. Kociba improperly counted "precancerous liver tumors," failed to incorporate a "no observable affect level" in the test, and made other errors.

Under Attack

Dr. Robert Squire, a John Hopkins researcher and participant in the original study, recently reevaluated Dr. Kociba's data and concluded that the CPF was too high, possibly by a factor of 10 or more. EPA and DEQ acknowledge that legitimate questions surround the Kociba study but they are not prepared to change the CPF yet.

Other Agencies Use Lower CPFs

Other federal agencies use cancer potency factors much lower than EPA's. The U.S. Food and Drug Administration uses a CPF of 17,500 and the federal Center for Disease Control uses 36,000. According to Lydia Taylor, the administrator of DEQ's Water Quality Division, it would not be appropriate for DEQ to regulate dioxins based strictly on these cancer potency factors. "FDA is required to take economics into account when developing their cancer potency factor and we are not," she said.

Industry Wants State Review

The NWPPA has repeatedly urged DEQ to conduct its own review of dioxin's cancer potency. "The upshot is we believe they have over estimated the cancer potency of dioxin and that the states should do their own independent analysis of this factor," said Matthews.

The Washington Department of Health — with help from University of Washington researchers — has undertaken its own study of dioxin's cancer potency. EPA also has a study underway but Oregon does not.

DEQ May Respond

"We will be looking at the cancer potency factor when the new data is available from EPA, but for now we are satisfied with the value we are using," said DEQ's Foster.

CPF Range: 6,700 to 250,000

The range of CPF values seems to be between 6,700 and 250,000. The NWPPA says 6,700 to 9,700 is justified based on the Squire re-analysis and other studies. Environmentalists have challenged the objectivity of the Squire re-analysis and argue that there is no compelling reason to lower the CPF. They also assert that the CPF could be as high as 250,000.

HOW POTENT IS DIOXIN?

CPF Values	New Standard*
6,700	0.321
9,700	0.222
17,500	0.123
36,000	0.059
250,000	0.008

* This is how the standard would change if DEQ used a lower CPF.

DEQ Leans to 15,000

According to Foster, some studies suggest that the CPF could be as low as 15,000. If such a CPF were used, the dioxin standard would be about 0.12 PPQ, or about 10 times less strict than the current standard.

The table at right shows how the dioxin standard would change if lower CPF values were plugged into the formula. None of the new standards exceeds a single part per quadrillion.

PULLING IT TOGETHER

How Does the Standard Change?

The large table on page 8 shows how the dioxin standard changes as the various parameters are "tweaked" one at a time. It also shows what happens if the controversial factors were all changed at the same time, rather than independently of each other. With the help of industry, the environmental community and DEQ, four new dioxin standards were developed -- two "NWPPA Numbers," the "Bonine Numbers" and the "DEQ Lean To."

Industry's Scenario

NWPPA Numbers. These numbers were provided by Doug Morrison, an attorney for the NW Pulp and Paper Association. If DEQ were to assume a fish consumption rate of 13.4 grams per day, a bio-concentration factor of 10,600 and a cancer potency factor of 6,700, the final dioxin standard would be .073 PPQ, about 5 times less strict than the current standard but still less than 1 PPQ. If the CPF were 9,700 -- the NWPPA's upper end estimate -- the final standard would be .050 PPQ.

Environmentalists' Scenario

Bonine Numbers. As an "exercise in number crunching," John Bonine agreed to provided his estimates for the factors: a fish consumption rate of 100 grams per day to protect Native Americans; a body weight of 50 kilograms -- about 110 pounds -- to better protect women and children; a risk factor of 1-in-10-million; and a bio-concentration factor of 50,000. Based on these assumptions, the dioxin standard would be 0.0000021 PPQ or 0.0021 parts per quintillion.

Bonine is actively engaged in the dioxin debate, representing the Northwest Coalition for Alternatives to Pesticides (NCAP) in litigation over DEQ's dioxin regulations.

FOUR POSSIBLE STANDARDS

Source of Values	New Standard*
NWPPA Numbers	.050
NWPPA Numbers	.073
Bonine Numbers	.0000021
DEQ 'Lean To'	.0037

* This is how the standard would change if EPA used the unofficial values provided by industry, environmentalists and DEQ.

DEQ's 'Lean To' Scenario

DEQ 'Lean To'. This scenario was developed with DEQ's help but does not reflect the agency's position on the dioxin standard. These numbers used are values the agency may "lean to" if the standard is eventually reviewed. The values are a fish consumption rate of 25 grams per day (about 1 fish meal per week), a bio-concentration factor of 50,000, and a cancer potency factor of 15,000 (over 10 times smaller than EPA's current CPF of 156,000, and smaller than any CPF employed by other federal agencies). Based on these assumptions, the final dioxin standard would be .0037 PPQ, or about 3½ times more strict than the current standard.

CONCLUSION

No Silver Bullets

All parties to the controversy acknowledge that the .013 PPQ dioxin standard is based on rough guesses and uncertain science.

Whether DEQ's dioxin standard is too strict, or not strict enough, depends on each individual's personal sense of comfort with levels of acceptable risk, and the economics of reaching the standard. As Dr. Donald Barnes, Director of the

TWEEKING THE NUMBERS: A LOOK AT HOW THE STANDARD CHANGES

	Fish Consumpt (FCR)	Water Consumpt (WCR)	Body Weight (WT)	Accepted Risk (RISK)*	Bioconcentration (BCF)	Cancer Potency (CPF)*	Final Standard
DEQ's Standard	6.5 (g/day)	2 (l/day)	70 (kg)	1.00E-06	5,000	156,000 (mg/kg/day)	.013 PPQ
	10	2	70	1.00E-06	5,000	156,000	.0089 PPQ
Tweeking	25	2	70	1.00E-06	5,000	156,000	.0035 PPQ
the	50	2	70	1.00E-06	5,000	156,000	.0017 PPQ
FCR	75	2	70	1.00E-06	5,000	156,000	.0012 PPQ
	100	2	70	1.00E-06	5,000	156,000	.0009 PPQ
	150	2	70	1.00E-06	5,000	156,000	.0006 PPQ
	6.5	2	70	1.00E-06	10,000	156,000	.0069 PPQ
Tweeking	6.5	2	70	1.00E-06	25,000	156,000	.0034 PPQ
the	6.5	2	70	1.00E-06	50,000	156,000	.0013 PPQ
BCF	6.5	2	70	1.00E-06	75,000	156,000	.0009 PPQ
	6.5	2	70	1.00E-06	100,000	156,000	.0006 PPQ
	6.5	2	70	1.00E-06	150,000	156,000	.0004 PPQ
	6.5	2	70	1.00E-06	5,000	6,700	.321 PPQ
Tweeking	6.5	2	70	1.00E-06	5,000	9,700	.222 PPQ
the	6.5	2	70	1.00E-06	5,000	17,500	.123 PPQ
CPF	6.5	2	70	1.00E-06	5,000	36,000	.059 PPQ
	6.5	2	70	1.00E-06	5,000	250,000	.008 PPQ
NWPPA Numbers	13.4	2	70	1.00E-06	10,600	9,700	.050 PPQ
	13.4	2	70	1.00E-06	10,600	6,700	.073 PPQ
Bonine Numbers	100	2	50	1.00E-07	150,000	156,000	.0000021
DEQ's 'Lean To'	25	2	70	1.00E-06	50,000	15,000	.0037 PPQ

*NOTE: The RISK FACTOR is expressed in Lotus 1-2-3 scientific notation. A 1.00E-06 notation means a 1-in-a-million risk and 1.00E-07 means 1-in-10-million.

EPA's Science Advisory Board, told the EQC this summer, "When it comes to dioxin, there are a lot of uncertainties; there are no silver bullet answers."

Standard Unlikely to Exceed 1 PPQ

Whatever else is decided, a few conclusions can be drawn. First, no single factor will be changed in isolation. Both DEQ and EPA are committed to a full review all the factors, not just the just the cancer potency, bio-concentration, or fish consumption numbers. Second, even if adjustments are made, it appears the final standard will remain below a single part per quadrillion, far below the detectable limits of today's instruments. Third, under all the scenarios presented, it appears the Columbia River will remain "water quality limited," forcing the mills to make expensive improvements to control dioxin.

Status & References

If approved by the EQC Nov. 1, eight public hearings on DEQ's entire water quality regulatory package, including the dioxin standard, will be held between Jan. 14 and Jan. 22 (watch *OI Calendar* for details). For more information, contact Eugene Foster (DEQ) at 229-6982. References: ORS 468.735, OAR 340-41 Table 20 (proposed water quality standards for toxic substances).

AIR QUALITY

Advisory Committee to Recommend Few Changes to Protect Wilderness Area Visibility

■ After some 18 months of work, it appears a Department of Environmental Quality (DEQ) advisory committee will recommended few if any significant changes in the way the agency protects visibility and other "air quality related values" in wilderness areas. Even though the group will recommend adding some new wilderness areas to the program, it will be years before that occurs.

Low Priority

"This is a slow moving process – it's not on the front burner," said John Core, visibility program coordinator and liaison to the advisory committee.

The recommendations are being developed as part of a federally-mandated review of the state "Visibility Protection Program." The VPP is supposed to protect air quality related values such as scenic vistas, air chemistry, aquatic biology and even sensitive plants in certain designated wilderness areas.

Triennial Review Underway

First completed in 1986, the VPP was approved by the Environmental Protection Agency in 1987. The program is unique because it requires air pollution control measures even where air quality is generally very high. The idea is to "preserve, protect, and enhance" the pristine air quality often found in wilderness areas, national parks, national seashores and similar areas.

DEQ appointed a 15-member Visibility Protection Advisory Committee last April to help review the program. The group includes representatives of the public, federal land management agencies, timber and agricultural industries, environmentalists and the tourism industry.

Field & Slash Burning at Issue

The primary threat to air quality in these areas is smoke from grass seed industry field burning, forest industry slash burning, and natural forest fires. The VPP restricts field and slash burning during certain months so smoke does not interfere with recreational uses.

Twelve Areas Protected Now

Some of Oregon's most noteworthy attractions are among the 12 wilderness areas currently protected under the program. These include Crater Lake National Park, Mt. Hood Wilderness Area, and popular wilderness areas near Bend. Designated "Class I," these areas receive the greatest air quality protection under the Clean Air Act and DEQ regulations.

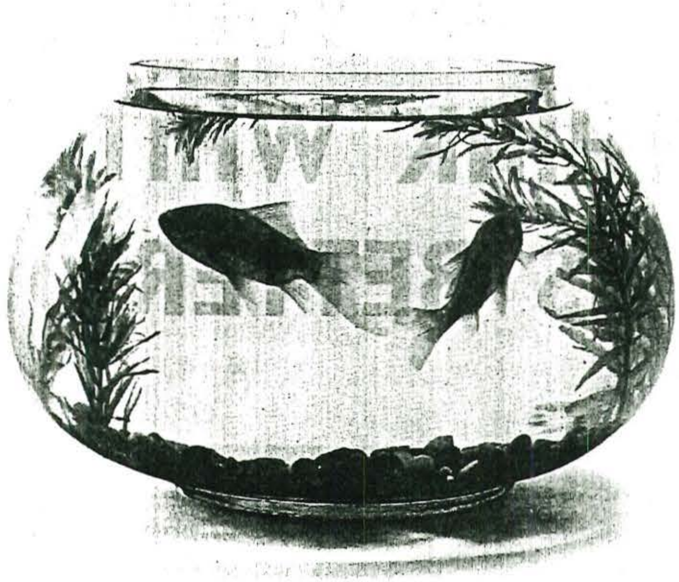
Two Questions

There are two general questions before the committee. First, should DEQ expand the VPP to include areas set aside as wilderness since 1977? Second, should DEQ change the way visibility and other related values are protected?

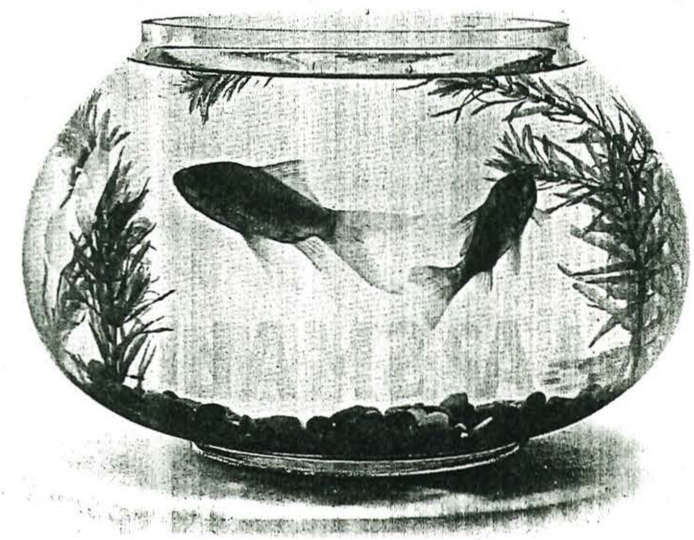
IF YOU THINK WHITER IS BETTER...

GREENPEACE

...THINK AGAIN.



This paper is white. It was bleached with oxygen.

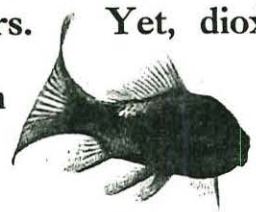


This paper is whiter. It was bleached with chlorine.

A SMALL
DIFFERENCE
TO YOU...

...MAKES A
BIG DIFFERENCE
TO OTHERS.

Chlorine-bleached pulp is bad for the environment. There can be no doubt about that. Studies have shown again and again that effluents from kraft or sulphite mills using chlorine technology lead to reduced reproductivity in fish, suppressed immune systems, impaired metabolism, and a multitude of other long-term effects. Chlorine-bleached paper is also bad for you. Many of the chlorinated poisons discharged by the mills will also be found in paper - like the page you are now holding in your hand. Even dioxin, one of the most toxic chemicals ever produced, is likely to be present in this chlorine-bleached paper. Dioxin has been proven to leach from bleached paper products, such as milk cartons and coffee filters. Yet, dioxin is only the tip of the iceberg when it comes to organochlorine pollution from pulp and paper mills. Up to 1,000 different chemicals can be found in the effluent of mills employing chlorine-bleaching. Many of these cause cancer or genetic damage

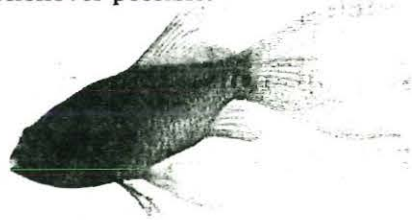


and are persistent and accumulate in the environment. On average, pulp mills discharge around 35 tons of toxic organochlorines every single day. Even those mills that already have upgraded their process to reduce formation of the most notorius organochlorine, dioxin, will still discharge between 10 and 20 tons of other chlorinated poisons every single day. These discharges must stop now. The page you are now reading was printed on sulphite pulp bleached with oxygen-based agents. Such chlorine-free bleaching technology is readily available and must be employed immediately by mills using the sulphite process. Chlorine-free bleaching technology available for kraft mills will yield a cream-colored pulp. That brightness is entirely sufficient for most purposes, particulary since kraft pulp is mainly used in paper products that need to be strong, not white, such as packaging, stationery or envelopes.

THINK TWICE BEFORE YOU BUY WHITE, AND SUPPORT GREENPEACE IN ITS DEMANDS FOR

- Complete elimination of all chlorine-based bleaching chemicals.

- Use of the right fiber for the right product, i.e. the use of off-white kraft and off-white sulphite pulp, or completely unbleached pulp whenever possible.



CHLORINE-FREE BY 1993!

For more information about different pulp and paper making technologies and their impact on the environment, please ask us for the Greenpeace Guide to Paper.

DIOXINS, FURANS AND PCBs: THE TRUE STORY

Dioxins, furans and PCBs have become some of the most controversial chemicals of modern society. Dioxin in particular has been labelled the most toxic chemical ever produced by man. More than $1 billion has been spent so far on dioxin research[1], yet at the same time, industry and government officials insist that not enough evidence on the toxicity exists to justify elimination of the sources.

This paper explores some of the myths and facts surrounding these environmentally dangerous chemicals and explains why the scientific debate has become of an increasing political nature.

What Are 'Dioxins'

The term 'dioxins' usually refers to a whole chemical family with 75 individual members, which more correctly should be termed chlorinated dibenzo-p-dioxins. The most toxic member of this family is 2,3,7,8-Tetra-Chloro-Dibenzo-p-Dioxin, often abbreviated as 2,3,7,8-TCDD.

Often, the term 'dioxins' also includes a closely related chemical family called chlorinated dibenzofurans. The most toxic among the 135 known furans is 2,3,7,8-Tetra-Chloro-Dibenzo-Furan (TCDF), which is one tenth as toxic as the corresponding dioxin, TCDD.

Of the 210 dioxins and furans, twelve are extremely toxic and are commonly referred to as the 'Dirty Dozen'. Their individual toxicity is ranked by comparing them to 2,3,7,8-TCDD via internationally agreed upon Toxic Equivalence Factors (TEFs). Box 1 (next page) shows the chemical structures of dioxins and furans, and their toxicity ranking.

PCBs are another chemical family closely related to dioxins. Due to their similar chemical structure, some PCBs can act through exactly the same pathways in organisms as dioxins, but are much less potent. However, due to their chemical nature, PCBs are inevitably contaminated with furans and dioxins, and will form these more toxic chemicals during fires.

How Toxic Are Dioxins [2]

a) Extreme Ability to Kill

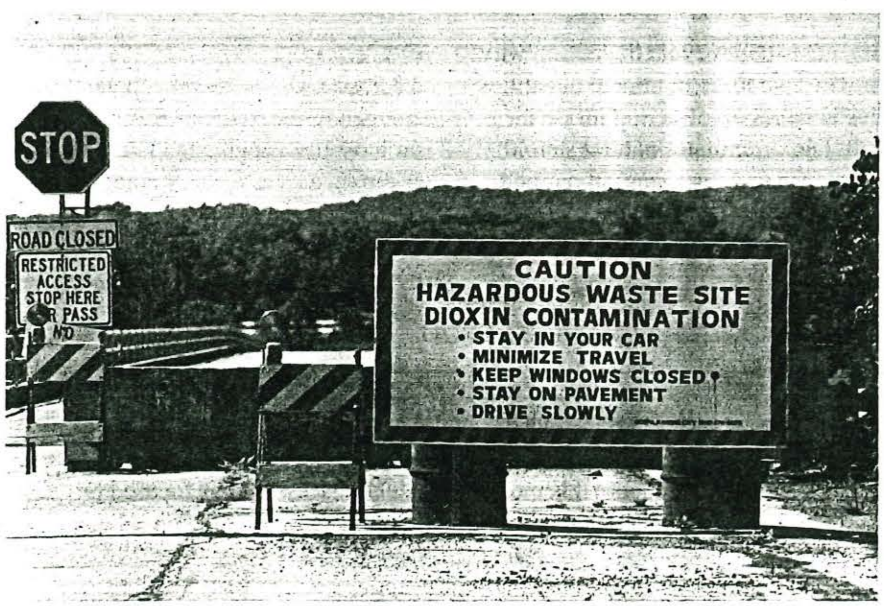
Dioxin TCDD is the most toxic man-made chemical ever tested on laboratory animals. Acutely lethal doses are measured in micro-grams per kilogram animal weight, in the parts per billion range. [2e] Though the lethal dose varies considerably from species to species, dioxin has been found to be extraordinarily toxic to all species tested.

Characteristic of lethal dioxin exposure is the 'wasting syndrome': animals seem to waste away, and eventually die, without displaying any overt pathological symptoms. The exact reason why dioxin can cause death in these minute quantities is not yet known.[2e]

b) Extremely Bio-Accumulative

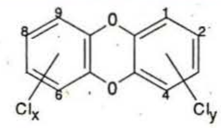
Dioxins are some of the most persistent and bio-accumulative man-made chemicals released into the environment. While dioxins can be broken down under certain conditions, in particular when exposed to intensive sunlight, they cannot be broken down once absorbed by soil or dust. When they enter the food-chain, they will bio-magnify, often to levels many thousands of times higher than their surroundings.[2d,3]

It is this combination of dioxin's extreme toxicity and its bio-magnification in the environment that makes Greenpeace believe that there can be no safe level of dioxin emissions.

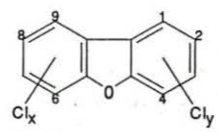


INTERNATIONAL TOXICITY EQUIVALENCY FACTORS (I–TEFS)

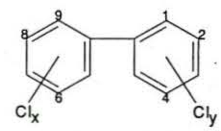
	I – TEF
2,3,7,8-TCDD	1
1,2,3,7,8-PeCDD	0.5
1,2,3,4,7,8-HxCDD	
1,2,3,7,8,9-HxCDD	0.1
1,2,3,6,7,8-HxCDD	
1,2,3,4,6,7,8-HpCDD	0.01
OCDD	0.001
2,3,7,8-TCDF	0.1
2,3,4,7,8-PeCDF	0.5
1,2,3,7,8-PeCDF	0.05
1,2,3,4,7,8-HxCDF	
1,2,3,7,8,9-HxCDF	
1,2,3,6,7,8-HxCDF	0.1
2,3,4,6,7,8-HxCDF	
1,2,3,4,6,7,8-HpCDF	
1,2,3,4,7,8,9-HpCDF	0.01



chlorinated dibenzo—p—dioxins



chlorinated dibenzofurans



chlorinated byphenyls (PCBs)

Box 1

c) Long-Term Toxicity: The Dioxin-Receptor

More worrisome than the high acute toxicity are the more insidious long-term effects of exposure to sub-lethal doses of dioxin. Daily doses 1,000 times below the lethal dose, the parts per trillion range, cause profound delayed effects in mammals, such as cancer, damage to the immune system, and reproductive failure.[2e]

Concentrations in water another 1,000 times lower, the parts per quadrillion range, can still cause a wide variety of toxic effects in fish, e.g. in rainbow trout.[3]

Scientists believe that the reason why dioxin is so toxic in minute quantities lies in its mode-of-action inside the cell. Dioxin imitates natural steroid hormones (e.g. estrogen) in our bodies. Dioxin fits into a protein receptor, which normally responds to these steroid hormones. The receptor then transports the dioxin directly into the cell nucleus, where it interacts with basic cell chemistry.[2a]

The 'dioxin-receptor' has been identified in laboratory animals as well as in humans. One can compare this mode-of-action with dioxin acting as a key to the receptor-lock. Some individual dioxins and furans fit better into the receptor than others; PCBs do not fit as well. 2,3,7,8-TCDD fits best into this receptor and consequently is the most toxic.

d) Chloracne

The disfiguring skin disease chloracne is often erroneously referred to as the only human health effect positively linked to dioxin exposure, and is often down-played in its severity. Yet, chloracne is always accompanied by other health effects, such as chronic weakness in the legs, severe pain in the joints, headaches, pronounced fatigue and irritability, and often lasts for decades, as several studies on occupationally exposed workers show.[2b]

e) Cancer

2,3,7,8-TCDD is the most potent carcinogen tested to date.[2] Researchers so far have been unable to clarify whether dioxin acts as a co-carcinogen or whether it suppresses the immune response to other carcinogens. Yet given the fact that other carcinogens are plentiful in our polluted environment, that question can be of academic interest only.

Does Dioxin Cause Cancer in Humans?

Much discussion has focused on whether 2,3,7,8-TCDD is a human carcinogen. Some evidence exists to support such a claim, but there are also indications that this discussion has not been without bias.

One of the best analyzed groups of exposed humans are chemical workers who produced 2,4,5-T (Agent Orange). The West German chemical company BASF experienced an explosion in 1953, which exposed workers to relatively high doses of dioxin TCDD. Many of the workers subsequently suffered from chloracne.

At the 1989 International Symposium on dioxin and its toxic effects, West German scientist F. Rohleder presented a re-analysis of these exposed BASF workers and found significantly elevated levels of respiratory cancer and cancer of the digestive system. [4]

Most disturbingly, Rohleder found that earlier studies, paid for by BASF itself, were fraudulent: non-exposed workers had been deliberately added to the 'exposed' cohort, and truly exposed workers, some of whom were displaying chloracne, had been deliberately excluded from the study.

Evidence that PCBs may be carcinogenic in humans is also mounting. A cancer study by the Cincinnati National Institute for Occupational Safety and Health found that Westinghouse workers in Bloomington, Indiana experienced a more than two-fold increase in mortality from brain cancer and a four-fold increase in deaths from skin cancer.[5]

The Shortcomings of Epidemiology

The reason clear proof of dioxins' and PCBs' carcinogenicity in humans does not exist, and may never exist, lies in some important short-comings of any epidemiological study: the humans investigated are exposed to many more toxic influences than just dioxin, and it will always be possible to point the finger at other factors possibly causing the disease. This poses an ethical dilemma, since it is impossible to raise humans in controlled environments such as a laboratory.

Further, epidemiological studies carried out so far rarely have verified the actual exposure of the presumed exposed versus the unexposed control group. That fact is probably the single most important reason why the findings of epidemiological studies carried out so far contradict each other so much.

Recently it has become possible to determine actual dioxin body burdens through analysis of blood serum, and some exposed cohorts investigated earlier, e.g. Vietnam Veterans and occupationally exposed workers, are being re-analyzed. However, individuals in these cohorts who have died since the original study was conducted are invariably excluded from these new studies.

f) Reproductive Effects

More subtle than chloracne or cancer are other health effects such as reproductive failure. It is striking that reproductive failure has been observed in all animal species tested, be it fish, bird or mammal. It is therefore highly likely that reproductive failure also occurs in humans exposed to dioxin.[2c]

Most disturbing are laboratory experiments on primates such as rhesus monkeys, whose reproductive systems were found to be extremely sensitive to dioxins when administered in minute doses on a daily basis. Researchers found a serious decrease in sperm count in exposed males, and an inability to conceive or carry the pregnancy to term in exposed females.[2d,6]

Some evidence of such reproductive failure in humans already exists. Jock Ferguson, a Canadian reporter who investigated health effects in occupationally exposed workers, once interviewed three Hooker Chemicals workers, all of whom suddenly came to realize that none had fathered children.[7] Why is it that incidences like these are always dismissed immediately as anecdotal evidence, and are not followed up in a formal investigation, e.g. an epidemiological study, whereas negative findings are always promoted as certainty?

Other reproductive effects observed in laboratory animals include stillbirths and birth defects. Dioxin has been linked to spina bifida, anencephaly (absence of brain) and cleft palate.[2]

g) Suppression of the Immune System

Perhaps most frightening of all are the effects dioxin has on the immune system. The thymus, a gland that is of utmost importance to the immune system, is one of the main targets of dioxin. It has been shown in laboratory animals that one of the first signs of dioxin poisoning is thymic atrophy.[d]

The human thymus develops at 9 weeks of gestation and disappears at puberty, at the age of 10 to 12. It seems that the thymus is not required for the maintenance of effective immune function in adults, since human T lymphocytes have a life-span of 15 – 20 years, and there is little replacement for them during adult life.[2d]

But what about children, and even worse, what does thymic atrophy do to nursing babies?

h) Behavioral Changes in Offspring and Minimum Effect Levels

A number of health effects have been noted at doses comparable to those producing cancer. Very few of the studies, however, have produced clear No Observable Effect Levels. This is particularly true of long-term studies in rodents and rhesus monkeys.[2e]

The available evidence suggests that No Observable Effect Levels for some of the immunologic and reproductive effects in rhesus monkeys are well below 1 ng/kg/day. [6] Behavioral changes in the offspring, for example, were observed in rhesus monkeys when exposed to dioxin levels in the diet as low as 0.12 parts per trillion.[6a]

Box 2 shows how these Minimum Effect Levels for immunotoxic, reproductive and carcinogenic effects, as observed in various animal species, compare to the average daily intake of nursing babies in the western industrialized world.[2d,8]

Dioxins in Human Milk

An average breast-fed baby in industrialized countries already ingests up to 100 times more dioxin than the World Health Organization (WHO) deems tolerable for a healthy adult.[8] The margin of safety, that is the difference between the levels of dioxin we expose our babies to and those that we know will cause adverse effects in laboratory animals, is on the order of ten to non-existent. Babies in heavily contaminated areas are already exposed to dioxin levels that are certain to induce toxic effects in laboratory animals.

Aside from dangerously high levels of dioxins and furans, mother's milk also contains other toxic chlorinated chemicals, such as PCBs, hexachlorobenzene, and polychloronaphthalenes to name a few. Yet no research has been done on the likely synergistic effects of these compounds.

Further, some scientists believe that exposure in utero from transplacental migration may have important effects on brain development, and thus may

Minimum Effect Levels and Tolerable Daily Intake of Dioxin, expressed in equivalents of 2, 3, 7, 8-TCDD (TEQ), compared to the Average Daily Intake by a nursing baby in industrialized countries. (2d,8)

EFFECTS	MEL (lab.tests) ng/kg bw/day	ADI (nursing baby) ng/kg bw/day
immunotoxic	6 (guinea pig)	
reproductive	0.12 (primates)	around 0.1
carcinogenic	10 (rats)	
	TDI pg/kg bw/day	**ADI pg/kg bw/day**
Sweden	1 – 5	
Canada	10	
USEPA	0.006	100
USFDA	0.06	
WHO	1	

Box 2

wood articles become very significant sources of dioxin when burnt in wood stoves or incinerators.

Municipal incinerators are another very significant but completely avoidable source of dioxins. They not only generate vast amounts of dioxin-laden ash but also emit dioxins into the atmosphere where they can be transported over long distances, e.g. to the Arctic. The disposal of toxic incinerator ash has become a highly publicized problem since export schemes to Panama and other developing nations were exposed by Greenpeace.

Incinerators should be eliminated for other environmental reasons as well. Incinerators are not compatible with recycling systems, since comprehensive recycling systems eliminate cheap fuel from the waste stream, e.g. paper or plastics, thus eliminating the economic viability of incinerators.

Copper reclamation plants and hospital waste incinerators are also major dioxin sources due to the burning of PVC (polyvinylchloride) and PVDC (polyvinylidene-chloride) waste. Copper wires are coated with PVC, and many hospital disposable items are made of these chlorinated plastics, as are many disposable household products.

Many West German cities, e.g. Bielefeld, Munich, Aachen and others, have now banned the use of PVC material in public buildings to protect the public and fire fighters from dioxin formed during fires. The Danish government is actively pursuing a phase-out of all PVC articles, and is presently researching a feasible time-table.

The Swedish government is pushing for a phase-out of chlorinated solvents, due to the risks they pose to ground water supply, their effects in the lower atmosphere, and the associated waste disposal problems.

The pulp and paper industry as well as certain branches of the metallurgical industry are significant sources of dioxin due to the use of raw chlorine. Chlorine gas reacts with wood compounds or carbon electrodes to form dioxins. European governments are researching and implementing new production processes that would ban the use of chlorine and thus the generation of dioxin as well as other toxic organochlorines.

It is clear that eliminating these sources of dioxin means eliminating a much larger portion of toxic chemicals from our environment. This makes a lot of sense from an environmental point of view, because dioxins never come alone, but are always accompanied by other toxic organochlorines.

Dioxin indeed is only the tip of an iceberg of environmentally dangerous organochlorines and other organohalogens; and successfully eliminating modern society's dioxin sources will inevitably mean eliminating this iceberg, which is exactly the reason environmentalists are becoming more and more vocal in this matter. To Greenpeace, dioxin is a symbol of whether we want to deal with our pollution or whether we want to continue our self-destructive lifestyle.

SOURCE	ELIMINATION STRATEGY
a) PRODUCTION OF ORGANOCHLORINES, e.g.	
* chlorophenols and chlorobenzenes	ban production and use immediately
b) COMBUSTION OF ORGANOCHLORINES, e.g.	
* car exhaust, leaded gas	don't add org. chlorine scavengers (use unleaded gas)
* municipal waste incinerators	comprehensive recycling
* hazardous waste incinerators	waste reduction/elimination and use other destruction methods
* copper reclamation	eliminate PVC coating
* steel recycling	no chlorinated rubber/plastics to be used in car or machinery
c) USE OF CHLORINE GAS, e.g.	
* pulp and paper industry	less bleaching and bleaching with oxygen/ H202
* zinc/magnesium smelters	use chlorine-free process

Box 3

The Politics – Whose Interests Are At Stake?

Obviously, when the entire organohalogen production is being questioned, some very powerful interest groups want to have a say. Much is at stake, both in terms of liability law suits and lost profits.

It would be naive to think that the chlorine- and organochlorine-producing industry, e.g. PVC and chlorinated solvents or pesticide producers, have had no influence on the colour of dioxin science. Other vested parties to name include the incineration lobby, the pulp and paper industry and the metallurgical industry. Even defense departments are involved in the discussion, due to the use of Agent Orange in Vietnam and elsewhere.

The result: instead of devoting research efforts toward eliminating the sources, finding alternative products or production technologies, and safe methods of dealing with the existing wastes, the public is being deluged with attempts to linguistically detoxify dioxin, via media releases, information brochures and widely publicized risk assessments.

Risk assessments, in particular, can at best only be viewed as pseudo-scientific exercises, because they do not take into account:

- total exposure from all possible sources
- synergistic effects
- effects on the next generation, for example through contaminated human milk
- all possible health effects, rather than selected health effects only, e.g. certain forms of cancer.

be of even more concern than postnatal exposure through mother's milk.[9]

Scientists will never be able to prove a link between health effects at a later stage in life to any toxic chemicals present in mother's milk or to exposure to these toxins in utero, simply because babies do not grow up in controlled environments such as a laboratory.

Who is at Risk?

Obviously, the human baby is of most concern when it comes to human health effects. But what about the entire environment? Despite all the money spent and all the papers published, we know very little about dioxin's effect on an entire ecosystem. It seems likely that animals and birds with a fish-based diet will suffer most.

The Baltic gray seal is a case in point. In the mid-seventies it was found that only 20 percent of the mature female gray seals were fertile.[10] This is commonly thought to be caused by PCBs in the Baltic food chain; and PCBs, as we know, react through the same protein receptor as dioxins.

Fertility is not the only effect linked to PCBs in the seals' diet: over 75% of the seals found dead in recent years have been found to have intestinal ulcers and kidney damage. Roughly half the female gray seals also had uterine tumors. Often, even the living display these same diseases. Interestingly, when seals are raised with a diet of less contaminated fish caught outside the Baltic, the seals are able to reproduce. Yet, this fact is often excluded in discussions about toxic effects of PCBs and dioxins, and seldom mentioned in official government or industry brochures.

Clearly, the solution to such environmental problems cannot be to place Baltic seals or beluga whales or fish-eating birds into a sanctuary and feed them less contaminated fish. Neither can the solution be to forbid breast-feeding. It is essential, then, to prevent any further build-up of these insidious chemicals in the food chain. This can only be achieved by immediate elimination of all sources of dioxins.

The Sources and Elimination Strategies

While the production of PCBs was finally outlawed worldwide, and the worry now is how to eliminate existing PCB wastes, dioxins and furans seem to come from many different and ongoing sources. Yet there is an obvious common denominator to these sources: modern society's use of chlorine.

It is often claimed that dioxin is a naturally occurring toxin, produced in forest fires and wood stoves. This theory, first introduced by Dow Chemical scientists as the 'Trace Chemistry of Fire' theory [11], has been convincingly disclaimed by at least three separate studies:

a) the Czuczwa study, which investigated contamination of Great Lakes sediments, found that dioxin levels were virtually non-existent prior to the Second World War, which coincides with the beginning of large-scale production and combustion of organochlorines.[12]

b) the Inuit mummy study, in which A. Schector investigated tissue of two 400-year-old mummies. Only minor amounts of the less toxic but very persistent octa-chlorodibenzo-p-dioxin (OCDD) were found. [13]

c) the Chilean mummy study, in which W.V. Lignon analyzed tissue of nine Chilean mummies for dioxins and furans. Again, only minor amounts of OCDD were found.[14]

All three studies conclude that rising dioxin levels are intimately linked to modern industrialized society. Box 3 lists strategies to eliminate major industrial sources of dioxin, all of which are connected with the use of elemental chlorine as well as the production and combustion of chlorinated organic chemicals (organochlorines).

Elemental chlorine does not exist in Nature, and Nature does not produce organochlorines on a large scale either, with the exception of some very simple molecules, such as methylchloride or dichloromethane.

Many of the industrial dioxin sources are easy to eliminate.

Chlorophenols, for example, are already banned in many European countries. Sweden actually experienced a decline of dioxin levels in human milk after banning both pentachlorophenol and chlorophenol-based herbicides.

Both Canada and the United States actively resist such a ban, and chlorophenols are still used for wood preservation (utility poles and railway ties) and as a fungicide on lumber destined for export. Once treated, these

Conclusions and Greenpeace Demands

Enough research exists to prove that dioxin is extremely toxic and persistent, and that levels in our environment and in human milk are increasing. Given that many health effects occur from exposure to even minute quantities over time, and that widespread contamination of our environment and the build-up of these chemicals in the food chain has already led to dangerously high levels in human milk and in marine mammals, all energy must be devoted toward preventing any further releases of dioxins into the environment.

The elimination of man-made dioxin sources would go hand-in-hand with the elimination of a much larger group of environmentally dangerous organochlorines, which would be extremely desirable from an overall environmental point of view. Elimination of all dioxin sources would mark a turning point in our dealings with pollution control, since a holistic approach would have to include the phase-out of an entire class of anthropogenic chemicals presently discharged in large quantities into the environment.

In 1983, after two years of research, the Ministers' Expert Advisory Committee on Dioxins stated that [15]:

"Regardless of arguments about the significance of species differences in sensitivity, the validity of risk assessments, and other uncertainties which may take years to resolve, it is quite clear that dioxins are very unpleasant things to have in our environment and the less we have of them the better. It is, in fact, imperative to reduce dioxin exposure to the absolute possible minimum."

Despite these recommendations, the Canadian government has failed to eliminate even such outstanding dioxin sources as pentachlorophenol, but has instead actually added new dioxin sources to the Canadian environment by building further municipal and hazardous waste incinerators.

Greenpeace demands that the Canadian government follow the leadership provided by forward thinking European governments, and:

establish a five-year plan to eliminate all known industrial dioxin sources,

and in particular:

- **ban import and use of chlorophenols immediately;**
- **establish an indefinite moratorium on construction of new municipal and hazardous waste incinerators;**
- **phase out disposable products made of PVC or PVDC;**
- **phase out PVC coating of copper wire;**
- **phase out chlorinated solvents;**
- **eliminate the use of chlorine in the pulp and paper industry and metallurgical industry;**
- **establish a mass-balance of chlorine and organochlorines in Canada; i.e. determine the amount of chlorine gas and organochlorines produced, and their fate in the environment. This mass balance should extend to other halogens and organohalogens;**
- **commission a feasibility study on phase-out of all production and use of organochlorines.**
- **Fund research to find clean production technologies and alternatives to chlorinated products, as well as safe methods of destroying the existing piles of dioxin and other chlorinated waste.**

This paper was researched and written by Renate Kroesa, M.Sc., Toxic Project Co-ordinator.

REFERENCES

1) Report from Conferences, the 5th Int'l Dioxin Symposium, Bayreuth, 1985; Chemosphere, 1986, 15, N1-2.

2) This entire section is based on the following five overview reports/books published on the toxicology of dioxin. All reports/books give an excellent overview and provide many detailed references to the interested reader.
   a) 'Human Health Aspects of Exposure to PCDDs and PCDFs'; UAREP, Bethesda, Maryland, June 1988 (funded by the American Paper Institute).
   b) 'The Chemical Scythe', by Alistair Hay; Plenum Press 1982.
   c) 'A Cancer Risk-Specific Dose Estimate for 2,3,7,8-TCDD'; US-EPA/600/6-88/007Ab, June 1988, plus Appendices A-F.
   d) 'Dioxins in the Environment' by the UK Dept of the Environment; Pollution Paper No. 27, 1989.
   e) S.A. Skene et al, Human Toxicol, 1989, 8, 173-203.

3) P.M. Mehrle et al, Environmental Toxicology and Chemistry, 1988, 7, 47-62.

4) F. Rohleder, Presentation to the 9th Int'l Dioxin Symposium, Toronto, 1989.

5) T. Sinks, Presentation to the 7th Int'l Symposium on Epidemiology in Occupational Health, Tokyo, 1989.

6) a) R.E. Bowman et al, Neurotoxicology, 1986, 7, 637-650.
   b) J.R. Allen et al, Toxicology and Applied Pharmacology, 1979, 48, A180.
   c) J.R. Allen et al, Bulletin of Environmental Contamination and Toxicology, 1979, 21, 463-469.

7) 'Who do you believe?', Jock Ferguson; Chemosphere, 1985, 14 791-796.

8) PCBs, PCDDs and PCDFs in Breast Milk: Assessment of Health Risks; WHO, Regional Office for Europe; EH 29 (1988).

9) W.R. Swain; Aquatic Toxicology, 1988, 11, 357-377.

10) Monitor 1988, Sweden's Marine Environment - Ecosystems Under Pressure; National Swedish Environmental Protection Board.

11) a) R.R. Bumb et al (Dow Chemical), Science, 1980, 210, 385.
   b) Nestrick et al (Dow Chemical), Chemosphere, 1983, 12, 617-626.

12) J.M. Czuczwa, R.A. Hites, Chemosphere, 1986, 15, 1417-1420.

13) a) A. Schector et al, Chemosphere, 1988, 17, 627.
   b) A. Schector et al, poster at the 9th Int'l Dioxin Symposium, Toronto, 1989.

14) W.V. Ligon et al (General Electric), Environ. Sci. Technol. 1989, 23, 1286-1290.

15) Report of the Joint Health and Welfare Canada/ Environment Canada Advisory Committee on Dioxins, November 1983.

GREENPEACE

Founded in Canada, 1971
Fondé au Canada, 1971

Vancouver

1726 Commercial Drive,
Vancouver
British Columbia
Canada V5N 4A3
✆ 604 253-7701
FAX 604 253-0114

Toronto

578 Bloor Street West
Toronto, Ontario
Canada M6G 1K1
✆ 416 538-6470
Fax 416 538-6479

Montréal

2444 Notre-Dame Ouest
Montréal (Québec)
Canada H3J 1N5
✆ 514 933--0021
Fax 514 933-1017

Press Gang Printers - a feminist worker-controlled collective

STATE OF OREGON

DEPARTMENT OF ENVIRONMENTAL QUALITY   INTEROFFICE MEMORANDUM

DATE: June 7, 1991

TO: Environmental Quality Commission

FROM: Fred Hansen, Director

SUBJECT: Petition for Rule Amendment: Water Quality Standard 2,3,7,8 - TCDD

The Department would recommend to the Commission that the petition for rule making regarding the water quality standard for 2,3,7,8 - TCDD be denied. The denial at this time is based on several factors including:

1. The Department is in the process of completing the triennial review of the state's water quality standards. The standard for 2,3,7,8-TCDD was evaluated during this process. The Department, after careful review of the criteria, recommends to retain the standard as adopted in 1987.

   The Department reviewed all of the factors used to derive the criteria with special attention to three of the factors. These three factors were cancer potency, bioconcentration, and fish consumption. Various numbers have been forwarded for revision of all three of the factors. Review of the published literature indicated that the 0.013 pg/l water quality standard was an appropriate standard. When considering the possible changes to the cancer potency factor, the bioconcentration factor, and the fish consumption rate the 0.013 pg/l standard is an appropriate standard.

2. Since the Department's review of the water quality standard during the fall of 1990 the USEPA has announced that they will be conducting a review of the criteria. The USEPA expects to complete the review in one to two years. The agency expects to address wildlife, aquatic life, and human health issues related to the criteria. The agency is expected to review carcinogenic and reproductive effects to humans, wildlife and aquatic life; the rate of bioaccumulation; and, fish consumption rates.

3. Any review of the 2,3,7,8-TCDD standard which addresses wildlife and aquatic life risks could well result in a criteria value lower than the present Oregon standard. It should be noted that piscivorous wildlife have an increased risk of cancer mortality and reproductive

effects than humans when applying the Oregon water quality standard. In addition, a No Observed Adverse Effect Level (NOEL) has not been established for 2,3,7,8-TCDD. The lowest concentration studied of 38 ppq has resulted in 45% mortality of the trout exposed during the test.

4. According to the most recent USEPA memo to the Department (April 24, 1990) concerning the tracking of state water quality criteria for 2,3,7,8-TCDD there are 25 states with adopted dioxin criteria. Fourteen of the states have adopted standards at or below and 11 above the USEPA criteria level.

5. EPA's Office of Research and Development(ORD) is currently developing a review strategy which we expect to be released on or around June 14, 1991 (attachment 1). The strategy is expected to include greater detail on the scope and timing of the EPA review. This could shed additional light on the national review and the type of information it will develop. This would be very germane to a decision on the petition and the type of review to be conducted by the state.

6. There has not been new peer reviewed published information within the last five to six months since the Department has reviewed the standard, that would cause the Department to recommend a change to the standard. An epidemiological study has been published in The New England Journal of Medicine which links occupational exposure of 2,3,7,8-TCDD to an increase in the rate of mortality due to cancer (Fingerhut 1991). A new method to estimate the bioaccumulation factor has been forwarded to the Department but this method does not appear to be suitable for use in water quality criteria development. The Department is involved in projects or aware of projects which should provide specific information on bioaccumualtion in riverine systems as well as fish consumption rates of Native Americans along the Columbia River.

7. William Riley, Administrator EPA, stated in a memo dated April 10, 1991 announcing the review of the 2,3,7,8-TCDD criteria that regulatory actions concerning 2,3,7,8-TCDD should go forward.

8. On-going litigation based on the current standard is not expected to be resolved soon.

Based on the above information it would not be the best use of limited state resources to duplicate the present USEPA effort. State resources should be spent in other areas of toxin control such as the development of a comprehensive standard for all biologically and toxicologically active dioxins, furans and PCBs, technology based standards for the control of dioxins and furans in the pulp and paper industry and wood treating industry.

When the USEPA has completed their review of the 2,3,7,8-TCDD criteria, the Department would propose to immediately undertake a review of the standard if it is warranted.

If the Commission does not accept the Department's recommendation, we recommend, in accepting the petition for rule making, that a very specific statement be made regarding current regulatory actions, the items to be considered during the review and the time frame for the review. This would include:

1. The Department would continue all current regulatory activities using the current standards until such time as a new standard was adopted.

2. The re-evaluation of the state standard would be opened at this time, but the review would not be closed until the USEPA had completed its review.

3. The re-evaluation of the 2,3,7,8-TCDD water quality standard would include the review of criteria derivation for the other biologically available dioxins, furans, and co-planar PCBs to address as one standard the pollutants with similar biological/toxicological properties.

4. The Department would move forward to establish technology based standards for the control of dioxins and furans in the pulp and paper industry and wood treating industry.

ENVIRONMENT WEEK

By The Editors Of The Energy Daily And New Technology Week

KING COMMUNICATIONS GROUP, INC. • 627 NATIONAL PRESS BUILDING • WASHINGTON, D.C. 20045 • 202/638-4260

Thursday, May 2, 1991 Volume 4, Number 18

Congressmen Implore Swift Panel To Enact Interstate Waste Rules

The long-simmering congressional debate on interstate transportation of solid and hazardous waste boiled to the surface during a House Energy and Commerce subcommittee hearing on Tuesday.

BY DENNIS WAMSTED

Currently, states are essentially precluded by the Commerce Clause of the Constitution from regulating the flow of out-of-state wastes. Worried that this could turn their districts into national dumping grounds, lawmakers from waste importing states have introduced a rash of proposals to give state or municipal governments the right to regulate interstate flows of both hazardous and solid waste.

At the same time, officials from the major exporting states urge caution, saying that legislative curbs on interstate waste trade could slow the development of national recycling markets, and that in many cases the exports are driven by other environmental concerns, such as a desire to protect groundwater resources. Although disagreeing with each other, both sides, as well as several members of the Energy and Commerce subcommittee on Transportation and Hazardous Materials, criticized the Environmental Protection Agency for its listless leadership on this issue over the past 10 years.

The criticism began at the top, with subcommittee chair Rep. Al Swift (D-Wash.) voicing his dis-

(Continued on page 7)

Waxman: EPA Clean Air Act Permit Plan 'Clearly Illegal'

BY CATHERINE COONEY

Rep. Henry Waxman (D-Calif.), chairman of the House Energy and Commerce subcommittee on health and the environment, blasted Vice President Dan Quayle, head of the White House Council on Competitiveness, at a hearing on Wednesday for interfering with the Environmental Protection Agency's proposed Clean Air Act permit rule. "White House officials, spearheaded by Vice President

(Continued on next page)

ORD DRAFTS DIOXIN REASSESSMENT

BY CATHERINE COONEY

The Environmental Protection Agency's Office of Research and Development (ORD) is nearing completion of its plan for reevaluating the agency's risk assessment model for dioxin, and should send the 10-page strategy to Environmental Protection Agency chief William Reilly sometime this week, according to Peter Preuss, one of the ORD officials coordinating the review effort.

Reilly ordered the agency to reevaluate the risk assessment model in an April 8 memo sent to ORD Assistant Administrator Erich Bretthauer. Reilly's reevaluation order was based on the significant amount of new scientific data that has been published recently on the ubiquitous chemical and its impact on human health.

The reevaluation will focus on the "thinking" developed at an international conference held last fall at the Banbury Center at Cold Spring Harbor Laboratory, said Preuss. At the conference, dioxin experts developed a new approach regarding how dioxin reacts in cells: called the receptor-mediated model, it basically recognizes that dioxin must first bind to and then activate a receptor cell before it can become carcinogenic in humans. While many who attended the conference say the new approach implies that there is a level at which dioxin exposure will no longer be considered carcinogenic, Preuss said it is much too soon to predict this. "It would be speculation to say," Preuss said about the implications of the new approach.

The reassessment will look at a variety of the health effects of dioxin, such as cancer and human developmental problems. The agency plans to look at the views on dioxin from "all of the leading scientists" and will evaluate most of the literature, Preuss said. They will also review current laboratory data on how dioxin effects a cell, as well as develop new data on this. Because EPA believes that some of the data on health effects is insufficient, it will use its Health Effects Research Laboratory in Research Triangle Park, N.C. to develop new data on immunotoxicity and some early biological effects that can be measured. EPA will also look at health data at other U.S. and European labs. "But there are no new contracts now," he added.

Lastly, the agency will have to gather new data on the ecological impact of dioxin, such as its affect on aquatic life, which is still not fully understood.

After Reilly approves ORD's plan, the group will begin directing the research to prepare for its written review. This reevaluation will be written with the help of scientists outside the agency, and should be ready for peer review in a year. Within two years, the final document discussing the receptor-model risk approach will be ready for public comment.

The group will work under ORD's Bretthauer, and includes: Preuss; William Frank, who will oversee the research; and Linda Birnbaum, director of the environmental toxicity division at Research Triangle Park who will oversee the data development. True to Reilly's announced commitment that the process be open, Preuss said all of the documents concerning the reassessment will be available to the public.

NORTHWEST ENVIRONMENTAL ADVOCATES

June 10, 1991

Fred Hansen, Director
Oregon Department
of Environmental Quality
811 S.W. Sixth
Portland, OR 97204

Bill Hutchinson, Chair
Oregon Environmental Quality
Commission
Tooze, Shenker Holloway, & Duden
333 SW Taylor St.
Portland, OR 97204

Re: Notice of Consideration of Petition for Rule Amendment
(Water Quality Standard for 2,3,7,8-TCDD)

Dear Fred and Bill:

I am writing to urge the Commission to deny the pulp and paper industry's petition to change the criterion in the water quality standard for dioxin. There are numerous reasons for the Commission not to take up this issue, not the least of which is the fact that the Department recently reevaluated this standard in its most recent "triennial review." In addition, as I am sure you are aware, U.S. EPA is reexamining the criterion.

It would be redundant for the State of Oregon to reevaluate the very same issue that EPA is currently reviewing, and Oregon is certainly less well equipped to do so. It is also premature to second guess the outcome of that evaluation. In fact, EPA Administrator Reilly has urged that regulatory actions based on the existing dioxin criterion proceed as scheduled.

For as many reasons as the pulp and paper industry can come up with to argue for an increase in the allowable limits for dioxin, there are at least an equal number of arguments that the existing standard is not conservative enough. For example, the current criterion is based on a bioconcentration factor of 5,000. Yet studies show that the bioconcentration factor in fish can range up to 156,000. The existing dioxin standard does not take into account the other media by which dioxin contaminates human beings, i.e. inhalation, eating food other than fish. General human background exposure to dioxin compounds (1 to 10 parts per kilogram (equivalent to part per quadrillion) in toxicity equivalent units for all dioxins) is known to already exceed the acceptable daily intake set by EPA for protection against reproductive effects (1 part per quadrillion). In addition there are the synergistic and

408 Southwest Second Avenue, Governor Bldg. Suite 406, Portland, Oregon 97204 Telephone (503) 295-0490

additive effects caused by exposure to dioxin in tandem with other toxic pollutants.

Industry is fond of pointing out that the risk to humans from dioxin is far less than to lab rats, for which dioxin is clearly a hazard. Presumably industry would include other 'lower life forms' in its assessment of the hazards of dioxin. This is relevant to the Commission's decision because, whether or not the existing criterion for dioxin adequately protects human beings, it certainly does not take into account the increased effects dioxin has on wildlife. These effects are increased due to the lower body weight and greater consumption of contaminated aquatic life (e.g. fish) by eagles, mink, otter, and other pisciverous wildlife. States' water quality standards are supposed to protect the most sensitive beneficial uses. The Commission should not even consider this or any other petition to change the dioxin standard unless petitioners can demonstrate that a higher level of dioxin contamination will not result in a lower level of protection for the most sensitive uses.

It is an old ploy of industry's to seek to have the rules changed when it doesn't want to meet them. It is inexcusable when government accedes to this. The Commission should enforce the standards it has adopted, not bend them when the going gets tough for a segment of industry which has had the benefit of over-polluting public waters for many years.

Sincerely,

Eugene Rosolie for

Nina Bell
Executive Director

cc: Emery N. Castle
Henry Lorenzen
Carol Whipple
William W. Wessinger

action for the Commission is to deny the Petition for Rule Amendment and we urge the Commission to do so.

Dated this 10th day of June, 1991.

Respectfully submitted,

Victor M. Sher / RET

VICTOR M. SHER

Todd D. True / RET

TODD D. TRUE

Rebecca E. Todd

REBECCA E. TODD

Sierra Club Legal Defense Fund, Inc.
216 First Avenue S. Suite 330
Seattle, WA 98014
(206) 343-7340

Attorneys for American Oceans Campaign, Campaign for Puget Sound, Dioxin/Organochlorine Center, Friends of the Earth, National Audubon Society, Puget Sound Alliance, Washington Environmental Council, and Washington Toxics Coalition.

Sent by telecopy to:

Chair William P. Hutchison, Jr.	(503) 223-5550
Vice Chair Emery N. Castle	(503) 737-1574
Commissioner Henry Lorenzen	(503) 276-3148
Commissioner Carol A. Whipple	(503) 584-2129
Commissioner William W. Wessinger	(503) 229-4689
Director Fred Hansen	(503) 229-6124

cc: Mr. Larry Edelman
Ms. Dana Rasmussen
Mr. Rick Albright
Ms. Adrianne Allen

Because of the availability of chlorine-free technologies, the complete lack of need for chlorine bleached pulp and paper, and the serious and persistent risks to human and environmental health, if the Commission grants the Petition for Rule Amendment, we anticipate returning to urge the Commission to promulgate an ambient water quality standard of zero for 2,3,7,8-TCDD.

IV. Conclusion

On behalf of the organizations listed above, we offer this Memorandum in Opposition to the Petition for Rule Amendment. We will gladly provide the Commission with any of the data discussed above. As we have not had the opportunity to view all the information submitted by the mills, we are unable to respond directly to their particular scientific or other assertions. Should the Commission like us to provide a more detailed response to their specific claims, we will arrange to procure the mills' lengthy submission and provide a detailed scientific analysis for the Commission's review. That being said, however, we believe that the wisest, most protective, and most efficient course of

//

//

//

//

//

//

//

//

There are many technologies available and in use worldwide that reduce and eliminate the use of chlorine or chlorine compounds that are the necessary precursors for all chlorinated organic compounds. Without chlorine or chlorine compounds present in the production process, organochlorines cannot be formed and discharged to the environment. Many European mills and some North American mills currently employ chlorine-free technology in their pulp and paper production. Many if not all the mills in the United States are at the very least exploring ways in which they can reduce their use of chlorine and the subsequent discharge of toxic organochlorines.

Furthermore, the public is becoming increasingly aware of the human and environmental health risks associated with chlorine bleaching and is demanding chlorine-free pulp and paper products. The mill in Lyons Falls, New York is one example of a mill that has converted to a chlorine-free technology and has subsequently experienced an increase in its market share. As consumers increasingly demand chlorine-free paper products, those mills that can supply them are enjoying competitive success in the marketplace.

As has been long recognized elsewhere, there are no functional uses of pulp and paper products that demand the super bright whiteness normally achievable with chlorine bleaching processes. Non-chlorine bleaching renders pulp and paper products that are nearly as bright white as chlorine bleached products. These chlorine-free products are suitable for every use to which pulp and paper products are put today.

We are not the first to suggest to the State of Oregon that the water quality standard for 2,3,7,8-TCDD should be zero. Over the past several years, the United States Fish and Wildlife Service has consistently advised that because of the long-term health effects on wildlife that 2,3,7,8-TCDD discharges be reduced and eliminated:

> We recommend that the DEQ consider limiting the [pulp and paper mills' National Discharge Elimination System, or NPDES] permit[s] to a discharge of no dioxins...

Letter from the United States Fish and Wildlife Service to the Oregon Department of Environmental Quality dated July 10, 1989. Six months later the Fish and Wildlife reiterated that

> we believe it is appropriate for DEQ to develop a long-term goal that decreases and eventually eliminates the production of dioxin and other chlorinated byproducts.

Letter from the United States Fish and Wildlife Service to the Oregon Department of Environmental Quality dated January 19, 1990.

In recognition of the severity of the organochlorine contamination in the Columbia River Basin, the Fish and Wildlife Service most recently explained that

> considering the longevity of organochlorine compounds and the potential impact of small quantities of dioxins on fish, waterfowl, and endangered species, we recommend that the EPA strive towards limiting NPDES permits to zero discharge of dioxins to the Columbia River Basin.

Letter from the United States Fish and Wildlife Service to Region 10 EPA dated November 21, 1990. The zero discharge standard is the only standard for 2,3,7,8-TCDD that will adequately protect human, wildlife, and environmental health.

At this time and given the limited resources of the State, the most logical and protective course of action for the Commission is to deny the Petition for Rule Amendment.

III. Alternatively, If the Environmental Quality Commission Revisits the Rulemaking Procedure, the Proper Water Quality Standard for 2,3,7,8-TCDD is Zero.

The chlorine bleaching pulp and paper mills insist that new data indicate that the ambient water quality standard for 2,3,7,8-TCDD should be loosened. It is our position, and the position of the best scientific experts in the field, that available data militate for a <u>more stringent</u> <u>and</u> <u>protective</u> standard. These data include human reproductive and developmental effects, the effects on wildlife reliant on contaminated ecosystems, and the bioaccumulation, bioconcentration, and persistence of 2,3,7,8-TCDD in animal tissue and sediments. If the Petition for Rule Amendment is granted, we expect that the Commission will find itself in the midst of an extremely involved and complex dispute, with both sides presenting evidence and expert opinion regarding the proper water quality standard for 2,3,7,8-TCDD.

If the Commission does indeed elect to reopen rulemaking, we anticipate arguing that the standard for 2,3,7,8-TCDD is properly zero, that is, that the Commission should allow no discharges of 2,3,7,8-TCDD at all.

//

//

//

Furthermore, the issue of the proper water quality standard for 2,3,7,8-TCDD will be debated shortly in another forum. EPA established the Total Maximum Daily Loadings [TMDL] for the Columbia River on February 25, 1991, regarding the total allowable discharge of 2,3,7,8-TCDD into the Basin. We anticipate legal challenges to the TMDL asserting that the .013 ppq standard is inadequate to protect human health and wildlife. In this connection, we believe that the appropriate water quality standard for 2,3,7,8-TCDD is zero, as detailed in Section III below.

Furthermore, from an ecosystem perspective it is nonsensical to allow mills in Oregon to discharge bioaccumulative and persistent organochlorines into the Columbia River Basin at 2.3 ppq, while Idaho and Washington mills comply with the applicable .013 ppq state standards, a difference of orders of magnitude. Fish, endangered Bald Eagles feeding on them, mink, otter, other wildlife, as well as sensitive human populations such as Native Americans, Asian Americans, and subsistence and sport fishers cannot differentiate among the 2,3,7,8-TCDD contamination from Oregon and that from other states. With regard to these especially sensitive groups, the State of Oregon has a duty to protect all of the people that compose the population of the State. While the .013 ppq standard is not adequately protective of either humans and wildlife, the suggested 2.3 ppq standard is even less so.

//

//

II. The Environmental Quality Commission Should Deny the Petition for Rule Amendment.

We strongly urge the Commission to deny the Petition for Rule Amendment filed by James River II and the Boise Cascade Corporation on May 23, 1991. A new rulemaking effort makes little sense in light of the limited resources of the State of Oregon. Indeed, Oregon initially adopted the .013 ppq standard established by EPA's Quality Criteria for Water 1986 with the express realization that the State had insufficient resources to undertake adequately a separate analysis of the health risks of 2,3,7,8-TCDD. As the State continues to suffer from limited resources, it continues to be ill-advisable for the State to undertake the complex analysis of human and environmental health risks from 2,3,7,8-TCDD necessary in deciding the water quality standard.

The adoption of a water quality criterion or standard is a significant task. EPA regulations mandate that every water quality criteria

> must be based on sound scientific rational and must contain sufficient parameters or constituents to protect the designated use. For waters with multiple use designations, the criteria shall support the most sensitive use.

40 C.F.R. § 131.11(b)(1)(1990). To adopt a new water quality standard requires that the rulemaking body employ "scientifically defensible methods" in assuring that the most sensitive uses are protected. 40 C.F.R. § 1313.11(b)(1)(1990) Establishing a new water quality standard for 2,3,7,8-TCDD would be extremely resource intensive, consuming the kind of time and energy that the State of Oregon has already recognized that it lacks.

it is misleading to consider dioxin as a single entity, and the potential health risks are properly evaluated by taking into account exposures to mixtures of the hundreds of isomers and related compounds in this group.[8]

An approach, therefore, which focuses on the cancer risks from 2,3,7,8-TCDD necessarily underestimates cancer risks from pulp and paper mill effluent[9] and also ignores other arguably more important organismic and ecosystem level impacts from 2,3,7,8-TCDD such as adverse reproductive, developmental, and wildlife effects.

//

//

//

//

//

---

[8] Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 at 456 (1989).

[9] EPA itself recognizes that its cancer risk and attendant water quality standard of .013 ppq vastly underestimate the actual cancer risk suffered by certain sensitive populations. EPA estimates that a Native American adult consuming Columbia River Basin fish in an amount average for Native Americans per day contaminated with 6.5 parts per trillion (ppt) 2,3,7,8-TCDD equivalents exceeds the EPA threshold of concern for reproductive effects by over nine times. See, McCormack, Craig and David Cleverly, United States Environmental Protection Agency, Analysis of the Potential Populations at Risk From the Consumption of Freshwater Fish Caught Near Paper Mills, Draft Report, April 23, 1990.

Furthermore, in calculating the cancer risk and water quality standard for 2,3,7,8-TCDD, EPA assumed a fish consumption rate of only 6.5 grams per day, while actual fish consumption rates are approximately five times higher than this, and Native American fish consumption rates are approximately fifteen times higher. More realistic fish consumption rates, therefore, would make the cancer risk standards five to fifteen times higher, respectively. Id.

bioaccumulative, bioconcentrative, and persistent.[6]

Moreover, while 2,3,7,8-TCDD is the most toxic substance ever identified, and hence the most toxic of the organochlorines, chlorine bleaching pulp and paper production generates tons of chlorinated organics which are toxicologically equivalent to 2,3,7,8-TCDD. In other words, these other organochlorines act within the body and the environment in virtually the same toxicological manner as 2,3,7,8-TCDD. For example, in issuing a recent Fish Consumption Advisory for Lake Roosevelt, the Washington State Department of Health recognized that 90% of the dioxin toxicity is due to 2,3,7,8 tetrachlorodibenzofuran.[7] As one of the leading scientific experts has written,

---

Svensson, Bengt-Goran, Anita Nilsson, Marianne Hansson, Christopher Rappe, Bjorn Akesson, and Staffan Skerving, Exposure to Dioxins and Dibenzofurans Through the Consumption of Fish, The New England Journal of Medicine 116:8-12 (1991).

Swain, Wayland R., Human Health Consequences of Consumption of Fish Contaminated with Organochlorine Compounds, Aquatic Toxicology 11:357-377 (1988).

Tanabe, S., N. Kannan, An. Subramanian, S. Watanabe, and R. Tatsukawa, Highly Toxic Coplanar PCBs: Occurrence, Source, Persistency and Toxic Implications to Wildlife and Humans, Environmental Pollution 47:147-163 (1987).

[6] The toxicokinetic half-life of 2,3,7,8-TCDD in human tissue has been predicted to be approximately 5 to 8 years and the half-life in sediments is even longer. See, Bowman, R.E., S.L. Schantz, N.C.A. Weerasinghe, M.L. Gross, and D.A. Barsotti, Chronic Dietary Intake of 2,3,7,8 Tetrachlorodibenzo-p-dioxin (TCDD) at 5 or 25 Parts Per Trillion in the Monkey: TCDD Kinetics and Dose-Effect Estimate of Reproductive Toxicity, Chemosphere 18:243-252 at 250 (1989), and Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 at 458 (1989).

[7] Washington Department of Ecology, First Progress Report on Ecology's Dioxin/Furan Survey in Lake Roosevelt, Memorandum from Art Johnson, Dave Serdar, and Stuart Magoon to Carl Nuechterlein, August 8, 1990.

2,3,7,8-TCDD is a known human carcinogen, teratogen, and immunosuppressant.[4] Other types of damage caused by 2,3,7,8-TCDD include skin disorders, reproductive disorders, hormonal and metabolic effects, developmental defects, damage to the liver, kidney and thymus, wasting syndrome, neurobehavioural effects, and learning disabilities.[5] Furthermore, 2,3,7,8-TCDD is

---

[4] Some pertinent papers regarding this include:

Fingerhut, Marilyn A., William E. Halperin, David A. Marlow, Laurie A. Piacitelli, Patricia A. Honchar, Marie H. Sweeney, Alice L. Greife, Patricia A. Dill, Kyle Steenland, and Anthony J. Suruda, Cancer Mortality in Workers Exposed to 2,3,7,8 Tetrachlorodibenzo-p-dioxin, The New England Journal of Medicine 324: 212-218 (1991).

Schwartz, E., A Proportionate Mortality Ratio Analysis of Pulp and Paper Mill Workers in New Hampshire, British Journal of Industrial Medicine 45:234-238 (1988).

Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 (1989).

Skene, S.A., I.C. Dewhurst, and M. Greenberg, Polychlorinated Dibenzo-p-dioxins and Polychlorinated Dibenzofurans: The Risks to Human Health: A Review, Human Toxicology 8:173-203 (1989).

[5] Some pertinent papers regarding this include:

Bowman, R.E., S.L. Schantz, M.L. Gross, and S.A. Ferguson, Behavioral Effects in Monkeys Exposed to 2,3,7,8-TCDD Transmitted Maternally During Gestation and for Four Months of Nursing, Chemosphere 18:235-242 (1989).

Fish and Wildlife Service, Dioxin Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review, Biological Report 85, May 1986.

Jacobson, Joseph L., Sandra W. Jacobson, and Harold E.B. Humphrey, Effects of In Utero Exposure to Polychlorinated Biphenyls and Related Contaminants on Cognitive Functioning in Young Children, Journal of Pediatrics 116:38-45 (1990).

Larsson, Ake, T. Andersson, L. Forlin, and J. Hardig, Physiological Disturbances in Fish Exposed to Bleached Kraft Mill Effluents, Wat. Sci. Tech. 20:67-76, 1988.

McCormack, Craig and David Cleverly, United States Environmental Protection Agency, Analysis of the Potential Populations at Risk From the Consumption of Freshwater Fish Caught Near Paper Mills, Draft Report, April 23, 1990.

Schantz, Susan L., and Robert E. Bowman, Learning in Monkeys Exposed Perinatally to 2,3,7,8 Tetrachlorodibenzo-p-dioxin (TCDD), Neurotoxicology and Teratology 11:13-19, 1989.

In specific, the organizations seek to reduce and eliminate entirely the discharge of toxic organochlorines to the waters of the Pacific Northwest, including 2,3,7,8 tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD), commonly known as dioxin.[2]

We strongly oppose the Petition for Rule Amendment and urge the Environmental Quality Commission to deny the Petition. We are a group of national, regional, and Washington State environmental groups concerned about the water quality of the Pacific Northwest, Oregon, and the water resources shared by Oregon, Washington, and Idaho. The Columbia River receives much of the region's pulp and paper mill organochlorine discharge and for many hundreds of miles is a shared resource and border for Oregon and Washington.[3] The ambient water quality standard for 2,3,7,8-TCDD in Oregon necessarily affects these shared ecosystems and the livelihood and recreation of those living in both states. We are also concerned with the precedential implications that the Petition for Rule Amendment may have nationwide and for the Pacific Northwest.

---

[2] "Dioxin" as it refers to 2,3,7,8-TCDD is actually a misnomer. Dioxins are a family of approximately 75 separate chlorinated organic compounds, each of which is characterized by the existence of two oxygen atoms connecting two chlorinated benzene rings.

[3] The interdependence of the Pacific Northwest states with regard to the Columbia River has been recognized by the formation by Oregon and Washington of the Bistate Commission for the Columbia River, and the basin-wide protection strategies for the River established by the Environmental Protection Agency [EPA], including the establishment of Total Maximum Daily Loadings and Individual Control Strategies pursuant to the Federal Water Pollution Control Act, 33 U.S.C. §§ 1313(d) and 1314(l), respectively.

VICTOR M. SHER (WSB# 16853)
TODD D. TRUE (WSB# 12864)
REBECCA E. TODD (WSB# pending)
Sierra Club Legal Defense Fund
216 First Avenue S., Suite 330
Seattle, Washington 98104
(206) 343-7340

BEFORE THE ENVIRONMENTAL QUALITY COMMISSION
OF THE STATE OF OREGON

In the Matter of the Petition of James River II, Inc. and Boise Cascade Corporation to Amend Subparagraph (2)(p)(B) of Oregon Administrative Rules Chapter 340, Division 41, Sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965.	MEMORANDUM IN OPPOSITION TO THE PETITION FOR RULE AMENDMENT

I. Introduction

This Memorandum in Opposition to the Petition for Rule Amendment is submitted by the Sierra Club Legal Defense Fund, Inc. on behalf of the American Oceans Campaign, the Campaign for Puget Sound, the Dioxin/Organochlorine Center, Friends of the Earth, National Audubon Society, Puget Sound Alliance, the Washington Environmental Council, and the Washington Toxics Coalition.[1] These organizations are non-profit environmental groups dedicated to and actively working toward the preservation and protection of water resources and all life dependent on them.

[1] American Oceans Campaign, 4007 Latona Avenue NE Seattle, WA 98105; Campaign for Puget Sound, P.O. Box 2807 Seattle, WA 98111-2807; Dioxin/Organochlorine Center, 1247 Willamette Street Eugene OR 97401; Friends of the Earth, 4512 University Way NE Seattle WA 98105; National Audubon Society, P.O. Box 462 Olympia, WA 98502; Puget Sound Alliance, 4516 University Way NE Seattle WA 98105; Washington Environmental Council, 5200 University Way NE Seattle WA 98105; and the Washington Toxics Coalition, 4516 University Way NE Seattle WA 98105.

United States
Environmental Protection
Agency

Region 10
1200 Sixth Avenue
Seattle WA 98101

Alaska
Idaho
Oregon
Washington

EPA

Reply to
Attn of: WD-139

Fred Hansen, Director
Oregon Department of Environmental Quality
Executive Building
811 SW Sixth Avenue
Portland, Oregon 97204

RE: Comments on Petition to Amend Oregon's Standard for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)

Dear Mr. Hansen:

The Environmental Protection Agency (EPA) Region 10 believes it is premature for the State of Oregon to revise its dioxin standard at this time in response to the petition referenced above, and recommends that the Environmental Quality Commission deny the petition.

As you are aware, EPA is currently reassessing the toxicity of TCDD. EPA expects to complete development of a new model for predicting TCDD toxicity by the spring of 1992. Following its development, the new model will undergo extensive peer review. EPA has committed considerable resources to collect additional data on endpoints other than cancer effects to help support this model. These other endpoints, which include reproductive and immunological responses, are of concern as they may be more sensitive to TCDD exposure than the development of cancerous tumors. Consequently, it is impossible to predict at this time whether EPA's criterion will become more or less stringent as a result of the reassessment.

As a final note, I would like to add that the technology-based controls being required of pulp and paper mills in Oregon will require controls adequate to meet Oregon's current TCDD standard. Thus, the mills should not incur any irretrievable expenditures during the coming year while EPA completes its TCDD reassessment.

These comments are discussed in greater detail in the enclosure to this letter. Should you have any questions regarding our comments, please call me at (206) 553-5810. Thank you for the opportunity to comment on this petition.

Sincerely,

Dana A Rasmusse

Dana A. Rasmussen
Regional Administrator

Enclosure

ENVIRONMENTAL PROTECTION AGENCY
REGION 10

COMMENTS ON PETITION TO REVISE
OREGON'S TCDD STANDARD

June 10, 1991

This document provides the Environmental Protection Agency (EPA) Region 10 comments on the May 23, 1991, petition by James River II, Inc., and Boise Cascade Corporation to amend Oregon's water quality standard for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The petitioners propose a standard of 2.3 parts per quadrillion (ppq) in place of the current standard of .013 ppq. For the reasons discussed below, EPA believes it is premature for the State of Oregon to revise its dioxin standard at this time, and recommends that the Environmental Quality Commission deny the petition.

As you are aware, EPA is currently reassessing the toxicity of TCDD. This reassessment is in response to a growing understanding of the mechanism by which TCDD acts and on newer information on its carcinogenicity. EPA will attempt to develop a new model for predicting harmful levels of TCDD exposure based on this more recent information. EPA expects to complete development of the model by the spring of 1992. Following its development, the model will undergo extensive peer review. Because the model will consider a number of toxicological endpoints, it will not focus solely on cancer effects, as the model used to develop EPA's current water quality criterion for TCDD does.

While the standard proposed in the petition is based on a model similar to that which EPA is currently evaluating, EPA believes that use of the model to revise the standard is premature for the following reasons:

1. EPA has only begun to develop this model. While there appears to be general agreement on the mechanism by which TCDD causes toxicity, development of a predictive model relies on a number of assumptions, few of which have undergone any kind of rigorous testing or peer review. Due to its extreme toxicity, it seems inappropriate to substantially elevate the TCDD standard without more critical review of model assumptions.

2. The new model being developed by EPA relies on multiple toxic endpoints. Little information exists for many endpoints of concern. Therefore, EPA has committed considerable resources to collect additional data on other endpoints such as reproductive and immunological responses. The scant information available to date

suggests that these other endpoints may be more sensitive to TCDD exposure than the development of cancerous tumors. EPA's scientists are uncertain at present whether the new model, when combined with the new toxicological information being generated, will cause EPA's criterion to become more or less stringent. To increase the TCDD standard by over two orders of magnitude in light of this information appears inappropriate.

3. A number of other chemicals endemic in the environment appear to cause toxicity via a similar mechanism. It is possible, therefore, that chemicals such as PCBs, PAHs, DDT, furans, and dioxins other than TCDD may exacerbate the effects of exposure to TCDD. Part of the additional data being generated by EPA during the coming year is aimed at addressing this issue.

4. Current information on the effects of TCDD on aquatic organisms and wildlife has been inadequate for EPA to develop a criterion for their protection. However, both fish and wildlife have proven to be extremely sensitive to TCDD. In addition, concern has been raised over the potential effects of TCDD on threatened and endangered species, particularly bald eagles, in the Columbia River basin. To address this inadequacy, EPA is also collecting the information necessary for development of a TCDD criterion for the protection of aquatic life.

Because of the extreme toxicity of dioxin to aquatic life and laboratory animals, and because EPA is in the process of collecting a vast amount of additional information on the toxicity of TCDD, it would seem premature for Oregon to revise its TCDD standard at this time.

Region 10 does not believe that Oregon's current TCDD standard will cause any irretrievable expenditures by companies in the Pacific Northwest. All companies likely to be affected by the current standard are faced with making process changes to meet existing or proposed technology-based requirements. These technology-based requirements are expected to achieve, or come very close to achieving, TCDD limits based on the current standard of .013 ppq. In fact, Region 10 does not expect the appeals of their NPDES permits by the petitioners to be completed until after EPA concludes its TCDD reassessment next spring.

In conclusion, EPA believes that it would be premature for Oregon to consider revising its TCDD standard until EPA completes its reassessment. However, should the Environmental Quality Commission decide that a rulemaking to revise the standard is appropriate at this time, EPA suggests that the following be considered:

1. The proposed rule should consider the similar mechanisms of effect of other dioxin congeners, furans, PCBs, and other similar chemicals;

2. Other chlorinated organic compounds, such as chloroform and resin acids, which are often produced in association with TCDD and which are generally controlled by the same processes which control TCDD, should also be considered for rulemaking; and,

3. Aquatic life and wildlife effects should be considered in setting a new TCDD standard.

U.S. EPA Region 10
Water Division

FAX: (206) 553-0165
FTS 399-0165

To Confirm Your FAX Call:
(206) 553-6913
FTS 399-6913

TO: ~~Fred~~ Hansen

Phone No:

City, State/Region:

FAX NUMBER: 503 229-6124

FROM: Bob Burd

1200 Sixth Avenue, WD- 131 Seattle, WA 98101

Phone No: 206 553-6415

TOTAL PAGES: 6
(Including this cover sheet)

COMMENTS:

CHARLES R. "CHUCK" NORRIS
UMATILLA COUNTY
DISTRICT 57

REPLY TO ADDRESS INDICATED:
House of Representatives
Salem, Oregon 97310-1347
P.O. 121, 725 E. Highland Ave.
Hermiston, Oregon 97838

378-8050

HOUSE OF REPRESENTATIVES
SALEM, OREGON
97310-1347

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 12 1991
OFFICE OF THE DIRECTOR

June 11, 1991

William P. Hutchison, Jr., Chair
Environmental Quality Commission
c/o Department of Environmental Quality
811 SW Sixth
Portland, OR 97204

Dear Mr. Hutchison:

I understand that the EQC is in receipt of petitions to reconsider the permissible ambient level of 2,3,7,8 TCDD (dioxin) in Oregon's water. You may recall that I had previously shared some concerns on this issue, basically questioning a criterion of .013 ppq. A copy of some relevant correspondence under date of March 19, 1990 is enclosed.

A lot has happened in this matter since my letter of March 19, most notably Dr. Robert A. Squire's letter of the same date refuting the research which led to the .013 ppq criterion. I'm sure you are aware of and have seen that letter, but I enclose a copy for your convenient reference.

While I am certainly committed to avoiding realistic biological risk, I remain concerned that we do not label certain bodies of water, especially the Columbia River John Day and McNary Pools, unsafe based on other than credible scientific evidence and principles.

As stated earlier, eventually the west end of Umatilla County must rely on the Columbia as a major source of water for a variety of uses, and it would be extremely unfortunate to have such use denied because of alleged contamination based on flawed criteria. No doubt you are aware that certain other states, in concert with the EPA, have adopted standards far less stringent then .013 ppq.

Your attention in this matter will be appreciated.

Sincerely,

C.R. "Chuck" Norris

2 enclosures: As stated above.

cc: Henry Lorenzen, Member, EQC
Fred Hansen, Director, DEQ

REPLY TO ADDRESS INDICATED:
[ ] House of Representatives
Salem, Oregon 97310-1347
[✓] P.O. 121, 725 E. Highland Ave.
Hermiston, Oregon 97838

HOUSE OF REPRESENTATIVES
SALEM, OREGON
97310-1347

567-8638, ofc

March 19, 1990

SUBJECT: Dioxin in the Columbia River

TO: Fred Hansen, Director, Department of Environmental Quality
811 SW Sixth, Portland, OR 97204

Dear Fred:

During my comments to the Environmental Quality Commission on March 1 in Pendleton I raised two basic issues regarding dioxin in the Columbia.

1. Is there a scientific basis for the limiting standard of .013 parts per quadrillion? My best recollection is that I was informed that the standard was set by the EPA.

2. I commented that the water future of parts of District 57 (primarily the west end of Umatilla County) will rest on tapping the Columbia River to replace our current dependence on deep wells. I expressed the hope that we wouldn't get there just in time to learn that dioxin contamination above McNary Dam precluded our use of that source. My best recollection is that there was no response suggesting that there is or is likely to be such a problem. My thoughts and comments at the time are reported with reasonable accuracy in the enclosed article from the Hermiston Herald. (See Enclosure 1.)

Several days after the EQC meeting I read with dismay the enclosed article from the East Oregonian of March 12. It jarred me on two counts. (See Enclosure 2.)

1. It reported that the McNary pool was already badly contaminated.

2. It reported that the Oregon (DEQ) standard is .013 parts per quadrillion but that the Federal (EPA) standard is "only" .07 parts per trillion and the Federal FDA acceptable level is more lenient yet at 25 parts per trillion--the Oregon standard being more stern by factors of 5,000 and 35,000, respectively. (I have made no effort to check the math on those factors.)

I am confused and concerned and request a clear statement on acceptable levels of dioxin in the Columbia River (or any other water source) and whether or not the interagency disparity suggested in Enclosure 2 does in fact exist. I repeat my question and concern of March 1 regarding acceptable levels--scientific or arbitrary?

Your attention in this matter will be appreciated.

2 encl: As ~~stated above~~. Not included

Sincerely,

Chuck

C.R. "Chuck" Norris

cc: Wm. P. Hutchison, JR, Chair, EQC
Henry Lorenzen, Member, EQC

ROBERT A. SQUIRE ASSOCIATES, INC.
1515 LABELLE AVENUE
RUXTON, MARYLAND 21204
301-821-0054

March 19, 1990

Robert A. Michaels, Ph.D., Chairperson
Maine Scientific Advisory Panel
RAM TRAC Corporation
931 Northumberland Drive
Schenectady, N.Y. 12309

Dear Dr. Michaels:

I enclose a copy of the independent Pathology Working Group (PWG) Report on 2,3,7,8-Tetrachlorodibenzo-P-Dioxin conducted by Pathco, Inc. This report constitutes an objective reevaluation of the female rat liver lesions, by recognized experts, based upon current pathological criteria. I am certain the other observers of the PWG, Dr. Moch from FDA and Dr.'s Singh and Chiu from EPA, would agree with me that the review was conducted in a balanced, unbiased manner by highly qualified pathologists.

The conclusions reached by the PWG are consistent with my recent findings, as reported to you in my letter of January 8, 1990. A recalculation of potential human risk, based upon these new data, is clearly necessary. One of the most important statements in the report is that the morphological findings indicate that TCDD had only a weak oncogenic effect in female rat livers. This is in contrast to the view often expressed that TCDD is a potent animal carcinogen.

The Maine Scientific Panel should be commended for raising this issue and seeking an objective review based upon current scientific evidence. Without your request, it would have been difficult to obtain the slides for reevaluation and, more importantly, there would have been little impetus to conduct the review.

Please contact me if I may be of further assistance.

Sincerely,

Robert A. Squire

Robert A. Squire, D.V.M., Ph.D.

RAS:fts

cc:Dr. Robert Frakes

MAY 04 1990

(503) 229-5502
FAX (503) 226-1355
TDD-Nonvoice (503) 229-5497

Oregon

DEPARTMENT OF HUMAN RESOURCES

Health Division

June 11, 1991

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 12 1991
OFFICE OF THE DIRECTOR

Environmental Quality Commission
Director's Office
Dept. of Environmental Quality
811 SW 6th Avenue
Portland, Oregon 97204

Dear Commissioners:

I am writing as the spokesperson for the Oregon Health Division to recommend that the Environmental Quality Commission deny James River II, Inc. and Boise Cascade's petition to amend Oregon's ambient water quality standard for TCDD. Increasing the ambient water quality criteria for TCDD could potentially undermine the future protection of public health in the State of Oregon.

As the Public Health Toxicologist for the Oregon Health Division (OHD), I am very familiar with scientific information regarding the health effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). A substantial amount of scientific data exists to support a receptor-based mechanism of toxicity for this chemical. Empirical as well as epidemiologic information provide support that animal to man inferences, and high to low dose theoretical extrapolation models have not accurately estimated TCDD's true human toxicity.

The OHD is currently monitoring the scientific debates and developments regarding the assessment of human health effects of TCDD. We are also in the process of developing a public health policy regarding dioxin and furan contaminated media of public health concern in the State of Oregon. This policy is not expected to be finalized before the end of the year.

The OHD policy will provide information about whether or not human health effects would be expected from a certain type of dioxin or furan exposure. The policy will address pre-existing environmental contamination, and provide the mechanism to initiate appropriate public health protection activities.

The OHD approach will not be unlike other agency's "acceptable daily intake" estimates which identify a dose that is not expected to result in adverse health effects. However, such estimates are not useful for developing pollution prevention or antidegradation environmental protection policies. To be protective of public health,

BARBARA ROBERTS
Governor

1400 SW 5th Avenue
Portland, OR 97201
(503) 229-5599 Emergency
(503) 252-7978 TDD
Emergency

concentrations of contaminants in the environment of highly persistent chemicals such as dioxins and furans for which substantial evidence exists for the potential for adverse health effects should not be allowed to increase, and should not be as high as an "acceptable daily intake".

Even if pollution prevention or antidegradation is not an issue in this particular case, it still remains that many assumptions and extrapolations that are not scientifically based, and can not be validated must be made in order to utilize an "acceptable daily intake" in the calculation of an ambient water quality criteria.

In conclusion, the OHD believes that revision of Oregon's ambient water quality criteria should be scientifically based on information that can be substantiated with actual data. Such information is not presently available; therefore, increasing the water quality criteria has the potential for undermining the future protection of public health in the State of Oregon.

Sincerely,

Rlorenzana

Roseanne M. Lorenzana, DVM, PhD
Public Health Toxicologist
Environmental Toxicology Section
Office of Environment and Health Systems

RML:ab

CC: Gene Foster, DEQ
Larry Foster, Acting State Health Officer
Kathleen A. Gaffney, MD, MPH, State Health Officer Elect

LIZ VanLEEUWEN
LINN COUNTY
DISTRICT 37

REPLY TO ADDRESS INDICATED:
☑ House of Representatives
Salem, OR 97310-1347
Capitol Message 378-8772

☐ 27070 Irish Bend Loop
Halsey, Oregon 97348
Home Phone 369-2544

COMMITTEES
Chairman:
Intergovernmental Affairs
Vice-Chairman:
Agriculture, Forestry, and
Natural Resources
Member:
Enviroment and Energy

HOUSE OF REPRESENTATIVES
SALEM, OREGON
97310-1347

June 11, 1991

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 13 1991
OFFICE OF THE DIRECTOR

Mr. William P. Hutchison
Chairman, Environmental Quality Commission
811 S.W. Sixth Avenue
Portland, OR 97204

Dear Mr. Hutchison:

I am writing to support the James River Corporation and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Oregon's current water quality standard of .0013 parts per quadrillion (ppq) may be more restrictive than necessary to protect human health. Recently, the EPA approved water quality standards in other states that are 100 times less stringent than the original EPA guideline criterion which Oregon adopted. Now EPA has called for a review of the science on dioxin. However, if Oregon awaits the outcome of the EPA study before reviewing its own dioxin standard, the two pulp and paper companies listed above will be bound by state law to invest millions of dollars in what may prove to be unnecessary environmental controls. That is why we need rule-making now.

James River will spend close to $20 million in the next three years to further reduce the discharge of dioxin from its Wauna pulp and paper mill on the Columbia River. If the Wauna mill were located in Maryland, Virginia or elsewhere in the Southeast, the mill already would be in compliance with EPA-approved standards, and the expenditures would not be necessary.

<u>We must establish a scientifically-based water quality standard for dioxin that protects Oregonians, but at the same time does not overwhelmingly disadvantage Oregon industry.</u> I urge you and other commission members to accept the petition to review Oregon'' water quality standard for dioxin when you meet June 14.

Sincerely,

Liz VanLeeuwen

Liz VanLeeuwen
State Representative
District 37

June 2, 1991

Environmental Quality Commission
Directors Office
811 S. W. 6th Ave.
Portland, Oregon 97204

Dear Commission Member,

In reference to the giant pulp and paper manufacturers, notably James River Corporation and Boise Cascade, who brashly now request the Oregon E.Q.C. to set lower ambient water quality standards.

Needless to say, the Oregon standard is absolutely necessary to the maintenance of our waterways now and for the future. Certainly industrial needs must be given some consideration. However all members of the state's citizenry should also be granted the highest water quality standards in our great Northwest. Oregon as a leader in all environmental concerns is a model for the nation.

As owners of property on the Columbia River in Columbia County, we implore the E.Q.C. to reject the proposed change in water quality standards. Industry cannot provide any real evidence that would support any modification of the D.E.Q. standard.

Thank you for your vote against such a negative approach to our water quality.

Sincerely,

Roger and Mary Thompson

Roger and Mary Thompson
4144 S. E. Boardman Ave.
Milwaukie, Oregon 97267

Environmental Quality Commission
Directors Office
811 SW 6th Avenue
Portland, OR 97204

June 4, 1991

Dear Commission Member,

I urge you to please reject the latest proposal by the pulp industry to reduce the water quality standards in Oregon.

In a time of increased environmental awareness, it seems indefensible that certain companies would propose to lessen the standards for economic reasons, while neglecting and potentially harming a very large and complex ecological system.

My interest as a partner in land in Clatskanie prompts me to write this letter not only for myself, but for everyone who lives on or near the rivers in Oregon. You have the opportunity to effect a positive result for the people of Oregon. Please do so.

Respectfully,

Robert J. Thompson

Robert J. Thompson

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 07 1991
OFFICE OF THE DIRECTOR

LES MILES

GRAVEL COMPANY

30, AUBURN, WASHINGTON 98071

AUBURN
JUN 5 '91
WASH.

U.S. POSTAGE
0 5 2
METER
8219290

Environmental Quality Commission
Directors Office
811 S.W. 6th Ave.
Portland, OR 97204

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 07 1991
OFFICE OF THE DIRECTOR

NORTHWEST PULP&PAPER

June 6, 1991

Fred Hansen, Director
Department of Environmental Quality
811 SW Sixth Avenue
Portland, OR 97204

Dear Mr. Hansen:

The Northwest Pulp and Paper Association is writing to support the James River Corp. and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Oregon's current water quality standard of 0.013 parts per quadrillion (ppq) is a human-health-based standard. However, the science upon which this standard was developed has been challenged — and its conclusions radically altered — by the very scientist who conducted the original research. Therefore, the premise for the current standard is now highly questionable.

In addition, the Environmental Protection Agency has recently approved water quality standards 100-times less stringent than its guideline criterion (which Oregon adopted, along with a variety of other EPA recommendations for toxic discharges). Thus, EPA has indirectly conceded that, when taking new science and regional factors into consideration, its criterion of 0.013 ppq may be more restrictive than necessary to protect human health.

In recognizing this apparent conflict, EPA has announced a review of the science on dioxin. I have enclosed a May 17 report from *Science* that notes the one-year time frame EPA Administrator William Reilly has established for this review. However, should Oregon decide to wait on the EPA review before commencing a review of its standard — and not suspend its imposition of dioxin discharge restrictions — the two mills in question are bound by state law to invest millions of dollars in what may prove to be unnecessary environmental controls.

Oregon needs a scientifically-based water quality standard for dioxin that is fully protective of human health. The Clean Water Act delegates this responsibility to the states, in part so that states may incorporate regional data, such as fish consumption information, into their decision. It is time for Oregon to develop such a state-specific water quality standard for dioxin. We hope that the Environmental Quality Commission will accept the James River and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Sincerely,

Kathy E. Gill

Kathy E. Gill, CAE
Public Affairs Director

enclosure
c: EQC members

NORTHWEST PULP & PAPER ASSOCIATION 1300 114TH AVENUE SOUTHEAST, SUITE 110 BELLEVUE, WASHINGTON 98004 (206) 455-1323

EPA Moves to Reassess the Risk of Dioxin

Urged on by the scientific community, EPA is developing a new model for estimating dioxin's risk

GALVANIZED BY THE RESULTS OF A RECENT scientific meeting on dioxin's molecular actions, Environmental Protection Agency (EPA) administrator William K. Reilly has launched a major new effort to reassess the toxicity of this ubiquitous—and infamous—chemical.

Responding to criticism that the model EPA now uses to assess dioxin's risk is obsolete, Reilly has asked agency scientists to come up with a new "biologically based" model that will draw on an emerging understanding of the first steps that take place as dioxin enters a cell (for example, see pages 924 and 954). Reilly and others call the new effort "precedent-setting" not only for how the agency regulates carcinogens but also for EPA's quick response to new scientific developments—not its strong suit in the past.

Until now, EPA has gauged the risk of dioxin exposure by using the same model it applies to most carcinogens: the linear multistage model, which assumes that risk rises in proportion to dose. Agency officials have long viewed the model as a "default"—one adopted for lack of a real understanding of how carcinogens work—and their intent was always to replace it with something more realistic once mechanisms were understood. But so far, they say, such evidence has been lacking. Now it may at last be in hand, at least for dioxin and perhaps a handful of other chemicals that behave similarly.

The turning point came in an 8 March briefing for Reilly and his top deputies given by three agency scientists: William Farland and Peter Preuss, both at EPA headquarters in Washington, D.C., and Linda Birnbaum of EPA's Health Effects Research Laboratory in North Carolina. Part of the briefing was devoted to recent epidemiologic studies, including the new one by Marilyn Fingerhut of the National Institute for Occupational Safety and Health (NIOSH), which found perhaps the strongest link yet between high doses of dioxin and human cancer (see *Science*, 8 February, page 625). The EPA scientists also discussed a reanalysis of data from a 1976 study of cancer in dioxin-exposed rats that figured heavily in EPA's original risk assessment. After reexamining the original slides of liver tissue, investigators have concluded that the animals developed fewer tumors than was originally believed.

But it was Birnbaum and Farland's description of a meeting last November at the Banbury Center at Cold Spring Harbor Laboratory that Reilly says made the most compelling case for change. At that meeting a group of dioxin experts agreed that before dioxin can cause any of the ill effects it has been linked to—cancer, immune system suppression, chloracne, and birth defects—one "necessary but not sufficient" event must occur: the compound must bind to and activate a receptor, known as the aryl hydrocarbon or AH receptor (see *Science*, 8 February, p. 625). After that, the dioxin-receptor complex is transported to the nucleus, where it binds to specific sequences of DNA and turns genes on and off, thereby causing its myriad effects. It had long been known that dioxin binds to a receptor, but before the Banbury meeting it had been unclear whether all of dioxin's effects or just some were mediated this way.

Key mover. *Linda Birnbaum had been urging EPA to change how it does dioxin risk assessment.*

The Banbury group also agreed that dioxin has to occupy a certain number of AH receptors on a cell before any biological response can ensue. The result is a practical "threshold" for dioxin exposure, below which no toxic effects occur. That conclusion flies in the face of the linear model's underlying assumption: that the risk of harmful effects begins with exposure to a single molecule and increases from there. Faced with this new picture of dioxin's action, the Banbury participants urged EPA to develop a new, receptor-based model for dioxin risk assessment.

Reilly bit. He has now asked scientists in EPA's Office of Research and Development, in collaboration with academic researchers around the country, to come up with just such a model. The goal, explains Michael Gallo of the Robert Wood Johnson Medical School, one of the organizers of the Banbury meeting who is now working with EPA, is to pinpoint the threshold or "safe" dose below which none of dioxin's ill effects should occur.

In building the model, Gallo and his EPA colleagues hope to draw on work on the dioxin receptor now under way in a number of labs around the country. In this issue of *Science*, for example, a group headed by Oliver Hankinson of the University of California at Los Angeles reports on the cloning of a protein that is necessary for the receptor to function. Various roles have been proposed for the new protein; one intriguing possibility is that it is part of the receptor itself. The dioxin receptor thus might contain at least two proteins, one that binds to dioxin (and presumably whatever natural molecule dioxin mimics) and another that binds to DNA. "Boy, is that exciting," says Gallo, who adds that the new findings will feed directly into the model.

Until the model is complete, no one can say for sure whether it will show dioxin to be more or less risky than EPA now calculates, though Gallo and others speculate that it will turn out to be less risky. One of the major questions is how close the presumed "safe" dose is to the background levels of dioxin to which the general population is exposed. If background exposure is already near the "safe" dose, then there may not be much room for additional exposure.

Those background levels are largely unknown, so Reilly has added that question to the EPA scientists' assignment. Over the next year Birnbaum and other EPA scientists, in collaboration with researchers from NIOSH, the Centers for Disease Control, and the Air Force, hope to get a fix on blood levels of dioxin and the handful of polychlorinated biphenyls that behave similarly and thus could increase its risk. Meanwhile, other researchers will be studying the sources and routes of dioxin exposure—most of which are dietary—and how it is passed up the food chain.

Reilly wants the new model and related work complete within a year, at which time the results will go on to EPA's Scientific Advisory Board (SAB) for peer review. Three years ago, the SAB sent EPA scientists back to the drawing board when they tried to revise the dioxin standard, saying the science wasn't sound enough. Birnbaum and other EPA researchers predict a different outcome this time. ■ LESLIE ROBERTS

313 S.W. 2nd Street, Suite D
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON
TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 07 1991
OFFICE OF THE DIRECTOR

June 6, 1991

Office of the Director
Department of Environmental Quality
811 SW 6th Ave.
Portland, OR 97204

RE: Petition for reduction of Oregon's ambient water quality standard

Dear Mr. Fred Hansen:

At a very late date I was advised that this petition is once again before your department. I understand the EQC will consider and possibly act upon the petition submitted to you by James River Corporation and Boise Cascade at its June 14th meeting. For some reason this Commission has been excluded from any official notification by your department or by the petitioners. Instead I have been advised by a local citizen that this action has been about to take place.

This Commission remains opposed to lowering of our ambient water quality standards until and unless it can be shown that there will be zero negative effect upon the health of salmon runs in the affected waters. The basis of our concern is primarily for effects on the juvenile salmon who must use the fresh water habitat enroute to the ocean. We remain especially concerned in view of the recent petitions for endangered species status on several northwest salmon runs.

I include copies of testimony and correspondence already submitted to your department which I would like to have attached to the record for this particular petition.

In short, the Commission remains extremely concerned that even current loading of dioxins into the fresh water habitat may have deliterious effects on juvenile salmon survivability. Until it can be shown that those effects do not exist and until it can be shown that a reduction of our water quality standards will not further the problem, we remain opposed to any lessening of the standards.

Thank you for your considerations. I hope the oversight which led to the lack of communication with this Commission about these petitions will be corrected.

Sincerely yours,

Tom Robinson, Manager
Oregon Salmon Commission

TR/nf

313 S.W. 2nd Street, Suite D
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON
TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

May 10, 1990

Llewellyn Matthews
Northwest Pulp & Paper Association
1300 114th Ave. SE, Suite 110
Bellevue, WA 98004

Dear Mr. Matthews:

Thank you for your letter and overview statement pertaining to the dioxin issue. Although I was not personally in attendance, this Commission was represented at your Astoria briefing by Commissioner Robert Finzer. Mr. Finzer is a North Coast commercial fisherman and wholesaler. He gave a brief report on the situation at our last Commission meeting.

We are sensitive to your problems and we support your stated commitment to a solution which can allow a healthy pulp industry within a healthy environment. To us that continues to mean operations which do not pose risk to salmon food products nor to salmon survival, health or reproduction. It also means maintaining standards of water quality which are equal to those of our competitors in other nations which provide salmon to the world market.

So far, we are fairly comfortable with the food safety issue. Our public salmon are pure, clean food with all agencies finding salmon as the least likely of all fishes to be contaminated with toxins.

However, we remain steadfast in our position that standards equivalent to those in Europe and Canada be maintained here. Also, we continue to insist that our standards be met in fact. These are critical market demands.

We continue to be extremely concerned about salmon reproduction, smolt mortality, and immune systems, when exposed to effluent materials throughout the inland waterways they use. Even small percentages of mortality or fecundity loss represent large numbers of salmon losses at the harvest end. For example a 1% loss of down stream coho smolts represents a number of salmon roughly equal to the entire Oregon commercial troll harvest. We must learn the true impact on smolts and learn how to control it. I have not read the reports you cite as showing "no adverse affects on fish reproduction or fish tissue." Perhaps your staff can supply us with a copy.

Your offer to meet with us may be something we can explore later this fall, after our harvest season. We, like you, are an industry which supplies a valuable commodity to the market, relying on a healthy natural resource for the raw material. In the past, salmon resources industries have not viewed the wood products industry as a friend. I think you will agree that there is basis in fact for that view. Too much of our salmon resource has been lost to forest industries already. If that stops, perhaps we can ally as fellow industries, in common cause. If it does not, then our position is clear, and probably adversarial.

Sincerely yours,

Tom Robinson, Manager
Oregon Salmon Commission

cc: Dalton Hobbs, Department of Agriculture
Jill Zarnowitz, OR Dept. of Fish & Wildlife
Bob Eaton, Salmon for All
Oregon Salmon Commissioners

313 S.W. 2nd Street, Suite D
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

Date: May 1, 1990

To: DEQ
Water Quality Division
811 SW 6th Ave.
Portland, OR 97204

From: Tom Robinson, Manager
Oregon Salmon Commission

RE: Proposed Rule Changes Affecting Pulp Mill/Dioxin Effluents Standards.

Please be advised that the Oregon Salmon Commission on behalf of Oregon's commercial salmon trollers and on behalf of the consuming public which we serve under OAR 576.305 does not support any of the options for rule changes affecting standards applied to pulp mill effluents/dioxin contamination. The Oregon Salmon Commission has provided formal oral and written testimony to DEQ and to the Environment Quality Commission on this subject. Our position remains unchanged. We adamantly support stringent standards which will fully protect both food quality and the smolt survivability of salmon which use the Columbia River corridor. While we are satisfied that no danger to consumers of salmon food fish is imminent, we see this as no reason to relax any of the standards. We continue to be greatly concerned about mortality of juvenile salmon and about biological effects on adult salmon's immune systems and reproductive capacities when exposed to these effluents. Those biological and mortality concerns have not yet been addressed nor answered satisfactorily.

Attached are copies of written testimony already supplied to you by this Commission. Please apply them to this record.

On behalf of the Commission I also express a great dissatisfaction with the notification processes being used as this issue continues to run a gauntlet of meetings and reviews. I have not been formally contacted on a regular basis by your department about the schedule of hearings and comment deadlines. I remind you that we are a state agency which is very much affected by the decisions you will make. I find it extremely remarkable that my best source of up-to-date information continues to be the "grapevine" rather than official communications from your department. Furthermore, I know that the Pacific Fisheries Management Council and the states of Oregon and Washington fisheries divisions are greatly concerned about this issue. Are they not being directly contacted? Please take prompt action to correct this oversight in notification.

cc: William P. Hutchinson EQC
Randy Fisher ODFW
Joe Blum WDF
Richard Schwarz PFMC
Frank Warrens PFMC
Bob Eaton Salmon for All

313 S.W. 2nd Street, Suite C
P.O. Box 1033
Newport, Oregon 97365

(503) 265-2437

OREGON TROLL SALMON
QUALITY IS KING

OREGON SALMON COMMISSION

Date: December 15, 1989

To: Fred Hansen, Director
Department of Environmental Quality
811 SW Sixth
Portland, OR 97204

From: Tom Robinson, Manager
Oregon Salmon Commission

Re: Proposed Rule Changes

We understand that Oregon's EQC is reviewing proposed rule changes on pulp mill pollution effluents January 1990. As you know we continue to provide comment on this matter as we find it to have significant impact on our industry through degradation of the environment. The details of our concern are outlined in previous communications and testimony submitted to you.

We also have some specific concerns and comments regarding proposed rule changes.

1. We ask for a return to full, open disclosure of all proceedings between the state and pulp mill industry representatives as this matter is resolved.
2. We support the status-quo of rules which require formal findings on pollution before EQC makes approvals. We recommend that food fish studies should be independently performed by other than industry contractors, to assure the objectivity of required findings.
3. We call your attention to the following items from the proposed rule changes:
   a) Proposed changes in paragraph 3, section (a) are alarming in that they appear to weaken existing permit processes, allowing too much subjective opinion, changing the phrase "would not", to read, "is not expected to", is clearly a move away from the level of control and protection which we must have through your commission, to assure safe, quality habitat for food fish in Oregon.
   b) Likewise, we support the status-quo for procedures which determine WQL status. There must not be a relaxing of processes which would remove the burden of positive proof of compliance with effluent standards, prior to removing a waterway, or a facility, from corrective activity. Speculative statements that compliance is expected may be encouraging news, but should not be substituted for actual achievement.

Thank you for your attention to our requests. We continue to rely on EQC, and DEQ to protect the habitat of Oregon's salmon resource as you execute your difficult tasks.

cc See attached sheet

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 10 1991
OFFICE OF THE DIRECTOR

7 June, 1991

Oregon Environmental Quality Commission
c/o Oregon DEQ Director's Office
811 S.W. 6th Avenue
Portland, OR 97204

Director
Oregon Department of Environmental Quality
811 S.W. 6th Avenue
Portland, OR 97204

Dear Commissioners and Director:

We understand that James River, Inc. and Boise Cascade Corp., along with several co-petitioners have asked the Commission and the DEQ to amend the state's ambient water quality standard for 2,3,7,8-TCDD from a current level 0.013 ppq to 2.3ppq.

We wish to offer comments regarding the wisdom of honoring such a petition that we hope you will make part of the public record in this decision.

INADEQUATE PUBLIC NOTICE

First we must question the lack of public notification involved in this pending decision. We have, on more than one occasion, asked to be placed on the DEQ notification list for any water quality actions the Department has pending, particularly with respect to pulp mills.

Our requests have to date been ignored, and we find that the only way to obtain a copy of a notice or a draft permit is to hear of its existence from a third party and then to call the DEQ to request a copy be sent us. Nor have we received word of final decisions regarding permits or any response to permit comments we have offered. To say that this archaic and haphazard method of public notice is deficient is an understatement. It is certainly not consistent with the mandate for public participation inherent in EPA's having delegated the water quality program to the state of Oregon.

That the petitioners themselves have the temerity to suggest they have identified all interested parties as the few listed in item 2 of the Commission Chair's notice, is absurd. A gutting of the state's water quality standard for the most potent chemical known to mankind is not something to be decided privately after consultation with just a few individuals.

Even the more narrow decision the Commission intends to make about whether or not to initiate a rulemaking that could potentially weaken the standard should have received broader notice, e.g. tribal governments, fishing interests, the state health department and those state and federal agencies charged with protecting wildlife (e.g. the U.S. Fish and Wildlife Service).

THRESHOLD MODEL CITED BY PETITIONERS AS FAVORING THE WEAKENING OF A STANDARD HAS NOT BEEN PEER REVIEWED

We remind the Commission that the much touted theory regarding a supposed threshold mechanism for 2,3,7,8-TCDD has not yet been peer reviewed. The forum in which it was first advanced, at a Banbury conference last fall, has itself become known for the controversy it created among attendees (see attachment 1). No version of the theory has yet been published in the scientific literature, and the theory has been challenged by other dioxin scientists (see attachments 2, 3).

EPA's own review of it's dioxin standard is still underway and far from finalization, and any attempt by the state of Oregon to presuppose EPA's conclusions would be ill-advised. EPA Administer William Reilly himself warned against second guessing the Agency's dioxin review, advising that in the interim state governments should go on with business as usual.

There is also new evidence coming from other quarters that tends to refute the threshold theory cited so enthusiastically by the petitioners. Abstracts for two papers to be presented at this fall's dioxin symposium are attached which argue against reliance on such a theory (see attachment 4).

Moreover, a paper by Sargent, et al published in a recent issue of <u>Carcinogenesis</u> (see attachment 5) suggests alarmingly that even non-planar PCB's can act by a mechanism identical to that of coplanar compounds such as 2,3,7,8-TCDD, and that exposure to mixtures resulted in superadditive effects. The authors further state that humans already are exposed to levels at which adverse effects would certainly be occurring. This in turn suggests why the epidemiology concerning exposure to 2,3,7,8-TCDD is at best equivocal, except in very exaggerated doses, as was indeed the case for a recently published NIOSH study (see attachment 6).

EVIDENCE CITED BY PETITIONERS REGARDING BIOCONCENTRATION IN FISH AND FISH CONSUMPTION RATES DIFFERS DRAMATICALLY FROM THAT OFFERED BY MORE CREDIBLE SOURCES

Petitioners suggest that the prevailing way of estimating bioconcentration (BCF) factors in fish used to calculate the current standard should be scrapped, and that a different (less conservative) method for estimating BCF's should be substituted. The method they suggest yields a number in the same ballpark as

the existing one. Yet there is much evidence from EPA's lab in Duluth to suggest that fish are far better at taking up and storing dioxin than the 5000 factor now in use supposes (see attachments 7, 8), and the Agency has requested funds in its 1992 budget to re-evaluate its BCF assumptions.

In fact it has been shown that even Columbia River salmon, species thought to be more protected from uptake because of their mobility and feeding patterns, are harboring levels of dioxin in their edible tissues (see attachment 9).

Patterns of human fish consumption in the Pacific Northwest also argue for a much stronger standard. EPA has long acknowledged that the average fish consumption rate of 6.5 grams per day per person assumed in the setting of its current standard seriously underestimates actual eating patterns, and this has been confirmed by surveys in several states. Moreover, work by EPA's Cleverly and McCormack indicates that Columbia River sports and subsistence fishers, Native Americans, and Asian Americans eat far more fish than the levels suggested by petitioners (see attachment 10). One wonders how petitioners could have arrived at the impossibly low figures they suggest.

Petitioners also make the illogical claim that only fish consumption from the Columbia River need be considered, irrespective of the rest of one's fish diet, as if to suppose that all other sources of fish (or food) are free from contamination.

THE STATE HAS A DUTY TO PROTECT US FROM OTHER HARM THAN JUST CANCER, AND FROM OTHER POLLUTANTS THAN JUST 2,3,7,8-TCDD

Petitioners make mention of Keenan, et al's re-evaluation of the Kociba rat study from which EPA's current acceptable daily intake is derived. They suggest that we should take heart from the fact that slightly more than half a team of 9 scientists funded by the industry should find that many of the liver lesions identified by Kociba as cancerous might only be pre-cancerous after all. A critique of this study is enclosed.

In any case, it is hardly reassuring to expect that one's liver be riddled with dioxin-induced lumps and bumps of any kind. We similarly find no comfort in the fact that women thoughout the industrialized world are passing dioxins and other organo-chlorines on to future generations through the placenta and via breast-feeding.

Studies on primates have shown that dioxins can cause profound behavioral and reproductive effects at very low doses. The petitioners ignore all non-cancerous effects in arguing for a weaker standard.

It must also be noted that 2,3,7,8-TCDD never occurs in

isolation. Discharges from the pulp and paper industry include other dioxins and furans and numerous other compounds which exhibit similar mechanisms of toxicity. The Sargent study mentioned above gives added weight to the likelihood that these compounds can act synergistically.

THE STATE HAS A DUTY TO PROTECT THE ENVIRONMENT AS WELL AS HUMAN HEALTH

Petitioners have offered no evidence to suggest that a weakened ambient water quality standard will be sufficiently protective of aquatic life or fish-eating birds and mammals.

Nor have petitioners demonstrated that a weakening of the current dioxin standard will not adversely effect bald eagle populations on the lower Columbia River, as required under the Endangered Species Act. Much evidence already exists to suggest that dioxins and other organochlorines are negatively impacting these birds. The pending listing of various wild salmon species will further increase the burden of proof necessary to justify any continued discharge of dioxin and other organochlorines.

A RELAXING OF THE DIOXIN STANDARD AS PROPOSED BY INDUSTRY WILL NOT RELIEVE THE INDUSTRY OF ANY FINANCIAL BURDEN FOR POLLUTION CONTROL

The same technologies that must be implemented by petitioners to meet the state's current dioxin standard will in any case be required in order to meet the technology-based standards already in their NPDES permits. Indeed, the longer the industry waits to install new bleaching technology, the greater will be their ultimate financial burden.

Capital costs for equipment will only be more expensive, and the money invested in stopgap measures such as chlorine-dioxide generators will only be money wasted. The U.S. industry can also be expected to lose market share in Europe as a result of its recalcitrance, as is already proving the case in Canada. Fletcher Challenge's failure to produce chlorine-free pulp for its foreign market has already cost them an estimated $ 5 million dollars in loss of sales.

THE ONLY ACCEPTABLE STANDARD FOR DIOXIN IS ZERO, AND THE STATE OF OREGON SHOULD TAKE IMMEDIATE STEPS TO ELIMINATE ALL KNOWN SOURCES

Dioxin is the most intensively studied compound in history, and will doubtless remain the darling of the scientific community for years to come. Even so we still do not know its precise toxicity to humans, and given the degree to which we are all already contaminated with dioxin and dioxin-like compounds, we probably never will. There is simply no such thing as a control group to serve as a baseline.

But what we do know is serious enough to make moot any further quibbling about precisely how much is too much dioxin. What we know is more than enough to justify elimination of all known sources.

We urge the Department and the Commission to deny the petition to set a weaker dioxin standard, and instead use your limited resources to moving the pulp and paper industry into chlorine-free technology. The technologies exist, and only await implementation.

Sincerely,

Shelley Stewart

Shelley Stewart
U.S. Pulp/Paper Project

***

Please note that these comments are printed on chlorine-free paper imported from Europe. No North American manufacturer has yet been willing to produce chlorine-free bleached office or printing paper.

Attachment 1

UNIVERSITY OF MARYLAND AT BALTIMORE

The University Program In Toxicology
660 West Redwood Street
Howard Hall, Room 544
Baltimore, Maryland 21201-1596
(301) 328-8196

January 29, 1991

Dr. Jan Witkowski
Director
Banbury Center
Cold Spring Harbor Laboratory
P O Box 534
Cold Spring Harbor, NY 11724

Dear Dr. Witkowski:

I was a participant in the recent Banbury Conference on "Biological Basis for Risk Assessment of Dioxins and Related Compounds" held at the Banbury Center in October 1990. I am writing you becuase I have just been informed of a very disturbing result of that conference, a press release sent out by a public relations firm along with statements by Drs Scheuplein, van der Heiden, and Gallo purporting to represent the "consensus" views of the participants at that conference with espect to regulatory conclusions related to risk assessment of dioxins. I only learned of this press release from a reporter who called me last week (Marguerite Holloway of Scientific American).

This press release, copy enclosed, was never shown to me or to most of the participants in the conference, as far as I know. Thus, in terms of process alone, it should not be represented as a "consensus" document. Morover, its contents do not accurately reflect the views of all participants, or even a consensus of those views, as best I can determine. I resent the circulation of this press release as reflecting the views of a meeting in which I was a participant, and I feel that my name attached to it somehow implies my agreement with it.

I am in fact rather astounded by such a product from a Banbury Conference. While itwas rather obvious to some of us that the organizers, and some of the sponsors, of this confernece had some trans-scientific objectives in mind related to regulations concerning dioxin, I had expected that the Banbury Center would be able to keep these motives under control. The press releases and statements imply that a major focus of the conference was a discussion of the regulatory risk assessments that have been applied to the dioxins; this was not the focus of this meeting. I agreed to participate based upon my previously held high regard for Banbury and Cold Spring Harbor. I did not expect to be manipulated by industry and government spokespeople

(who are not dioxin researchers, incidentally) to be made into a supporter of their political views on dioxins and risk assessment. This is particularly annoying to me because I was invited to present the main conference paper on the topic of the scientific basis for dioxin risk assessment. In this paper, I have attempted to present the complexity of integrating the basic molecular biology of dioxins into a receptor-based model. I do not feel that the state of knowledge on this complex topic can be reduced to a simplistic press release.

The preparation and release of these documents by Drs Scheuplein, van der Heijden, Carlo, and Gallo, with the assistance of a public relations firm, discredits all of us. It challenges the precious institution of free scientific discussion, epitomized by such places as Banbury, Dahlem, and the Gordon conferences. I hope you believe that I would be just as angry if this action had been taken by an environmental group. I trust you will take aciton to dissociate Banbury from this attempt to manipulate science and scientists. Because these people have acted without consulting the rest of us, and because I have heard about this only through the press, I am with great regret also sending this letter to the persons shown under my signature, as well as to my colleagues at the conference, an action not taken by these people.

Yours sincerely,

Ellen K Silbergeld

Ellen Silbergeld, PhD
Visiting Professor of Toxicology and
Adjunct Professor of Pharmacology
and Experimental Therapeutics

cc: Leslie Roberts, Science
Marguerite Holloway, Scientific American
Cristine Russell, Washington Post
Chris Joyce, New Scientist
Judy Randall, The Economist
Betty Mushak, NIEHS
William Farland, EPA

attendees, Banbury Conference on Dioxins

History Lessons

Warfare analysts offer some disturbing—and hopeful—news

Political leaders always claim to be steering us by the lights of history toward a peaceful future. But what does a comprehensive analysis of our past actually reveal about our present course? A pessimist could conclude that our leaders are completely misreading—or misrepresenting—history. An optimist could find hope that warfare might become obsolete anyway—if the tentative spread of democracy worldwide continues.

These conclusions are both supported by the Correlates of War project, a computerized storehouse of information on 118 wars (defined as conflicts leading to at least 1,000 deaths) and more than 1,000 lesser disputes from the early 1800s to the present. Researchers at the University of Michigan created the data base in the 1970s to find statistical associations between warfare and various economic, political and social factors.

The data offer no support for the bromide "peace through strength," according to J. David Singer, a political scientist at Ann Arbor who oversees the Correlates project. A buildup of military armaments, far from deterring war, is one of the most frequent precursors of it. At the very least, Singer says, such a finding suggests that the U.S. policy of supplying arms to nations in an unstable region—such as the Middle East—is seriously flawed.

There is also no evidence that alliances help to keep the peace. In fact, a nation's participation in one or more alliances increases its risk of warfare, Singer says, particularly against its allies. History even casts doubt on the argument—used by the U.S. to justify both its current war against Iraq and its past one against Vietnam—that allowing aggression to proceed unchecked always leads to more aggression. Although Hitler's Europe certainly provides an important counterexample, Correlates of War data yielded little statistical correlation between warfare in a given region and prior unchecked aggression, Singer says.

A somewhat more hopeful finding

A Press Release on Dioxin Sets the Record Wrong

When the Chlorine Institute shopped around for a place to hold a scientific conference, they did not want just any host. "We were looking for an organization that was squeaky clean, that would not in any way, shape or form be questioned about the conference," says Robert G. Smerko, president of the Washington, D.C.–based institute, which is supported by some 170 chemical, paper and other manufacturers.

Smerko seemed to have met his requirements when he finally landed Cold Spring Harbor Laboratory. Last October the laboratory's respected Banbury Center held a conference—jointly sponsored by the Chlorine Institute and the Environmental Protection Agency—on the toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, or TCDD. That chlorinated compound achieved notoriety during the Vietnam War, when it was identified as a contaminant of the defoliant Agent Orange. It remains controversial because it is found in some commercial herbicides and is produced in other chemical processes, such as paper bleaching.

Cold Spring Harbor Laboratory may have been squeaky clean, but the conference apparently was not. And the outcome of that meeting—attended by 38 of the world's dioxin experts, few of whom say they knew it was industry sponsored—is every bit as controversial as the substance that was the topic of discussion.

The issue is a press release sent out at the conclusion of the meeting by the Chlorine Institute's public relations firm, Daniel J. Edelman, Inc. It announced that the experts had agreed on a model for the toxicity of dioxin that "allows for the presence of a substance in the environment, with no risk experienced below a certain level of exposure." The release said that the scientists had rejected a linear exposure model, in which any level of exposure would have a biological effect, in favor of a receptor-based model that implies a threshold level. (This part of the release was approved by Cold Spring Harbor Laboratory, says the Banbury Center's director, Jan A. Witkowski—although he now says Edelman made several changes after he saw it.)

Such a consensus, of course, would have implications for setting permissible levels of the substance in the environment. But those at the conference insist that no such agreement was reached. "There was no consensus in terms of risk assessment," says George W. Lucier of the National Institute of Environmental Health Sciences. In addition, none of the scientists saw the press release, although their names accompanied it. "We were being used, clearly, and that's unfortunate," declares Arnold J. Schecter, professor of preventive medicine at the State University of New York at Binghamton. "Political layering is not particularly good, especially when it is unbeknownst," Lucier adds.

Few of the participants seem to dispute that the receptor-based mechanism of dioxin is relevant to human exposure. Nor did they before the conference, observes Alan P. Poland of the University of Wisconsin at Madison, who discovered the receptor in 1976. "The basic tenets were all known since 1981 or 1982," Poland says. But Lucier notes that now "we are at the point where we can reevaluate the linear model."

Indeed, the EPA intends to explore the question of whether there is a threshold response. The agency will investigate the receptor-based model with Michael A. Gallo, one of the conference organizers and a professor of toxicology at the University of Medicine and Dentistry of New Jersey–Robert Wood Johnson Medical School. But Gallo and others agree that discussion of thresholds in a regulatory context may be premature. At the conference, "some regulators got real excited by back-of-the-envelope calculations" and thought dioxin standards could be eased, says Linda S. Birnbaum, director of the EPA's environmental toxicology division. "Clearly, we don't know that."

Although many of the Banbury attendees were the last to know about the consensus they reportedly reached, news about the conference traveled quickly in political circles. At a recent hearing on dioxin standards in Alabama, expert witness for the pulp and paper industry Russell E. Keenan invoked the Banbury results in his testimony. "There was general agreement among the attending scientists that dioxin is much less toxic to humans than originally believed," Keenan claimed. Obviously, "it is not useless to tout Banbury results if you have a political ax to grind," comments Cate Jenkins, a chemist in the EPA's hazardous waste division. —*Marguerite Holloway*

Attachment 2

To: Dioxin Nerds, et al.
From: Tom Webster, CBNS Queens College, Flushing NY 11367
Date: 3/14/91
RE: Banbury Dioxin Model, Part 1 A Critique

A recent two article series in Science(1) covered the infamous Banbury conference on dioxin toxicity. The second article addresses the scandal aspect of the story, particularly the involvement of the Chlorine Institute. The first article (attached) addresses some of the scientific aspects, but does so in what I consider a rather opaque fashion.

In particular, the article shows an S-shaped graph which appears to show why dioxin has a threshold. Science indicates, using the graph, that "responses to dioxin increase slowly at first but then shoot up after passing a critical concentration."

However, all is not as simple as it seems at first. Since there has been some confusion regarding this business, I will address the graph in this memo.

(1) Background: The Ah receptor

First, a bit of background. 2,3,7,8-TCDD and other dioxin-like compounds (PCDFs, co-planar PCBs, chlorinated naphthalenes, etc.) are generally thought to cause toxicity through a receptor mediated mechanism. This receptor also binds aromatic hydrocarbons such as 3-methylcholanthrene and other non-halogenated aromatic hydrocarbons; hence it is termed the Ah receptor.

The Ah receptor is a protein which is normally found in the fluid (cytosol) of the cell (There is some controversy here; some people think it is found solely in the nucleus). Only certain molecules ("ligands") with certain properties (size ,shape, etc.) fit it, like a key into a lock. 2,3,7,8-TCDD has the best fit of any known compound. When this occurs, the receptor-ligand complex changes shape and moves into the nucleus. The change in shape helps it to recognize and bind to certain sequences in the DNA. This in turn causes the transcription and translation of adjacent DNA into protein. (This is quite similar to the mechanism of steroid hormones.)

The most well understood effect is the production an enzyme called P450IA1 which makes aromatic hydrocarbons more water soluble--and therefore easier to excrete--by adding hydoxyl (-OH) groups. One measure of this enzyme activity is called aryl hydrocarbon hydroxylase (AHH).

Many of the types of toxicity associated with dioxin-like compounds correlate with binding to the Ah receptor or AHH activity (also with EROD, a related enzyme activity). This provides good evidence that dioxin toxicity is mediated by the Ah receptor, i.e., binding to Ah is the first (but not only) step. It also provides both a theoretical justification and a measurement technique for 2,3,7,8-TCDD equivalents. If all dioxin-like compounds act through the receptor, then the potency of a given compound can be rated against 2,3,7,8-TCDD by their relative ability to bind Ah and induce AHH or EROD activity.

Nevertheless, other experiments show that many toxic effects are probably not directly caused by enzyme induction. Hence, other genes are probably being turned on by the Ah receptor as

well. The nature of these other genes and the biochemical mechanism of many toxic responses is not so well understood. I'll discuss some of this in a future memo.

(2) Receptor Kinetics

If the toxicity of dioxin-like compounds is mediated by the Ah receptor, clearly we need to understand this first step. Receptor-ligand relationships are mathematically described by the Michaelis-Menten equation, a standard tool for describing enzymes. This is schematically described as:

$$L + R \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} LR \qquad (1)$$

where "R" is the unbound receptor, "L" is the ligand (molecule binding to the receptor) and "LR" is the receptor-ligand complex. k_1 and k_{-1} are, respectively, the association and dissociation rate constants. At equilibrium, we find

$$K_D = [L][R]/[LR] \qquad (2)$$

$$K_D = k_{-1}/k_1$$

where the items in the brackets "[ ]" are concentrations and K_D is the dissociation equilibrium constant. The constant K_D tells us, in an inverse way, about the strength of the binding between the ligand and the receptor. A small K_D means the binding is strong, and thus the receptor-ligand complex is less likely to dissociate. Conversely, a large K_D means that the receptor-ligand binding is weak.

Equation (2) can be solved in terms of the amount of occupied (bound) receptor:

$$[LR] = [L]*R0/(K_D + [L]) \qquad (3)$$

where R0 is the total amount of receptor, bound and unbound.

Equation (3) gives the relationship between the amount of 2,3,7,8-TCDD (or other ligand) and the amount of bound receptor (LR). Remember that the toxic activity of 2,3,7,8-TCDD (and other dioxin-like compounds) is thought to be associated with the concentration of dioxin-receptor complexes. We could infer a dose-response curve with two additional pieces of information: 1) the relationship between external dose (e.g., amount of exposure per day) and [L] and ii) the relationship between [LR] and toxicity.

Note that when the concentration of 2,3,7,8-TCDD is significantly less than K_D, the relationship is linear:

$$[LR] = [L]*R0/K_D \qquad \text{for } [L] << K_D \qquad (4)$$

Indeed, this equation indicates that even one molecule of 2,3,7,8-TCDD could bind to the receptor, indicating that there may be no theoretical threshold for activity. The slope of the curve is governed by the number of Ah receptors (R0) and the dissociation constant (K_D). Since 2,3,7,8-TCDD has a very small K_D compared to

other dioxin-like compounds, it binds tightly, and has a large slope.

For a high concentration of 2,3,7,8-TCDD, the curve saturates. One can't produce more receptor-dioxin complexes than there are receptors:

$$[LR] = R0 \qquad \text{for } [L] \gg K_D \qquad (5)$$

(We'll ignore for now so-called "supermaximal" induction as well as circumstances which alter the number of receptors).

Finally, note that when the concentration of a compound equals its K_D, the number of bound receptors is equal to one-half the total number of receptors.

$$[LR] = R0/2 \qquad \text{for } [L] = K_D \qquad (6)$$

(3) Analysis of the Science graph

When equation (3) is plotted on normal graph paper it looks like my Figure 1, linear at low levels of 2,3,7,8-TCDD--the concentration of receptor-ligand complexes directly proportional to the concentration of ligand--and plateauing--at 100% bound receptor--at high levels of 2,3,7,8-TCDD.

When the same equation is replotted using the logarithm of the concentration of 2,3,7,8-TCDD, the graph looks like Figure 2, the same S-shaped curve seen in Science. Note that the horizontal axis in the Science graph gives concentration of 2,3,7,8-TCDD increasing by a factor of ten at each step; this is equivalent to using logarithms.

Finally, 50% of the receptors are shown as occupied in the Science graph when the concentration of 2,3,7,8-TCDD equals about 10^{-9} (Although not given, the units are undoubtably the standard moles per liter). This is the old K_D value for 2,3,7,8-TCDD. Actually, recent experiments indicate that the K_D is probably even smaller, on the order of 10^{-12} to 10^{-11} moles per liter. This means that 2,3,7,8-TCDD binds Ah more tightly than previously thought.

(4) Discussion

As a result, it should be clear that the graph in Science does not by itself indicate a threshold. The S-shape of the curve is an artifact of the graphing technique. Plotted on linear axes, the equation for ligand-receptor interaction indicates that the number of occupied receptors rises linearly from zero. In other words, this response should theoretically be linear at low doses with no threshold.

What then is really going on? Clearly, there must be more to the story. I'll be writing another memo on this, but let me give a few hints.

i) There may be other compounds inside the cell which bind to Ah, albeit with less affinity, complicating the picture.

ii) Binding to the receptor is just the first step. The other steps, binding to DNA, generation of protein, action of protein, etc., might not be linear. Hence, even though the first step might be linear, the final toxic response might not be.

ii) Binding to the receptor is reversible. However, the long half-life of dioxin-like compounds and the background exposure to them diminishes the strength of this argument.

iv) The Birnbaum[2] memo makes the following assumptions: 1) all toxicity is mediated by the Ah receptor binding; 2) induction of P450IA1 (AHH activity) is the most sensitive response of this system; 3) no effect occurs until one can measure an increase in enzyme activity. This defines a "practical" threshold that one can use to determine no-effect levels, etc.

In response to this last argument (briefly), enzyme induction may be the most sensitive response, but we don't really know. Also, lack of measurable activity doesn't necessarily mean no activity. Ability to measure a response is determined by many things including the sensitivity of the assay, the statistical power of the experiment, etc. In addition, 2,3,7,8-TCDD has a very long lifetime in the human body. Finally, the already existing body-burden of dioxin-like compounds in humans and other animals needs to be taken into consideration when examining such threshold models.

References

(1) Roberts, L. (1991a). Dioxin Risks Revisited. Science 251: 624-626. February 8.
Roberts, L. (1991b). Flap Erupts Over Dioxin Meeting. Science 251: 866-867. February 22.

(2) Birnbaum, L. (1990). Memo to E. Bretthauer (EPA-ORD) regarding Consensus at Banbury Dioxin Conference. October 31.

Figure1 : Linear Plot

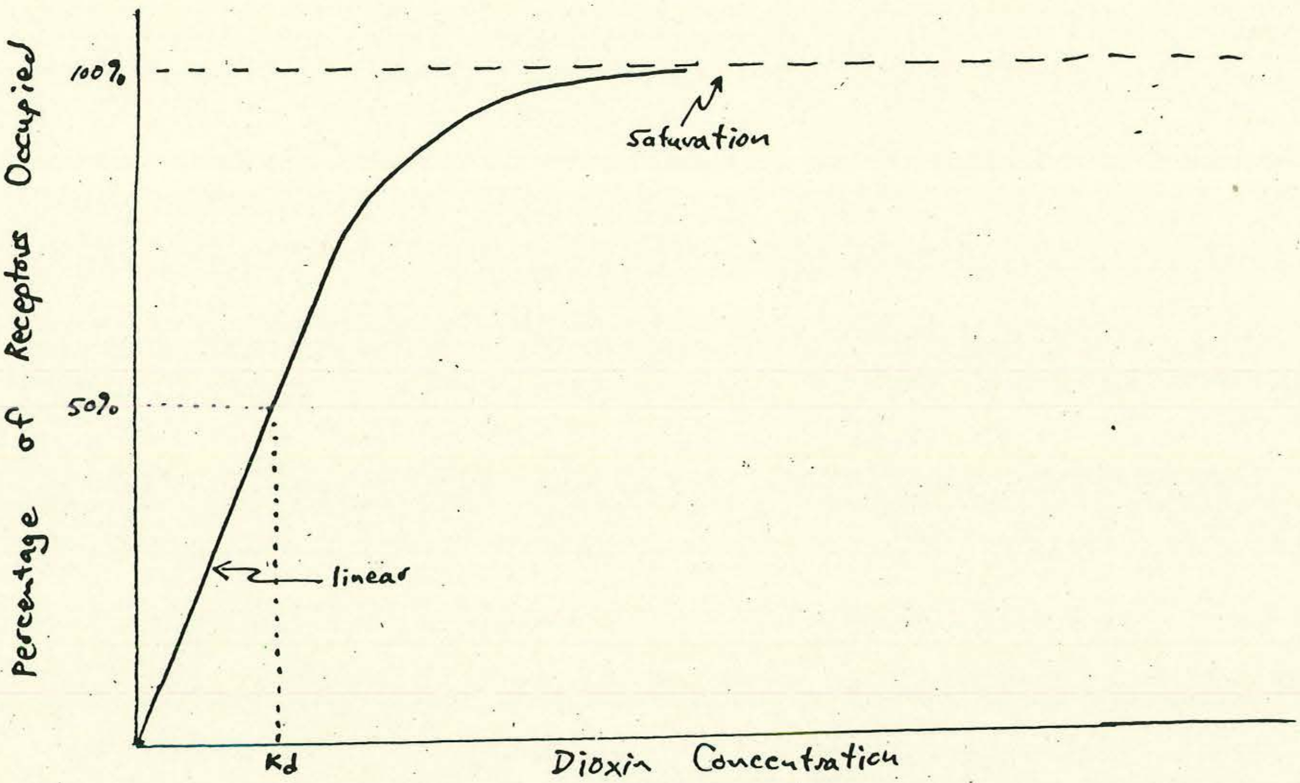
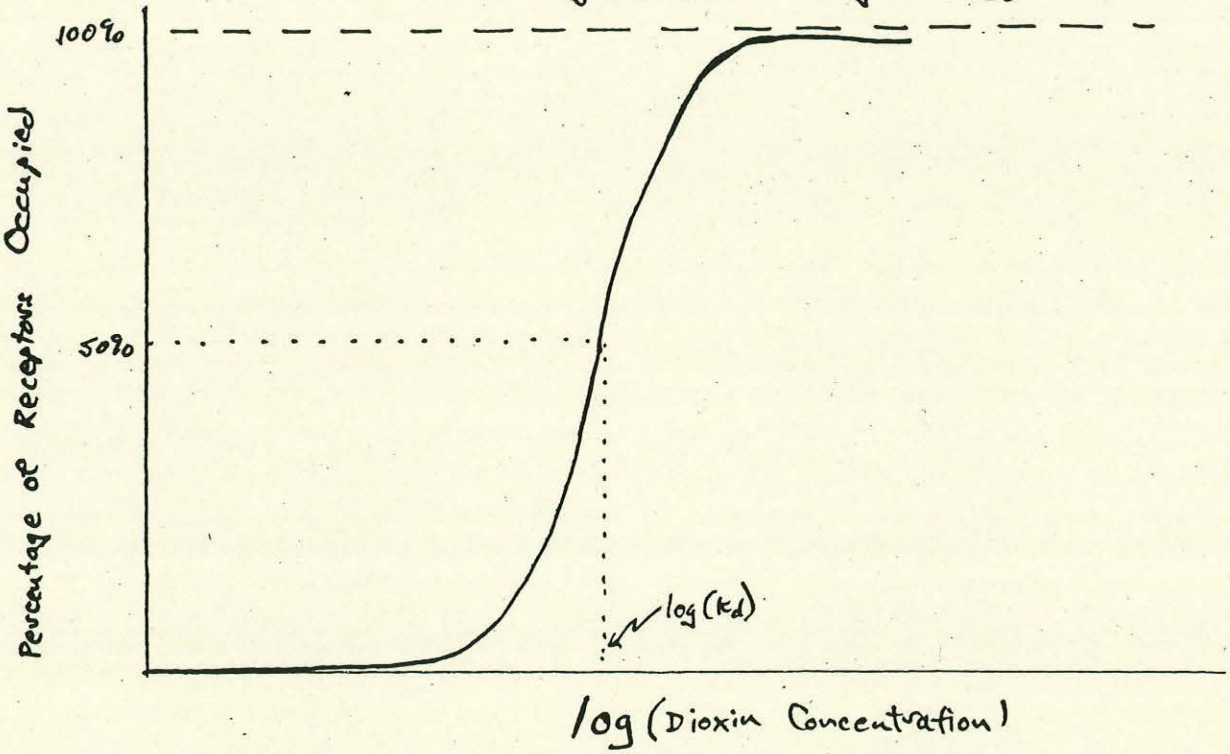


Figure 2 : Log-Linear Plot



Attachment 3

Downgrading Dioxin's Cancer Risk: Where's the Science?

By Tom Webster

Some of the concerns about the toxicity of the wood preservative pentachlorophenol have resulted because of its contamination with dioxins and furans. During manufacturing, pentachlorophenol is contaminated with several members of this family of compounds, with hexadioxins being most abundant.[1] 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD, commonly called dioxin), the most toxic dioxin, has been found in commercial pentachlorophenol formulations[1] and is often found in the soil and waste products from wood treatment plants.[2,3] This article discusses recent attempts to weaken regulatory standards for 2,3,7,8-TCDD.

-Ed.

The pulp and paper industry and certain consultants are once again attempting to relax the regulatory standards for dioxin. The consulting company ChemRisk has proposed an increase in the so-called "acceptable" dose of 2,3,7,8-TCDD by a factor as large as one thousand.[4,5] Many states are currently setting water quality standards for dioxin,[6] a regulation that depends on the "acceptable" dose.[7]

Despite assertions that the proposed change is based on new scientific evidence showing that dioxin "may be far less dangerous than previously imagined,"[8] the new information is actually a reinterpretation of the 1978 rat experiment that forms the basis for the U.S. Environmental Protection Agency's (EPA's) current estimate of dioxin's ability to cause cancer. In this reanalysis, a group of pathologists voted, according to a new set of guidelines, on the classification of tumors found in the test animals.[9]

However, if all other assumptions are left unchanged, recounting the tumors according to the revised rules [10] would result in an "acceptable" daily dioxin dose that is only two to three times larger than the current estimate. This is an insignificant change given the uncertainty in risk assessment. 2,3,7,8-TCDD is currently rated as millions of times more carcinogenic than many other compounds.

> *"Indeed, new scientific evidence on the amount of fish people consume, the degree to which dioxin is concentrated in fish, and the toxic equivalencies of other dioxins and furans supports stronger, not weaker, dioxin standards."*

The much larger change proposed by ChemRisk was derived by altering a number of other assumptions without proper justification. Indeed, new scientific evidence on the amount of fish people consume, the degree to which dioxin is concentrated in fish, and the toxic equivalencies of other dioxins and furans (JPR 10(2):23-27) supports stronger, not weaker, dioxin standards.[7]

Human Health Effects Controversy

This episode is neither the first nor last attempt to downgrade or dismiss the toxicity of dioxin. Perhaps the best known and continuing controversy surrounds Agent Orange. 2,3,7,8-TCDD was a contaminant in the herbicide 2,4,5-T, a component of Agent Orange, which was sprayed in parts of the United States as well as in Vietnam.

Despite the claim by some that the only long-term effect of dioxin on humans is chloracne, a serious skin disorder, the compound has been hypothesized to cause a number of other health effects in humans. Several recent epidemiological studies support this position. The Agent Orange Scientific Task Force[11] linked phenoxyacetic acid herbicides (such as Agent Orange) and their dioxin contaminants to a number of diseases including certain cancers. Dioxin's close chemical relatives PCBs and dibenzofurans may cause birth defects and learning/behavioral changes in the children of exposed women.[12,13] Certain key earlier studies that found no increase in cancer in chemical workers exposed to dioxin are faulty or possibly even fraudulent,[14,15] a charge now under investigation by EPA. Recent studies of German and American chemical workers exposed to dioxin found statistically significant increases in cancer rates.[16,17]

EPA rates cancer-causing compounds qualitatively (how good is the evidence for cancer causation in humans?) and quantitatively (how much cancer is caused by a given dose?). As a result of the recent epidemiology, it is likely that EPA will upgrade the qualitative standing of 2,3,7,8-TCDD to a Class B1 probable human carcinogen (limited human data and sufficient animal data),[18] an action with important regulatory ramifications.[19]

Constructing an "Acceptable" Daily Intake of Dioxin

EPA typically assumes that cancer-causing agents have no threshold, meaning that any amount of exposure can cause damage. Some people argue that there is no acceptable exposure for dioxin, an unintentional chemical by-product with no use or benefit, and that the goal should be zero exposure to this compound. EPA, however, has stated that some level of risk is "acceptable," a decision that is a matter of policy, not science. In setting ambi-

Tom Webster is a researcher with the Center for the Biology of Natural Systems (CBNS) of Queens College. He is currently working on a project for Greenpeace concerning chlorinated compounds.

CBNS; Queens College; City University of New York; Flushing, NY 11367; (718) 670-4180.

ent water quality standards, EPA often uses an acceptable lifetime risk of cancer of one case in a million (10^{-6}).

Based on this policy, the acceptable daily dose of a chemical is established by dividing the acceptable risk level by the "potency" of the compound. EPA calls such values risk specific doses (RsD). The potency is the quantitative estimate of the strength of the carcinogen. The more potent a chemical is, the smaller the dose that is required to pose a certain level of risk.

For dioxin, as with the overwhelming majority of toxic chemicals, there are insufficient human data to establish a potency. (The new study cancer among chemical workers[17] may, however, prove sufficient.) Consequently, dioxin's potency is based on laboratory experiments with animals. The current estimate for 2,3,7,8-TCDD[1] was based on a 1978 experiment on female rats, the most sensitive sex and species tested.[20]

EPA projected from the number of tumors found in animals at experimental doses to effects at the lower doses that people might encounter using a standard mathematical technique, the linear multistage model. This model assumes that the carcinogen has no threshold and that effects at low doses are linear, i.e., directly proportional to dose.

Finally, the potency in humans is estimated by multiplying the animal value by a "scaling factor." This adjusts for differences between the experimental animal and humans. For dioxin, EPA employed the default "surface area" scaling factor, since many differences between animals and humans (e.g., metabolism) depend on relative surface area.[1,21]

The 1988 Attempt to Downgrade Dioxin

In 1988, a proposal was made by EPA's Dioxin Workgroup to decrease the carcinogenic potency of 2,3,7,8-TCDD by a factor of sixteen. The Workgroup argued that dioxin might cause cancer through several mechanisms rather than being simply a complete carcinogen (the basis of the 1985 estimate). It might, therefore, be a less potent cancer-causing agent than previously thought. The Workgroup concluded that there was "no definitive scientific basis" for determining how much less potent dioxin might be.[22]

They noted that other agencies (the Center for Disease Control, the Food and Drug Administration) as well as other countries have less stringent "acceptable" levels of dioxin. They argued that "for strictly policy purposes, there is great benefit in federal agencies adopting consistent positions in the absence of compelling scientific information" and that an order of magnitude (factor of ten) estimate conveys the uncertainty involved. Based on this somewhat arbitrary logic, the Working Group recommended increasing the "acceptable" level (RsD) from 0.006 picograms (one picogram is one trillionth of a gram) per kilogram per day (pg/kg/day) to 0.1 pg/kg/day.

In their review of this proposal, EPA's Science Advisory Panel acknowledged some criticisms of the application of the linear multistage model to dioxin. However, they rejected the Workgroup's proposal, stating that "there is no reason to necessarily believe that a new mechanism model would lead to a relaxation of the risk specific dose for 2,3,7,8-TCDD induced cancer...The Panel therefore finds no scientific basis at this time for the proposed change."[23]

Acceptable Doses of Dioxin: ChemRisk versus EPA

At about the same time that the Science Advisory Panel was rejecting the 1988 case for increasing the "acceptable" risk of dioxin by a factor of sixteen, ChemRisk's new proposal supported an increase by as much as a factor of one thousand.[4,5] Three main factors are used by ChemRisk and EPA in their respective dioxin computations (see Table 1):

> ***"ChemRisk selects an "acceptable" risk of 10^{-5}. Since the level of acceptable risk is a question of policy, not science, ChemRisk's choice of this factor is arbitrary."***

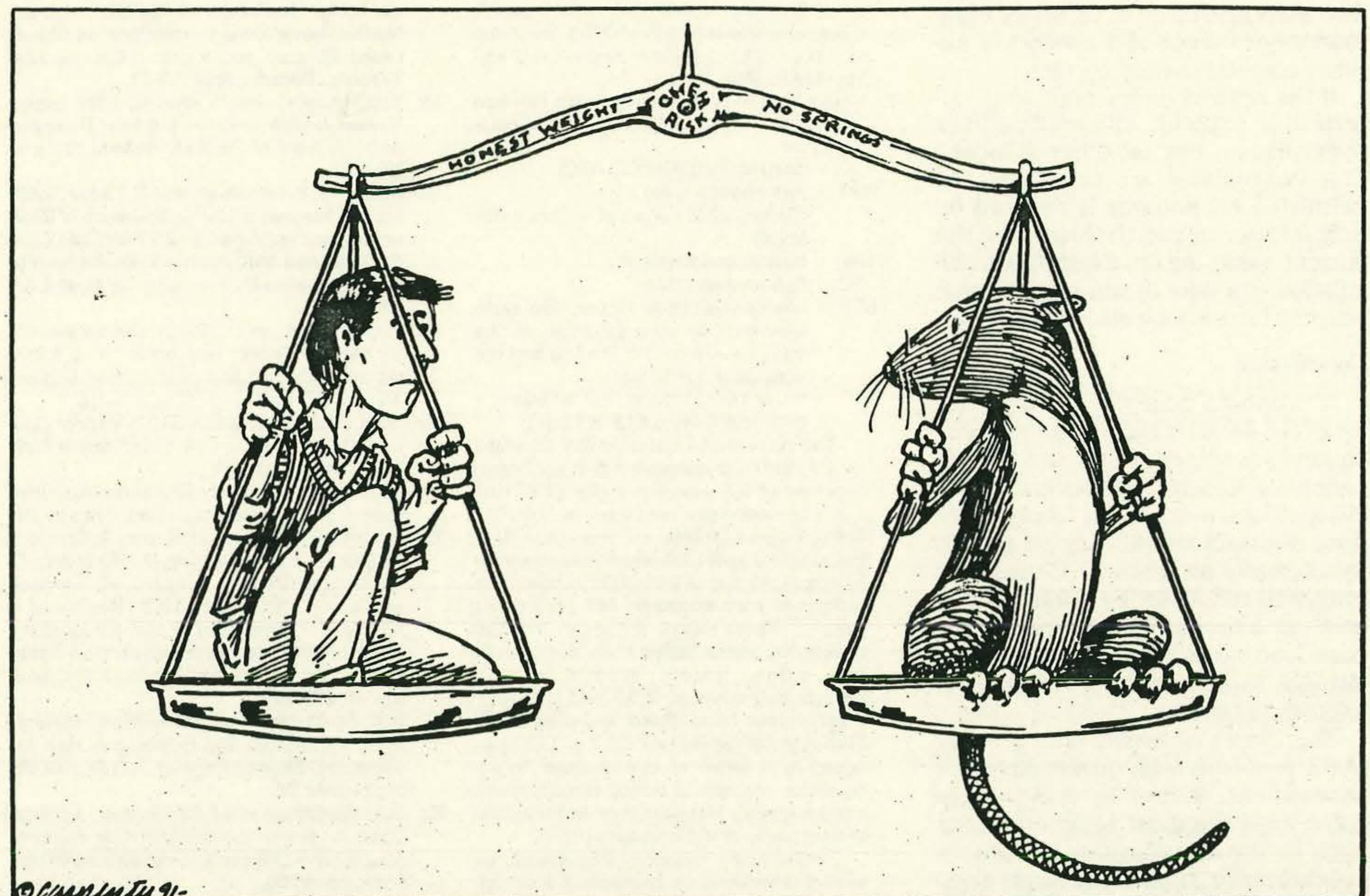
- **"Acceptable" Lifetime Cancer Risk:** For water quality standards, EPA recommends an "acceptable" lifetime cancer risk ranging from one in ten million (10^{-7}) to one in one hundred thousand (10^{-5}). However, one in one million (10^{-6}) is both the default and most commonly used value.[6,24] ChemRisk selects an "acceptable" risk of 10^{-5}. Since the level of acceptable risk is a question of policy, not science, ChemRisk's choice of this factor is arbitrary.
- **Interspecies Scaling Factor:** ChemRisk uses a body weight scaling factor to extrapolate from rats to humans. Since dose is commonly expressed as an amount per kilogram of body weight, ChemRisk's approach assumes that humans and rats are equally sensitive. EPA's surface area scaling factor assumes that humans will be more sensitive than rats per unit body weight by a

Table 1
Constructing an "Acceptable" Dose of Dioxin

	USEPA[1]	ChemRisk[4,5]	Factor[a]
1. Cancer potency in rats $(mg/kg/day)^{-1}$ (95% upper-bound estimate with linear multi-stage model)	29000	1500	19.3[b]
2. Scaling factor, rat to human (surface area)	5.38 (body weight)	1	5.38
3. "Acceptable" Lifetime Cancer Risk	10^{-6}[c]	10^{-5}	10
4. Risk-Specific Dose of 2,3,7,8-TCDD (pg/kg/day)	0.006[d]	6.74	1040

a. Factor by which ChemRisk is less stringent.
b. This factor would be 2-3 if the only change was the reclassification of tumors.
c. One in a million is a default and common value for water quality standards.[6,25]
d. An earlier draft by ChemRisk proposed an acceptable dose of 2.5 pg/kg/day.[4]

Note: RsD = (acceptable risk)/(rat potency * scaling factor)



Jim Carpenter

factor of about five.

ChemRisk argues that the use of the dose per body weight scaling factor is "more biologically relevant" because 2,3,7,8-TCDD is itself the active compound rather than any metabolite as is common with many carcinogens. EPA has disagreed with this line of reasoning in general,[25] but the case against body weight scaling is even stronger for 2,3,7,8-TCDD.

Since EPA's 1985 dioxin potency estimate, 2,3,7,8-TCDD half-life in humans has been determined to be 5-10 years, much longer than previously thought. In rats, the half-life of 2,3,7,8-TCDD is only about one month. Taking into account differences in tissue distribution, a scientist with EPA's Carcinogen Assessment Group estimated a scaling factor for the liver of as high as 37, much higher than ChemRisk's body weight scaling factor of one as well as EPA's surface area scaling factor of 5.38.[25] ChemRisk's reliance on the body weight scaling factor is not supportable.

• **Cancer Potency In Rats:** EPA's 1985 computation of dioxin potency was based on the occurrence in the 1978 rat study of carcinomas (cancerous tumors) and neoplastic nodules (lesions which may develop into cancerous tumors) in the liver, as well as tumors in other organs where the increase over control animals was statistically significant. In 1986, researchers proposed dividing neoplastic nodules into two groups: hepatocellular hyperplasia (a noncancerous proliferation of liver cells caused by toxicity) and hepatocellular adenomas (benign liver tumors).[10] This change has been questioned by some toxicologists.[26]

ChemRisk used the new classification system to argue in 1989 that the EPA's 1985 analysis was incorrect.[4]

At about the same time, Dr. Squire, a consulting pathologist involved in the original analysis of the female rat cancer data, was asked to re-examine the in conjunction with the setting of a water quality standard for Maine.[27] (Squire was involved earlier in a controversy over dioxin contaminants of pentachlorophenol: see article beginning on p. 4). After an initial review of the rat data, Dr. Squire helped convene a group of pathologists to re-examine the liver tissue slides from the experiment using the new classification system.

During this re-evaluation, in which "consensus" was defined as agreement by four out of seven pathologists (not all votes were unanimous), the group identified fewer carcinomas as well as fewer total tumors (carcinomas plus adenomas) than EPA's earlier analyses. The group concluded that because "the tumors were predominantly benign and usually associated with lesions of hepatic [liver] toxicity" the rat study demonstrated "a weak oncogenic [cancer-causing] effect of TCDD."[9] The implication of this controversial conclusion is that liver toxicity somehow caused or magnified the carcinogenic response.

ChemRisk used these results to calculate a new potency factor for 2,3,7,8-TCDD in rats, but counted only carcinomas in the liver (the primary target organ in this animal). They ignored carcinomas in other tissues as well as all adenomas, benign tumors that may progress into carcinomas. Both omissions are contrary to EPA guidelines for carcinogen risk assessment.[21]

ChemRisk also failed to adjust for early mortality of some test animals, another correction used by EPA.[1]

If the revised tumor pathology criteria are applied, eliminating liver hyperplasias, but all other standard EPA assumptions are employed, the calculated rat potency is reduced by only a factor of two to three from the current value. Again, ChemRisk's calculation of a new dioxin carcinogenic potency factor is indefensible.

Conclusion

A proposed acceptable daily dose for 2,3,7,8-TCDD is claimed to be based on new science regarding the classification of tumors. However, if this change alone is made, the "acceptable" dose of dioxin would only be altered by a factor of two to three. ChemRisk's proposed reduction by a factor of as much as a thousand is fundamentally based on scientifically indefensible changes in a number of other unrelated assumptions.

This series of events shows many of the problems with quantitative risk assessment. There is uncertainty about even the most basic questions such as the classification of tumors in laboratory animals. A large number of assumptions are required, each of which must be independently justified. Because of the uncertainty and the number of assumptions, it may be possible, in the absence of checks and balances, to construct nearly any result. ■

References and Notes

1. U.S. Environmental Protection Agency. 1985. *Health assessment document for polychlorinated dibenzo-p-dioxins.* EPA/600/8-84/014F. Washington, D.C.: Office of Health and Environmental Assessment.
2. U.S. Environmental Protection Agency. 1987. National dioxin study. EPA/530-SW-87-025. Washington, D.C.: Office of Solid Waste and Emergency Response.
3. State Water Resources Control Board. 1988. Chlorinated dibenzo-p-dioxin and dibenzofuran contamination in California from chlorophenol wood preservative use. Report 88-5WQ. Sacramento, CA: Division of Water Quality.
4. Keenan, R., R. Wenning, A. Parsons. 1989. Sensitivity analysis for dioxin risk assessment and implications for determining acceptable daily exposure: Executive summary. Portland, ME.: ChemRisk, October 20.
5. Keenan, R. Letter to Dr. R. Loehr, Chair, Executive Committee, Science Advisory Board, U.S. Environmental Protection Agency. March 20, 1990.
6. U.S. Environmental Protection Agency. 1990. *Tracking report: State water quality criteria for dioxin (2,3,7,8-TCDD).* Washington, D.C.: Office of Water Regulations and Standards. May.
7. Where people can consume both fish and water, the water quality standard is computed as:
   C = (RsD*BW)/((FC*BCF)+WC)
   RsD = risk specific dose ("acceptable" dose at a given risk level)
   BW = human body weight
   FC = fish consumption
   BCF = bioconcentration factor, the ratio between the concentration of the compound found in the fish and the concentration in water.
   WC = water consumption rate by humans (negligible when BCF is large).

   The current EPA water quality standard for 2,3,7,8-TCDD assumes a fish consumption rate of 6.5 grams per day (0.23 oz.) and a bioconcentration factor of 5000.[6,24] Both of these factors are low. New data indicate that sport fishermen can consume 30 grams per day of fish while subsistence fishermen may consume 140 grams per day.[24,28] These values are about five and twenty two times higher than the current EPA value. Recent studies of the bioconcentration of 2,3,7,8-TCDD have found values from 39,000 to 140,000.[29,30] Thus, even if the RsD for 2,3,7,8-TCDD was raised by a factor of two to three to account for changes in tumor classification, a water quality standard tens to hundreds of time lower could be constructed.

   Furthermore, water quality standards are set compound by compound, ignoring the fact that compounds closely related to 2,3,7,8-TCDD—such as 2,3,7,8-tetrachlorodibenzofuran, also emitted by pulp and paper mills that bleach with chlorine—are added together in other regulatory contexts, after adjusting for relative potency using the 2,3,7,8-TCDD equivalence methodology.
8. Gladwell, M. 1990. Scientists temper views on cancer-causing potential of dioxin. *Washington Post,* May 31, p. A3.
9. Sauer, R. and PATHCO, Inc. 1990. Pathology Working Group 2,3,7,8-tetrachlorodibenzo-p-dioxin in Sprague-Dawley Rats. 10075 Tyler Place #16, Ijamsville, MD 21754. March 13.
10. Maronpot, R., C. Montgomery, G. Boorman, and E. McConnell 1986. National Toxicology Program nomenclature for hepatoproliferative lesions of rats. *Toxicologic Pathology* 14(2): 263-273.
11. Agent Orange Scientific Task Force. 1990. *Human health effects associated with exposure to herbicides and/or their associated contaminants - chlorinated dioxins.* Washington, D.C.: National Veterans Legal Services Project.
12. Rogan, W., B. Gladen, C. Hsu, Y. Chen, and H. Ko. 1990. Yucheng: Studies in children. Presented at Dioxin '90, The Tenth International Meeting. Bayreuth, Germany.
13. Jacobson, J., S. Jacobson, and H. Humphrey. 1990. Effects of in utero exposure to polychlorinated biphenyls and related contaminants on cognitive functioning in young children. *J. Pediatrics* 116: 38-45.
14. Rohleder, F. 1989. Dioxins and cancer mortality: Reanalysis of the BASF cohort. Ninth International Symposium on Chlorinated Dioxins and Related Compounds, Toronto, Ontario, Sept. 17-22.
15. Van Strum, C. and P. Merrell. 1990. Dioxin human health damage studies: Damaged data? *Journal of Pesticide Reform* 10(1): 8-12.
16. Zober, A., P. Messerer, and P. Huber. 1990. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. *International Archives of Occupational and Environmental Health.* 62: 139-157.
17. Fingerhut, M., et al. (1991). Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324(4): 212-218.
18. "EPA likely to upgrade dioxin cancer classification to reflect new data." *Inside EPA.* February 1, 1991. p.4.
19. Jenkins, C. 1991. U.S. Environmental Protection Agency Memorandum. January 24.
20. Kociba, R., D. Keyes, J. Beyer, R. Carreon, C. Wade, D. Dittenber, R. Kalnins, L. Frauson, C. Park, S. Barnard, R. Hummel, and and C. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicology and Applied Pharmacology* 46: 279-303.
21. U.S. Environmental Protection Agency. 1986. Guidelines for carcinogen risk assessment. *Federal Register* 51(185): 33991. September 24.
22. U.S. Environmental Protection Agency. 1988. *A cancer risk-specific dose estimate for 2,3,7,8-TCDD: Draft.* EPA/600/6-88/007Aa. June. pp. 49-50.
23. Goldstein, B., N. Kim. 1989. Letter from the Chair and Co-Chair of the Ad Hoc Dioxin Panel to Dr. R. Loehr, Chair, Science Advisory Board Executive Committee, U.S. Environmental Protection Agency. November 28.
24. U.S. Environmental Protection Agency. 1990. EPA's position on Georgia's adoption of a dioxin water quality standard. Region IV. March.
25. Bayard, S. 1988. Quantitative implications of the use of different extrapolation procedures for low-dose cancer risk estimates from exposure to 2,3,7,8-TCDD. Appendix A of reference 22.
26. Alsen-Hinrichs, C, Department of Toxicology, University of Kiel School of Medicine, Kiel, Germany. Letter to the *Washington Post* (unpublished). June 21, 1990.
27. Squire, R. 1990. Letter to Dr. Robert Michaels acknowledging the request of November 28, 1989. January 8.
28. U.S. Environmental Protection Agency (1989). *Exposure factors handbook.* Versar, Inc. EPA 600/8-89-043. Washington, D.C.: EPA.
29. Mehrle, P., et al. 1988. Toxicity and bioconcentration of 2,3,7,8-tetrachlorodibenzo-p-dioxin and 2,3,7,8-tetrachlorodibenzofuran in rainbow trout. *Environ. Toxicol. Chem.* 7: 47-62.
30. Cook, P., A. Batterman, and B. Butterworth. 1990. *Laboratory study of TCDD bioaccumulation by lake trout from Lake Ontario sediments, food chain and water.* Duluth, MN: U.S. Environmental Protection Agency Environmental Research Laboratory.

Eleventh International Symposium on Chlorinated Dioxins and Related Compounds

MAR 20 1991

cc Steve
CR
By Ca.
Jim N

DIOXIN '91

September 23-27, 1991

Conference Information

School of Public Health
Office of Continuing Education
The University of North Carolina at Chapel Hill
CB# 8165, Miller Hall
Chapel Hill, NC 27599-8165
Phone: 919/966-1104
Fax: 919/966-7141

Organizing Committee

Memo

To: Conference Participants Who Plan to Submit Papers

From: Sharon Johnson Wills
Program Assistant

Date: February 10, 1991

Re: Abstract Format Instructions

The Organizing Committee of Dioxin '91 invites you to submit your abstract for the 11th International Symposium on Chlorinated Dioxins and Related Compounds. The conference will be held in Research Triangle Park, North Carolina, Sept. 23-27, 1991. Enclosed please find one instruction sheet and two forms for submitting your abstract. Also enclosed is an acknowledgment card that you should send back with your completed package. Fill in the lines marked "title" and "author" and return it with your abstract package to the Office of Continuing Education. I will return the card to you to acknowledge receipt of your abstract.

Please read the instructions carefully and take note of all mailing advisories so that we may include your abstract in this year's program. Remember that all abstracts must be received no later than April 1, 1991. Abstracts received after this date will not be considered for acceptance, published or printed.

If you have any questions or concerns, please call or write.

P.S. A complete brochure describing this program will be mailed to you in April. To register for Dioxin '91 before that time, please call me at 919/966-1104.

DOSE RESPONSE RELATIONSHIPS FOR CHRONIC EXPOSURE TO 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD) IN A RAT TUMOR PROMOTION MODEL: 2. QUANTIFICATION AND IMMUNOLOCALIZATION OF CYTOCHROMES P450c(1A1) AND P450d(1A2) IN THE LIVER.

A Tritscher, G Clark, Z McCoy, C Portier, W Greenlee, J Goldstein, and G Lucier. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

TCDD and its structural analogs produce a broad spectrum of biochemical and toxic effects in animals and humans. The mechanisms responsible for these effects involve interactions with the Ah receptor but many of the steps necessary for biological response remain unknown. One of the troublesome knowledge gaps that causes uncertainty in risk assessments for TCDD is the lack of adequate dose-response relationships following chronic exposure to TCDD. One of the most sensitive responses to TCDD and its structural analogs is the induction of specific isozymes of cytochrome P450 (CYP1A1 and CYP1A2). CYP1A1 is induced in many tissues whereas CYP1A2 is induced only in liver. We have employed a two-stage model for hepatocarcinogenesis in female Sprague-Dawley rats to evaluate dose-response relationships for CYP1A1 and CYP1A2. A single dose of diethylnitrosamine was used as the initiating agent followed by biweekly gavage of TCDD at doses equivalent to 3.5, 10, 35 and 125 ng/kg/day for 30 weeks. CYP1A1 and CYP1A2 were quantified in liver microsomes from control and treated rats by immunoassay. Data revealed a maximum induction of CYP1A2 of 10-fold and induction was nearly 3-fold at the 3.5 ng/kg/day dose. The no detectable effect for 1A2 induction was estimated to be 0.1 to 0.3 TCDD ng/kg/day. A chronic dosing experiment is in progress to determine if this is an accurate estimate of the no detectable effect. Interestingly, TCDD-mediated induction of 1A2 appeared to occur at lower doses in DEN-initiated rats compared to non-initiated rats. Also, CYP1A2 induction appeared to be a slightly more sensitive marker of TCDD exposure than CYP1A1 in our rat liver tumor promotion model. We also analyzed liver TCDD concentrations by GC-MS. These data revealed a linear relationship between administered dose and TCDD liver concentrations throughout the entire dose range of our study. Therefore, induction of 1A2 does not enhance TCDD retention in liver, a hypothesis that had been proposed because 1A2 is a binding protein for TCDD. We also used immunocytochemical techniques to analyze the pattern of CYP1A1 and CYP1A2 distribution in livers of control and TCDD-treated rats. 1A2 was localized primarily in the centrolobular region with small amounts in the midzonal and periportal regions. Induction by TCDD increases the number of cells containing detectable amounts of 1A2 but not the intensity of staining of cells constitutively expressing this cytochrome. Localization patterns, in induced rats, were similar for 1A1 and 1A2. Taken together, these studies are characterizing dose response relationships for CYP1A1 and CYP1A2 that represent characteristic Ah receptor dependent responses to TCDD exposure. (Funding for TCDD analyses provided by the American Paper Institute.

DOSE RESPONSE RELATIONSHIPS FOR CHRONIC EXPOSURE TO 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD) IN A RAT LIVER TUMOR PROMOTION MODEL: 1. RELATIONSHIPS OF TCDD TISSUE CONCENTRATIONS TO SERUM CLINICAL CHEMISTRY, CELL PROLIFERATION, AND PRENEOPLASTIC FOCI.

G Clark, A Tritscher, Z McCoy, C Portier, M Thompson, R Wilson, J Foley, R Maronpot, [1]T Goldsworthy, W Greenlee, and G Lucier. National Institute of Environmental Health Sciences, Research Triangle Park, NC and [1]Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

One of the important issues in a risk assessment for exposure to dioxins is the pharmacokinetic distribution of TCDD in a long term chronic exposure regimen and the biological responses associated with a potential carcinogenic outcome. A specific cytoplasmic binding protein, the Ah receptor, is generally thought to mediate most of the biological responses to TCDD including its action as a tumor promoter. We have used a rat liver tumor promotion model to investigate biochemical responses that may be associated with promotion of carcinogenesis. In previous studies we have found that alterations of hepatic cell proliferation and the appearance of enzyme altered foci (γ-glutamyl transpeptidase and glutathione S-transferase-positive foci) correlate with liver tumor formation but that the ovaries are necessary for the expression of these effects. In the current study we are investigating dose response relationships in female Sprague-Dawley rats with an initiating dose of 175 mg/kg DEN and biweekly exposure to TCDD for 30 weeks to give doses equivalent to 3.5, 10.7, 35.7, and 125 ng/kg/day TCDD. A linear distribution of TCDD in livers of exposed animals was found. The mean liver concentration of TCDD was 19.9 ppb at 125 ng/kg/day and the mean liver concentration was 0.5 ppb at 3.5 ng/kg/day. In serum samples from the rats exposed to 125 ng/kg/day the TCDD concentration was 23.9 ppt while the concentration at the lowest dose was 8 ppt. Several serum clinical chemistry parameters were measured including alkaline phosphatase, glucose, alanine transaminase, total cholesterol, triglycerides, sorbitol dehydrogenase, 5' nucleotidase, and total bile acids. A significant dose effect for TCDD exposure was determined for serum alkaline phosphatase, 5' nucleotidase activities and on the levels of serum cholesterol. We are in the process of analyzing cell proliferation in livers from these animals by incorporation of bromodeoxyuridine into newly-formed cells and immunohistochemical analysis. We are also quantifying γ-glutamyl transpeptidase and placental glutathione S-transferase-positive foci as indicators of preneoplastic lesions. These parameters will be correlated with the applied dose, the tissue specific dose, and the levels of occupied Ah receptors. We hope to determine a) what is the most sensitive biochemical response to TCDD exposure and b) which parameter correlates with carcinogenicity. These data will be useful in the development of mechanistic models for dioxin risk assessment. (Funding for TCDD analyses provided by the American Paper Institute).

Carcinogenesis vol.12 no.5 pp.793-800, 1991

Attachment 5

Study of the separate and combined effects of the non-planar 2,5,2′,5′- and the planar 3,4,3′,4′-tetrachlorobiphenyl in liver and lymphocytes *in vivo*

Linda Sargent[1], Yvonne P.Dragan, Chris Erickson, Chris J.Laufer and Henry C.Pitot[2]

McArdle Laboratory for Cancer Research, Department of Oncology and the Center for Environmental Toxicology, The Medical School, University of Wisconsin, Madison, WI 53706, USA

[1]Present address: Chemical Industry Institute of Toxicology, 6 Davis Drive, Research Triangle Park, NC 27709, USA
[2]To whom reprint requests should be sent

Polychlorinated biphenyls (PCBs) are a group of industrial chemicals that are widely distributed in the environment. Because these compounds occur as mixtures, studies of their possible interactive effects are essential for an understanding of the mechanism of the toxicity of these mixtures. For the determination of a possible interaction of the effects *in vivo* of 2,5,2′,5′-tetrachlorobiphenyl (TCB) and 3,4,3′,4′-TCB, rats were exposed to a single dose of diethylnitrosamine (DEN) and subsequently to 0.1 p.p.m. 3,4,3′,4′-TCB and/or 10 p.p.m. 2,5,2′,5′-TCB in the feed for 1 year. The two major targets of PCB toxicity, the liver and the peripheral blood, were examined after these treatments. TCB treatment after DEN exposure caused a predominance of increased placental glutathione S-transferase (PGST) and deficiencies of ATPase as preneoplastic markers in focal hepatic lesions. When 0.05% phenobarbital (PB) was administered after DEN exposure, the distribution of markers in altered hepatic foci (AHF) was essentially equal for increased PGST and γ-glutamyltranspeptidase (GGT) and for ATPase deficiency. Many of these AHF also exhibited increased P450 b/e expression. Our results demonstrated that the two PCB congeners interacted *in vivo* to produce an increase in AHF that were PGST positive and ATPase negative. PGST-positive and ATPase-negative AHF correlated best with focal areas of P450 b/e expression. The combination of the two PCBs caused a greater than additive decrease in the total number of lymphocytes and antibody-producing B-cells. Also the thymocyte-dependent T-helper cells isolated from the animals receiving the combination of TCBs demonstrated a morphologically abnormal subpopulation. The results indicate that the interaction of 2,5,2′,5′-TCB and 3,4,3′,4′-TCB *in vivo* induced much greater toxicity and mutagenicity in peripheral lympyhocytes and hepatocytes than treatment with either congener alone.

Introduction

Polychlorinated biphenyls (PCBs*) are a group of industrial chemicals that, in the past, had diverse uses owing to their chemical stability and their miscibility in organic solvents. These properties resulted in the use of PCBs as hydraulic fluids, plasticizers, adhesives, heat transfer fluids, wax extenders, dedusting agents, organic diluents, lubricants, flame retardants and as dielectric fluids in capacitors and transformers (1). The advantages that made PCBs such a versatile industrial chemical proved to be the source of their problem in the environment. Traces of PCBs have been found in environmental samples world-wide (2,3). Analyses of human breast milk, blood and adipose tissue have demonstrated that most individuals have been exposed to PCBs (2,3). The primary route of human exposure is through oral ingestion of contaminated products.

Technical mixtures of PCBs contain a combination of planar and non-planar congeners. The planar congeners bind to the Ah receptor, induce cytochrome P450 c and P450 d (4−7), and cause a cascade of events primarily in the liver and immune cells, including weight loss, thymic atrophy, decreased spleen weights (8), reduction of circulating lymphocytes of both the bursae and thymic cell populations (9−11), hepatomegaly, and subcapsular and midzonal hepatic necrosis. They are also potent promoters of the growth of preneoplastic hepatic foci (12). The non-planar congeners are less toxic, have a low affinity for the Ah receptor, and induce P450 b/e. The non-planar congeners cause hepatic enlargement and are relatively weak promoting agents in hepatocarcinogenesis (12,13). They do not cause thymic atrophy or reduction in immune function (5,6,14).

Planar and non-planar congeners occur as mixtures, yet there are few studies which have examined the potency of specific combinations of PCB congeners. The planar 3,4,3′,4′-tetrachlorobiphenyl (TCB) and the non-planar 2,5,2′,5′-TCB are found in the Aroclor mixtures 1254, 1248 and 1242. The ratio of the concentration of these two congeners in the major Aroclors was used to determine the concentration ratio for this study. In addition, we chose to use low-level, environmentally relevant doses of these TCBs in order to assess the potency of the combination for the determination of doses in this experiment. The sample of Aroclor that was used as a standard contained 0.002 μg of 3,4,3′,4′-TCB/ml and 0.2 μg of 2,5,2′,5′-TCB/ml. Hepatocytes and lymphocytes were chosen as target cells to study a possible superadditive toxicity and promotion potency of the combination of the planar and the non-planar TCBs, since these two target cell types are among the most sensitive to PCB toxicity.

Materials and methods

Chemicals

The Pariza purified diet was purchased from Teklad (Madison, WI). Diethylnitrosamine (DEN) was obtained from the Eastman Kodak Co. (Rochester, NY). 3,4,3′,4′-TCB was purchased from Ultra Scientific (Hope, RI) and 2,5,2′,5′-TCB was a gift from Dr James Miller (McArdle Laboratory, Madison, WI). All of the antibodies used for immunohistochemistry were obtained from Bioproducts for Science Inc. (Indianapolis, IN).

Animals and treatment protocol

Female Sprague−Dawley rats (Harlan Sprague Dawley, Madison, WI) weighing an average of 90 g were housed in wire mesh cages and fed the Pariza diet (30% casein, 5% corn oil, 10% partially hydrogenated corn oil, 40% sucrose, 15% cornstarch) and water *ad libitum*. A 70% partial hepatectomy was performed under ether anesthesia and 24 h later 50% of the animals were intubated with

*Abbreviations: PCBs, polychlorinated biphenyls; TCB, tetrachlorobiphenyl; DEN, diethylnitrosamine; PB, phenobarbital; AHF, altered hepatic foci; GGT, γ-glutamyl transpeptidase; PGST, placental form of glutathione S-transferase; ATP, canalicular ATPase; G6P, glucose-6-phosphatase; HCC, hepatocellular carcinoma; TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin; HCB, hexachlorobiphenyl.

10 mg DEN in trioctanoin/kg. After 1 week, the animals were randomly assigned to the treatment groups outlined in Figure 1. TCBs were dissolved in methylene chloride, added to the powdered chow, and mixed thoroughly in plastic bags. The solvent was evaporated in the hood for 24 h. Randomly selected rats were then placed on a control diet or control diet with one of the following additions: 0.1 p.p.m. 3,4,3′,4′-TCB only, 10 p.p.m. 2,5,2′,5′-TCB only, 0.1 p.p.m. 3,4,3′,4′-TCB and 10 p.p.m. 2,5,2′,5′-TCB, or 100 p.p.m. 2,5,2′,5′-TCB. Another group was fed phenobarbital (PB) at a level of 0.05% in the diet as a positive control (15,16).

Analysis of lymphocytes

Rats were treated with 100 mg cyclophosphamide/kg and anesthetized with ether; blood was drawn by cardiac puncture 48 h later. The red blood cells were lysed with 2 ml hypotonic buffer (1000 ml of deionized water, 8.29 g NH_4Cl, 1.0 g KH_2CO_3, 0.372 g disodium EDTA, pH 7.4) and washed with phosphate-buffered saline. Washed lymphocytes were then mixed with fluorescein-conjugated antibodies generated against the CD-4 protein, the CD-8 protein, the 1.1 Thy protein and a general B-cell protein (17). The stained cells were then analyzed on the flow cytometer by standard methods (18). Lymphocytes of abnormal morphology were examined by scanning electron microscopy according to standard methods. Sections of the spleen were frozen on solid CO_2 and fixed in 10% buffered formalin.

Analysis of preneoplastic foci (altered hepatic foci, AHF)

The liver was removed, weighed, and sections from each liver lobe were immediately frozen on solid CO_2. Five 10-μ-thick serial sections were stained for γ-glutamyl transpeptidase (GGT), the placental form of glutathione S-transferase (PGST), canalicular ATPase (ATP), cytochrome P450 b/e, P450 c/d and glucose-6-phosphatase (G6P), according to the methods for staining outlined by Xu *et al.* (19). AHF were then quantitated by the procedure of Campbell *et al.* (20). Additional slices of tissue were stored in 10% formalin for histopathological analysis.

Statistics

Non-parametric Wilcoxon statistics were used to compare groups. For the determination of additivity, Steel and Torrie's χ-square test for additivity (21) was used.

Results

Lymphocyte analysis

The total number of circulating antibody-producing cells (B-cells) was reduced in the peripheral blood prepared from animals treated with 3,4,3′,4′-TCB, but not from those treated with 2,5,2′,5′-TCB (groups 3 and 5, Figure 2) when compared with untreated controls. The number of circulating B-cells isolated from animals treated with both TCBs was reduced by a greater than additive level ($P < 0.001$, group 7) when analyzed by flow cytometry. When DEN was included in the treatment protocol (Figure 3), the level of circulating B-cells was reduced in the 2,5,2′,5′-TCB group as well as the 3,4,3′,4′-TCB group ($P < 0.05$, groups 4 and 6). The level of B-cells in the group with DEN plus both TCBs (group 8) was reduced to 1%. A reduction to this level was greater than would be expected by an additive model when analyzed by the χ-square test for additivity.

There was no statistical reduction in the number of CD-4, CD-8 or Thy 1.1 cells. Although the total number of cells was the same, a population of light-staining CD-4 cells was observed by flow cytometry (Figure 4). Of the CD-4 cells, 50 ± 8% from group 7 (both TCBs) and 95 ± 5% of the samples from group 8 (DEN + both TCBs) had an abnormal population of light-staining CD-4 cells. The forward scatter of these cells was the same as that of the normal CD-4 cells, but the side scatter was different (Figure 4). A difference in the side scatter would indicate a difference in size or morphology. When these light-staining CD-4 cells were separated and examined by scanning electron microscopy, the surface morphology of all of the cells examined was distinctly different from the normal population (Figure 5). By standard methods (17), these abnormal cells were further examined for esterase activity and were determined to be negative and therefore not monocytes.

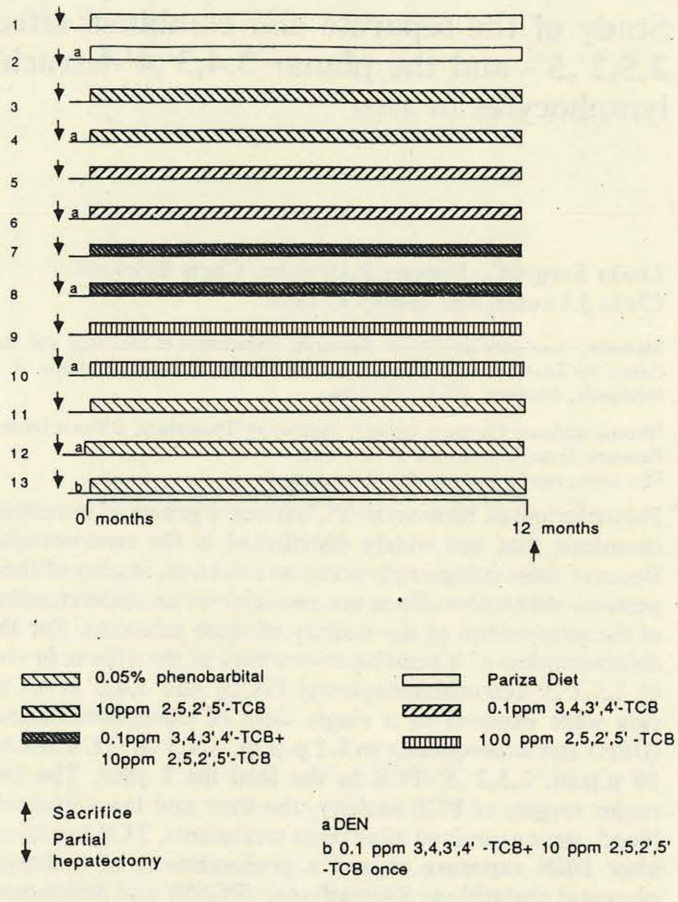


Fig. 1. Format of the protocol used for the initiation and promotion of AHF in female Sprague−Dawley rats.

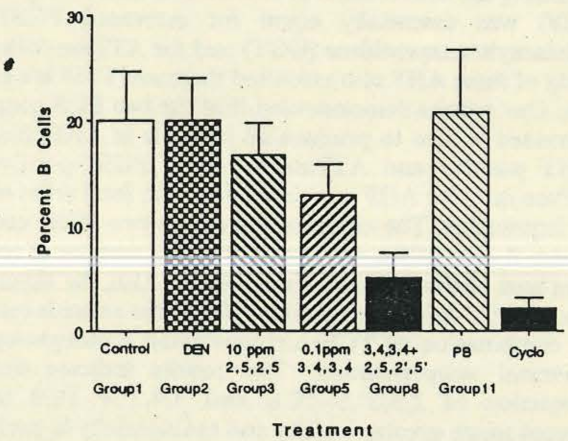


Fig. 2. Percentage of B-cells in the peripheral blood after chronic exposure to DEN alone or followed by 0.05% PB, 3,4,3′,4′-TCB, 2,5,2′,5′-TCB, or a combination of 3,4,3′,4′-TCB + 2,5,2′,5′-TCB or to cyclophosphamide. See text for details. Steel and Torrie's χ-square test for additivity (21) was used to examine an additive or greater than additive result. The conclusions of this test are given in the text. The bars above the columns indicate the standard error of the mean for analysis (1/rat in duplicate). The numbers of rats/group may be obtained from Table I.

Liver analysis

Number of preneoplastic foci. There was no statistical increase in the ratio of residual liver wt to body wt with any of the TCB treatments, but there was a significant increase in the PB and DEN + PB groups (Figure 6). A single dose of 0.1 p.p.m. 3,4,3′,4′-TCB and 10 p.p.m. 2,5,2′,5′-TCB did not increase the

Table I. Histopathologic changes in livers of rats on protocols depicted in Figure 1[a]

Group no.	Treatment	Portal damage[b]	Bile duct proliferation	Neoplastic nodules/rat	Cellular atypia/ neoplastic nodule/rat[c]	HCC/rat
1	Control	–	2/8	–	–	1/8
2	DEN	0/8	2/8	1/8	1/8	1/8
3	2,5,2′,5′-TCB (10 p.p.m.)	0/14	2/14	2/14	0/14	0/14
4	DEN + 10 p.p.m. 2,5,2′,5′-TCB	2/12	1/12	4/12	1/12	1/12
5	3,4,3′,4′-TCB (0.1 p.p.m.)	0/14	5/14	3/14	0/14	0/14
6	DEN + 0.1 p.p.m. 3,4,3′,4′-TCB	0/12	4/12	4/12	0/12	0/12
7	3,4,3′,4′-TCB + 2,5,2′,5′-TCB	9/12	9/12	1/12	1/12	0/12
8	DEN + 3,4,3′,4′-TCB + 2,5,2′,5′-TCB	9/11	11/11	11/11	9/11	2/11
10	DEN + 100 p.p.m. 2,5,2′,5′-TCB	3/5	2/5			
12	DEN + PB	2/11	11/11	11/11	11/11	9/11

[a]Data are presented as the number of rats exhibiting the pathologic process/total number of rats examined.
[b]Includes fibrosis, chronic inflammation and/or hydopic change of periportal hepatocytes. Control animals receiving control diets showed only occasional minimal portal damage and bile duct proliferation. The histopathology of livers of rats in groups 9, 11 and 13 (Figure 1) was no different from that seen in groups 1, 3 and 5.
[c]Cellular atypia is defined as morphological and cytological changes, usually focal, seen in neoplastic nodules, such changes being histologically compatible with one or more patterns of well-differentiated hepatocellular carcinomas (43–45).

total number of AHF or the volume fraction of the regenerated liver occupied by AHF.

Treatment with TCBs caused a predominance of AHF that were scored by the presence of PGST ($PGST^+$) and ATP deficiency as preneoplastic markers (Figure 7), whereas $PGST^+$, ATP deficiency and GGT^+ markers were equally distributed in AHF after DEN + PB (Figure 8). TCB treatment alone did not elevate the number of AHF when compared with the control livers; however, treatment with both TCBs increased the number of AHF to a level that was greater than that of the untreated control and statistically the same as the DEN control (groups 2, 3 and 5 in Figure 1; see also Figure 9). The numbers of preneoplastic foci per liver in the DEN + 10 p.p.m. 2,5,2′,5′-TCB group (group 4) or the DEN + 0.1 p.p.m. 3,4,3′,4′-TCB group (group 6 in Figure 1) were not significantly different from the DEN group (group 2, Figure 1). When rats were treated with DEN followed by both TCBs, the number of AHF was dramatically greater than additive (Figure 9) ($P < 0.001$). Treatment with DEN + 100 p.p.m. 2,5,2′,5′-TCB (group 10) did not cause a significant increase in the number of AHF when compared with DEN (Figure 9). Rats treated with the standard DEN + PB protocol had a significant increase in the number of AHF ($P < 0.001$, Figure 9).

Volume fraction of preneoplastic foci. When the volume fraction of AHF was analyzed, rats inititated with DEN and fed 10 p.p.m. 2,5,2′,5′-TCB (group 4) exhibited statistically the same volume percentage AHF as the DEN group (group 2 in Figure 10); however, the volume of AHF in the DEN + 3,4,3′,4′-TCB group (group 6) was slightly increased over that in the regenerated livers of animals receiving DEN only (group 2, Figure 10). The combination of DEN + both TCBs (group 8 in Figure 1) greatly increased the volume of the residual liver occupied by preneoplastic foci to a level that was much greater than would be expected by an additive model ($P < 0.001$; Figure 10). The group given a 10-fold greater level of 2,5,2′,5′-TCB (group 10) exhibited a significant increase in the volume of the regenerated liver occupied by AHF to 7% of the liver (Figure 10). This level was statistically greater than that of rats given DEN alone but not as great as the DEN plus both TCBs group. When the livers of rats given DEN followed by 0.05% PB in the diet were examined, there was a significant increase in the volume fraction of preneoplastic foci to 20% of the total regenerated liver (group 12 in Figure 1; see Figure 10).

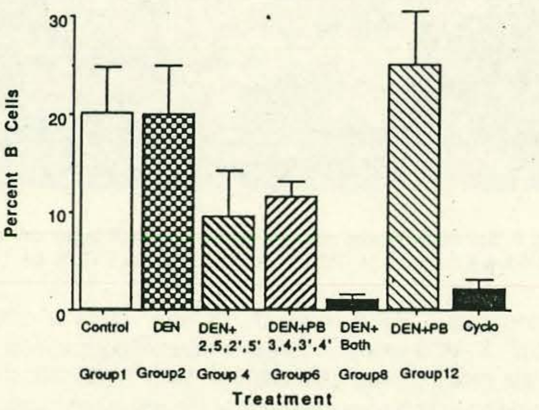


Fig. 3. Percentage of B-cells in the peripheral blood after 10 mg DEN/kg and 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB, 10 p.p.m. 2,5,2′,5′-TCB, or a combination of 3,4,3′,4′-TCB + 2,5,2′,5′-TCB or to cyclophosphamide. See text and legend to Figure 2 for details and statistical conclusions. Steel and Torrie's χ-square test for additivity was used to assess significance. $P < 0.05$.

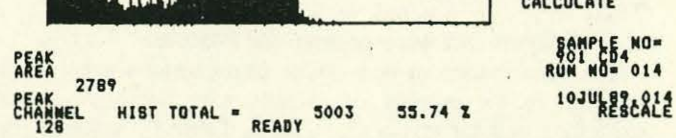


Fig. 4. Histogram of the fluorescence of T-helper cells following 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB. Antibodies conjugated with fluorescence and generated to the CD-4 protein were used to identify the T-helper cells. See text for experimental details.

Cytochrome P450 b/e was found in 10 ± 7% of the preneoplastic foci marked by PGST or ATP of the DEN + 10 p.p.m. 2,5,2′,5′-TCB, but 68 ± 10% of the AHF expressed the

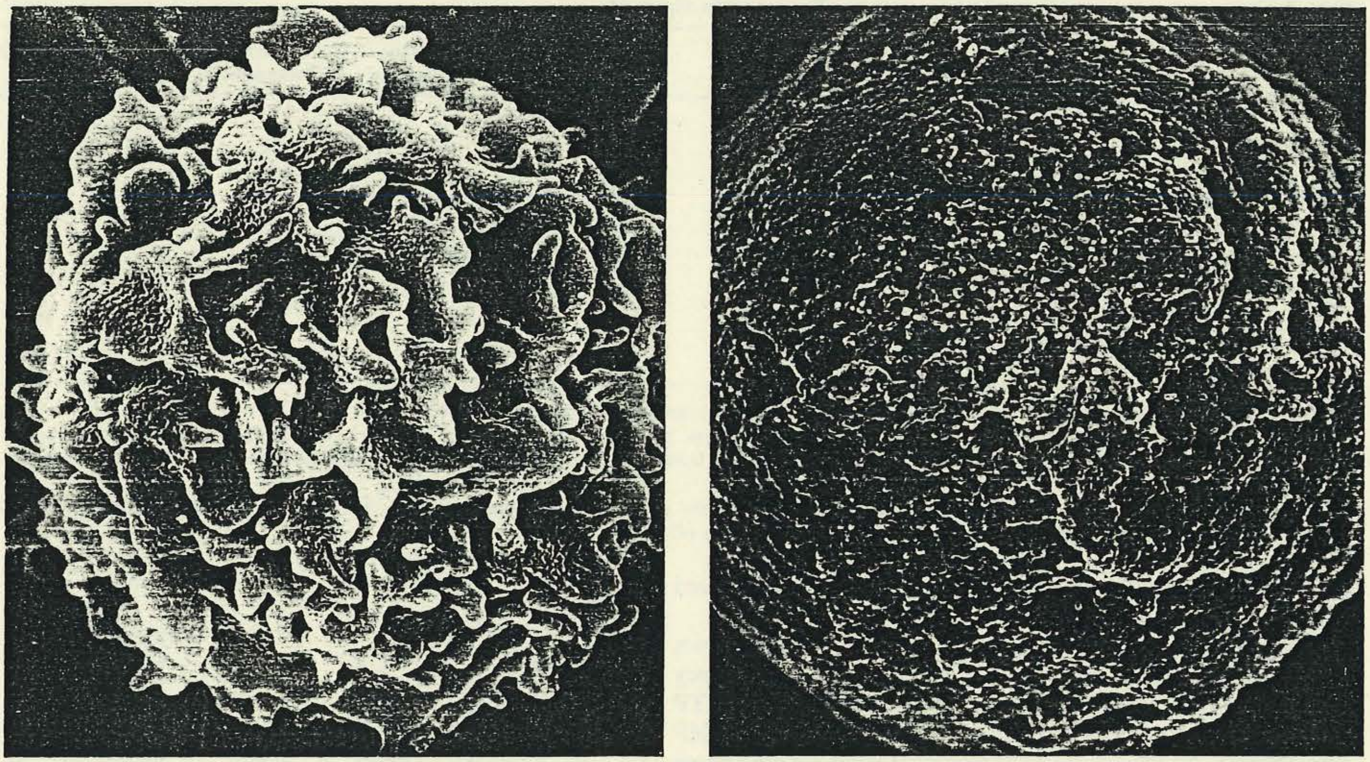


Fig. 5. Scanning electron micrograph of a normal T-helper cell (left) and an abnormal T-helper cell (right) isolated from the peripheral blood of an animal fed 0.1 p.p.m. 3,4,3',4'-TCB + 10 p.p.m. 2,5,2',5'-TCB for 1 year (×5000). See text for details.

cytochrome P450 marker in the DEN + 100 p.p.m. 2,5,2'.5'-TCB group. A larger number of positive foci was found in the group treated with DEN + both TCBs (60 ± 5%) than would be expected on the basis of the result seen with 10 p.p.m. 2,5,2',5'-TCB alone. The number of P450 b/e positive foci found in the DEN + PB group was as large as that of the group given DEN + both TCBs (65 ± 5%) (Table II).

The expression of P450 c/d was localized to the centrolobular and midzonal region of the regenerated liver in the DEN + 3,4,3',4'-TCB group, the DEN + both TCBs group, and the TCBs group (groups 6, 8 and 9). Centrilobular to midzonal staining was also seen with P450 b/e in the DEN + 10 p.p.m. 2,5,2',5'-TCB, the DEN + 100 p.p.m. 2,5,2',5'-TCB, the DEN + both TCBs and the DEN + PB groups. This degree of staining indicates that P450 c/d was induced by these regimens. In addition, P450 b/e was examined; in the DEN + PB group (group 12 in Figure 1), 76% of the PGST and 32% of the ATP-deficient foci were positive for this enzyme. In the DEN + 100 p.p.m. 2,5,2',5'-TCB group, 22% of the PGST-positive AHF and 41% of the ATP-negative AHF were positive for P450 b/e. When both TCBs were administered, 40% of the PGST and 40% of the ATP-deficient foci were positive for P450 b/e.

The combination of both TCBs also caused a superadditive increase in the number of animals with neoplastic nodules exhibiting cellular atypia ($P < 0.05$, Table I); however, only two of the animals treated with DEN + both TCBs developed hepatocellular carcinoma (HCC). Treatment with DEN + PB for 1 year caused 80% of the animals to develop HCC.

Discussion

The planar congener, 3,4,3',4'-TCB, and its non-planar isomer, 2,5,2',5'-TCB, which are found in the major Aroclor mixtures 1254, 1242 and 1248, induced a greater than additive toxicity

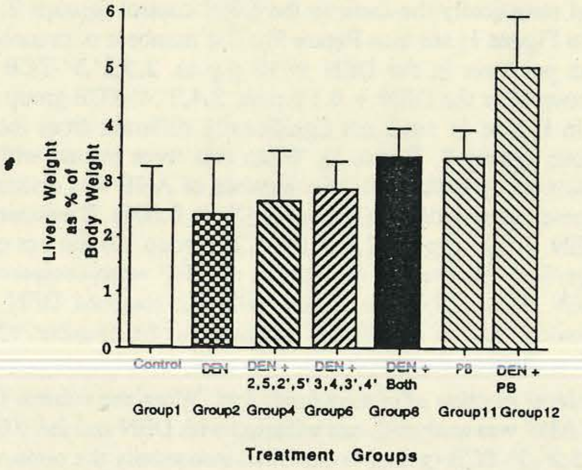


Fig. 6. Histogram of the ratio of the regenerated liver to body wt following 10 mg DEN/kg and 1 year of exposure to TCBs or to PB. The group numbers below each bar refer to the groups listed in Figure 1. The group designated PB is group 11 of Figure 1. Groups seen in Figure 1 not shown in this figure exhibited no significant change from the group 1 control.

in the two major target cell types of PCB toxicity, hepatocytes and lymphocytes, in the studies described here. Our results demonstrated that low doses of the planar 3,4,3',4'-TCB were more toxic to lymphocytes than a 100-fold higher dose of the non-planar 2,5,2',5'-TCB congener. The 3,4,3',4'-TCB congener caused a reduction in the number of B-cells. A similar reduction of B-cells has been noted after acute exposure to 3,4,3',4'-TCB (10). The combination of the two TCBs caused a greater than additive decrease in the number of circulating B-cells as well as the appearance of an abnormal subpopulation of T-helper cells. The esterase test verified that this abnormal population of

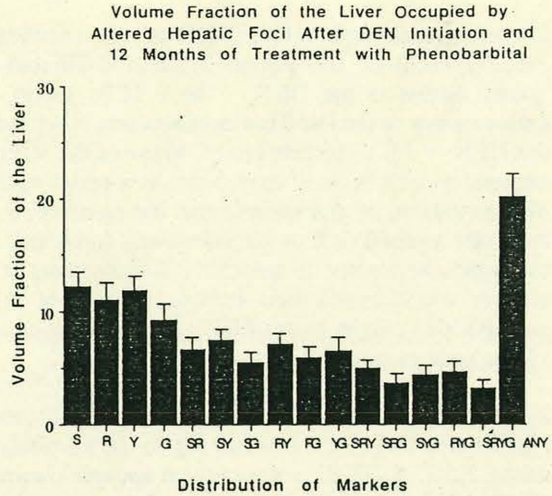


Fig. 7. Distribution of the volume fraction of AHF scored by multiple markers for AHF following initiation with 10 mg DEN/kg and 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB and 10 p.p.m. 2,5,2′,5′-TCB (group 8, Figure 1). Abbreviations: S, glutathione S-transferase-positive volume fraction; R, GGT-positive volume. Y, ATPase-negative volume; G, G6Pase-negative volume; SR, S and R combined; SY, S and Y combined. SG, S and G combined; RY, R and Y combined; RG, R and G combined; YG, Y and G combined; SYG, S and Y and G combined; SRY, S and R and Y combined. See ref. 19 for further details.

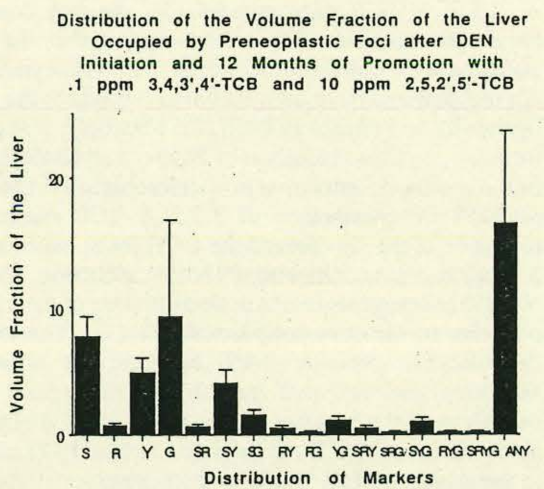


Fig. 8. Histogram of the distribution of the volume fraction of AHF scored by multiple markers for AHF following initiation with 10 mg DEN/kg and 1 year of exposure to 0.05% PB (group 12, Figure 1). See legend to Figure 7 for marker designation.

light-staining CD-4 cells was not a monocyte population, but was a new population of CD-4 cells exhibiting an abnormal surface membrane configuration.

The results from this research also demonstrated that the planar congener had more potent effects in liver cells than the non-planar TCB. The low dose of 3,4,3′,4′-TCB chosen for this study produced a moderate increase in the volume of preneoplastic foci as well as an increase in chromosome damage (L.Sargent and H.C.Pitot, unpublished observations). The relative potency of promoting agents has been expressed by the following relationship:

$$\text{promotion index} = V_f/V_c \times 1/\text{mmol per week}$$

where V_f is the total volume fraction (%) occupied by AHF in the livers of rats treated with the promoting agent, V_c is the total volume of AHF in control animals that have only been initiated and not treated with the promoting agent, and mmol is the number of millimoles of the promoting agent.

The promotion index (22) is based on the total number of altered cells within all AHF, thus giving a measure of tumor promotion. Table III shows the relative promotion indices of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB as well as their combination

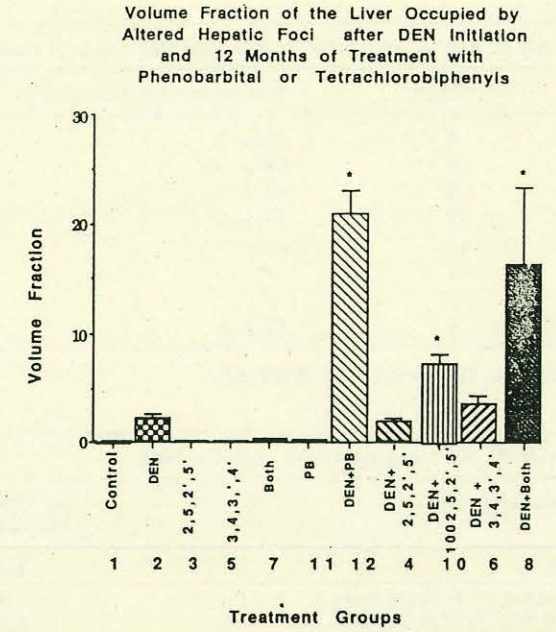


Fig. 9. Number of AHF per liver after initiation with 10 mg DEN/kg and/or 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB (groups 6 and 5), 10 p.p.m. 2,5,2′,5′-TCB (groups 4 and 3), 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB (groups 8 and 7) or to 0.05% PB in the diet for 1 year (groups 12 and 11). Eleven animals per group were killed after each treatment. The bars above the columns indicate the standard error of the mean from 11 animals. See Figure 1 for details of each group designated by number under the columns. $*P < 0.001$ by Student's t-test.

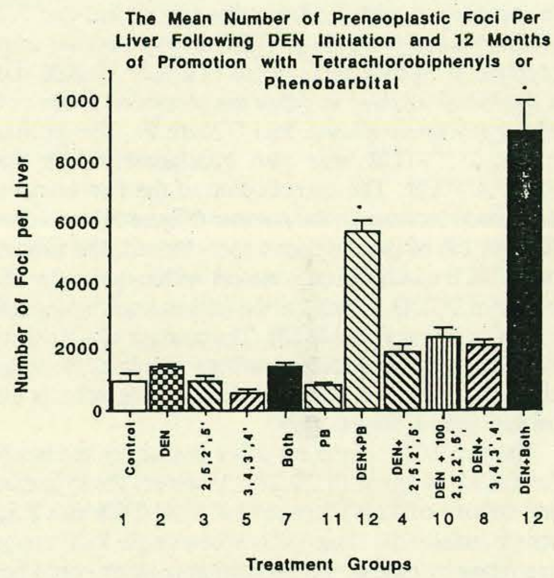


Fig. 10. Volume fraction (%) of AHF following initiation with 10 mg DEN/kg and/or 1 year of exposure to 0.1 p.p.m. 3,4,3′,4′-TCB (groups 6 and 5), 10 p.p.m. 2,5,2′,5′-TCB (groups 4 and 3), 0.1 p.p.m. 3,4,3′,4′-TCB + 10 p.p.m. 2,5,2′,5′-TCB (groups 8 and 7) or to 0.05% PB (groups 12 and 11) in the diet for 1 year. Each group had 11 animals. See legend to Figure 9 for further details.

Table II. AHF-positive P450 b/e expression after 1 year of treatment (%)

Groups	Foci positive for P450 b/e (%)
4	10 ± 7
10	68 ± 10
8	60 ± 5
12	65 ± 5
11	–[a]
3	–[a]
5	–[a]
9	40 ± 6

[a]Too few AHF to report significant data.

Table III. Promoting agents and promotion index

Promoting agents	Promotion index[a]
PB	100
3,4,3',4'-TCB (0.1 p.p.m.)	1.5×10^4
2,5,2',5'-TCB (10 p.p.m.)	200
2,5,2',5'-TCB (100 p.p.m.)	250
2,5,2',5'-TCB (10 p.p.m.) and 3,4,3',4'-TCB (0.1 p.p.m.)	8×10^5
2,3,7,8-TCDD[b]	2.8×10^7

[a]See text for details of calculations. Promotion indices were determined in animals that had been initiated with DEN (10 mg/kg) following a 70% partial hepatectomy (see text for details).
[b]Ref. 22.

in comparison with PB from this experiment and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) from an earlier study (22). By contrast, a 10-fold higher dose of 2,5,2',5'-TCB did not cause a significant increase in either the promotion index or the number of hepatic preneoplastic foci (Figure 9). The promotion index of 2,5,2',5'-TCB was also considerably less than that of 3,4,3',4'-TCB. The combination of the two congeners caused a dramatic increase in the number (Figure 9) and volume fraction (Figure 10) of preneoplastic foci. Indeed, the promotion index of the TCB combination is almost within one order of magnitude of that of TCDD, which has the highest known promotion potency of any compound (Table III). The number of animals treated with both TCBs that had numerous large neoplastic nodules exhibiting cellular atypia was also greater than that seen in either group treated with a single TCB.

The two TCB congeners differ in toxicity and binding affinity for the Ah receptor (8,23,24); however, the systemic clearance and volume of distribution of 3,4,3',4'-TCB and 2,5,2',5'-TCB are essentially the same (15). When single PCB congeners were examined by others, the promotion potency could be correlated with the affinity for the Ah receptor (23). Our results also demonstrated that the strong Ah receptor ligand, 3,4,3',4'-TCB, was a strong promoter of AHF, but the non-planar congener was a weak promoter relative to 3,4,3',4'-TCB and TCDD. Furthermore, previous results have shown that TCDD, which has a 500-fold greater affinity for the Ah receptor than TCBs, was a stronger promoter than 3,4,3',4'-TCB (24). The non-planar congeners, 2,4,5,2',4',5'-TCB (23), 2,4,2',4'-TCB and 2,5,2',5'-TCB, have been reported to exhibit promoting activity for hepatic preneoplastic foci (14). The presence of chlorine substitution in the *para* position correlated with an enhancement of promoting potency, but all the non-planar congeners were less potent than the planar 3,4,3',4'-TCB.

An enhancement of the amount of P450 b/e enzymes was seen in preneoplastic hepatic foci (AHF) of rats receiving 10 p.p.m. 2,5,2',5'-TCB or 100 p.p.m. 2,5,2',5'-TCB and to an even greater extent in the DEN + both TCBs group. This same enhancement of the P450 b/e enzymes was observed in AHF of the DEN + PB treatment group. Many of the changes in gene expression seen in AHF may occur as a result of the selection of a population of altered cells that are resistant to the specific treatment utilized (25) or are selectively stimulated to grow by the particular promoting agent (26). Enhancement of the expression of this detoxification enzyme in cells of AHF is also exemplified by an increase of P450 b/e following promotion with PB as well as hexachlorocyclohexane (27,28).

The greater than additive toxicity of 3,4,3',4'-TCB and 2,5,2',5'-TCB that was seen *in vivo* in hepatocytes and lymphocytes may have been owing to the metabolic activation of the 2,5,2',5'-TCB congener to an epoxide intermediate (14, 29,30). This epoxide intermediate is more toxic and more chromosome damaging than the parent compound (31) and has been shown to bind to DNA (29,32). PCB congeners that have both the *meta* and *para* sites available for oxidation can be metabolized through an epoxide intermediate. These intermediates can bind to DNA and have been found to be mutagenic (25,31). Examination of the dose–response curves of previous *in vitro* studies of chromosome damage in human lymphocytes (33) caused by 3,4,3',4'-TCB and a combination of 3,4,3',4'-TCB + 2,5,2',5'-TCB demonstrated that the two dose–response curves are parallel. This would suggest that the two events occurred by a common mechanism. Lymphocytes express the Ah receptor and have been shown to respond to the Ah receptor ligands by an increase in P450 c/d. Metabolic changes resulting from the combined induction of P450 c/d and P450 b/e can result in the metabolic activation of 4-chlorobiphenyl (34). Inhibition of P450 c/d metabolism of 2,5,2',5'-TCB results in greater formation of the 3,4-diol and the 4-OH form, indicating that more 3,4-oxide occurs following P450 c/d induction. The induction of P450 b/e enzymes results in detoxification of the 2,5,2',5'-TCB congener by direct *meta*-hydroxylation (32). The absence of the detoxification pathway (P450 b/e) and the presence of the activation pathway (c/d induction) may explain the greater sensitivity of the lymphocytes to 2,5,2',5'-TCB observed in the *in vivo* studies (35). The enhancement of the P450 b/e expression in preneoplastic foci resulting from treatment with both TCBs and with DEN + 2,5,2',5'-TCB as well as with DEN + PB may result in a selective reduced toxicity to 2,5,2',5'-TCB conferred to these cells by this gene expression.

Although centrilobular to midzonal staining for P450 b/e was observed by Buchman *et al.* (36) after DEN initiation and promotion with 3,4,5,3',4',5'-hexachlorobiphenyl (HCB) or with 2,4,5,2',4',5'-HCB, no increased staining for the P450 b/e isozyme occurred in AHF with this protocol. The 2,4,5,2',4',5'-HCB congener is an inducer of the P450 b/e isozyme; however, this congener is not known to be metabolized by this form or any other form of P450. Increased expression of a detoxification enzyme in cells of AHF has been observed as an increase of P450 b/e after promotion with PB as well as with hexachlorocyclohexane (36). Cells of AHF resulting from *N*-hydroxy ethylnitrosamine treatment exhibit reduced levels of P450 b/e and P450 c/d forms and an increase in glutathione S-transferase and expoxide hydrolase (23). Chronic treatment of rats with 2-acetylaminofluorene, which is metabolized by multiple forms of P450 (36), causes the proliferation of focal areas of preneoplastic hepatocytes; this may significantly lower the expression of many P450 genes as well as increase the conjugating enzymes that

detoxify the reactive intermediate (37). When PB administration followed AAF treatment, however, the level of P450 b/e was induced in AHF that had previously been negative for the enzyme (38). Thus, as a result of the alteration of drug-metabolizing enzymes, cells of AHF may have a selective advantage in a toxic environment. Since the growth of normal cells is suppressed by the cytotoxic effects of these treatments, the preneoplastic cells have an additional proliferative advantage.

The centrilobular to midzonal staining for P450 b/e that was evident in the livers of rats treated with DEN + PB or DEN + both TCBs indicates that enzyme induction occurred in response to these compounds in hepatocytes in these zones. Centrilobular staining with P450 c/d after treatment with DEN + 3,4,3′,4′-TCB or DEN + both TCBs indicates that induction of this isozyme also occurred. The dose of 3,4,3′,4′-TCB was 0.3% of the 6-day chronic dose used for maximal induction by Clevenger (14), and 0.003% of the acute dose used by Parkinson (6). The dose of 2,5,2′,5′-TCB utilized in our studies was 33% of the maximal chronic dose and 3% of the maximal acute dose used in other studies (13,23,24).

The greater than additive effect of the mixture of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB reported in this study may be the result of one or more of three possible mechanisms: (i) Ah receptor gene expression (1,4,5); (ii) the PB-type of cytochrome P450 response (24,39); (iii) the metabolic activation of PCBs to epoxides (29,30). Glutathione conjugation is the major phase II detoxification pathway for the 3,4-oxide of 2,5,2′-TCB. Several different mechanisms can contribute to the toxic effects of 2,5,2′,5′-TCB. Although the mechanism of glutathione depletion may be different in hepatocytes and lymphocytes, continuous exposure to the TCB combination may have resulted in depletion of the glutathione levels in both cell types. Depletion of glutathione would prevent a major part of the detoxification of the 3,4-oxide of 2,5,2′,5′-TCB (32).

Our results demonstrate an interaction of low doses of two PCBs *in vivo* in the two major target organs of PCB toxicity, the liver and the immune system, at doses that are relevant to human exposure levels (40). The observation of immune depression and promotion of AHF with very low PCB concentrations suggests that the biological effects of a complex Aroclor mixture in two different target cell populations of PCB toxicity may not be owing simply to the summed effects of each of the constituent chemicals or to the individual concentrations of the most toxic congeners, but rather largely to the effects of only a few constituents interacting at low concentrations.

This study also represents the first report of the appearance of an abnormal population of CD-4 lymphocytes in the peripheral blood after PCB exposure. This may be an important finding not only for rodent exposure, but also for human exposure, because this same PCB combination was very genotoxic to cultured human lymphocytes. The abnormal population of CD-4 cells in the peripheral blood may be the result of a genetic change that occurred in these cells. The aneuploidy of many hepatocytes (L.M.Sargent, G.Sattler, C.A.Sattler, B.Roloff, Y.Xu and H.C.Pitot, in preparation) and numerous large neoplastic nodules exhibiting cellular atypia in the liver are indications that the combination of 3,4,3′,4′-TCB and 2,5,2′,5′-TCB induces the stage of progression of hepatocarcinogenesis (41,42). Confirmation of this hypothesis will require further testing because the percentage of animals with hepatocellular carcinoma was not elevated after 1 year of treatment in this experiment. The numerous large neoplastic nodules with cellular atypia probably represent rapidly growing populations of abnormal cells. If this protocol had been allowed to continue further, it is possible that there would have been an increase in the frequency of hepatocellular carcinoma in the livers of rats receiving the combination compared with those administered each TCB alone.

Acknowledgements

We would like to thank Dr Colin Jefcoate for supplying the P450 antibodies. We would like to extend our gratitude to Dr James A.Miller for the gift of 2,5,2′,5′-TCB. We also thank Dr David Auerbach and the State Laboratory of Hygiene for their help in performing the flow cytometry. The expert histotechnology of Ms Jane Weeks and Mrs Jennifer Potter is also gratefully acknowledged, as well as the expert technical typing of Mrs Mary Jo Markham. The authors are grateful to Dr Ilse Riegel for technical editing and comments on the manuscript. The experiments described in this document were funded in part by grants from the National Cancer Institute (CA-07175, CA-2284 and CA-45700) and by a training grant from the National Institute of Environmental Health Sciences (ES-07015).

References

1. Safe,S. (1989) Polychlorinated biphenyls (PCBs): mutagenicity and carcinogenicity. *Mutat. Res.*, **220**, 31–47.
2. Passivirta,J. and Linko,R. (1980) Environmental toxins in Finnish wildlife. A study of trends of residue contents in fish during 1973–1978. *Chemosphere*, **9**, 643.
3. Jacobs,L.W., Chou,S.F. and Tiedje,J.M. (1978) Field concentrations and persistence of polybrominated biphenyls in soils and solubility of polybrominated biphenyls in natural waters. *Environ. Health Perspect.*, **23**, 1.
4. Safe,S., Bandiera,S., Sawyer,T., Robertson,L.W., Safe,L., Parkinson,A., Thomas,P.E., Ryan,D.E., Reik,L.M., Levin,W., Denomme,M.A. and Fujita,T. (1985) PCBs: structure–function relationships and mechanisms of action. *Environ. Health Perspect.*, **60**, 47–56.
5. Poland,A. and Knutson,J.C. (1982) 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin and related halogenated aromatic hydrocarbons: examination of the mechanism of toxicity. *Annu. Rev. Pharmacol. Toxicol.*, **22**, 517–554.
6. Parkinson,A., Robertson,L., Safe,L. and Safe,S. (1981) Polychlorinated biphenyls as inducers of hepatic microsomal enzymes: structure–activity rules. *Chem.-Biol. Interactions*, **35**, 1–2.
7. McKinney,J.D. and Singh,P. (1981) Structure–activity relationships in halogenated biphenyls: unifying hypothesis for structural specificity. *Chem.-Biol. Interactions*, **333**, 271–283.
8. Yoshimura,H., Yoshihara,S., Ozawa,N. and Miki,M. (1979) Possible correlation between induction modes of hepatic enzymes by PCBs and their toxicity in rats. *Ann. NY Acad. Sci.*, **320**, 179–192.
9. Silkworth,J.B. and Grabstein,E.M. (1982) Polychlorinated biphenyl immunotoxicity: dependence on isomer planarity and the *Ah* gene complex. *Toxicol. Appl. Pharmacol.*, **65**, 109–119.
10. Greenlee,W.F. and Irons,R.E. (1981) Modulation of benzene-induced lymphocytopenia in the rat by 2,4,5,2′,4′,5′-hexachlorobiphenyl and 3,4,4′,5′-tetrachlorobiphenyl. *Chem.-Biol. Interactions*, **33**, 345–360.
11. Wölfle,D., Münzel,P., Fischer,G. and Bock,K.-W. (1988) Altered growth control of rat hepatocytes after treatment with 3,4,3′,4′-tetrachlorobiphenyl *in vivo* and *in vitro*. *Carcinogenesis*, **9**, 919–924.
12. Osterele,D. and Deml,E. (1981) Promotion effect of various PCBs and DDT on enzyme altered islands in rat liver. *Nauyn-Schmiedberg's Arch. Pharmacol. Suppl. R*, **16**, 316.
13. Preston,B.D., Miller,E.C. and Miller,J.A. (1985) The activities of 2,2′,5,5′-tetrachlorobiphenyl, its 3,4-oxide metabolite and 2,2′,5,5′-tetrachlorobiphenyl in tumor induction and promotion assays. *Carcinogenesis*, **6**, 451–453.
14. Clevenger,M.A., Roberts,S.M., Sattin,D.L., Harbison,R.D. and James,R.C. (1989) The pharmacokinetics of 2,2′,5,5′-tetrachlorobiphenyl and 3,3′,4,4′-tetrachlorobiphenyl and its relationship to toxicity. *Toxicol. Appl. Pharmacol.*, **100**, 315–327.
15. Pitot,H.C., Campbell,H.A., Maronpot,R., Nimrat,B., Rizvi,T.A., Xu,Y.-H., Sargent,L.M., Dragan,Y. and Pyron,M. (1989) Critical parameters in the quantitation of the stages of initiation, promotion, and progression in one model of hepatocarcinogenesis in the rat. *Toxicol. Pathol.*, **17**, 594–612.
16. Pitot,H.C., Barsness,L., Goldsworthy,T. and Kitagawa,T. (1978) Biochemical characterization of stages of hepatocarcinogenesis after a single dose of diethylnitrosamine. *Nature*, **271**, 456–458.
17. Yam,L.T., Li,C. and CrosbyW.H. (1971) Cytochemical identification of monocytes and granulocytes. *Am. J. Clin. Pathol.*, **55**, 283–290.
18. Braylan,R.C. (1983) Attributes and applications of flow cytometry. *Ann. Clin. Lab. Sci.*, **13**, 379–384.

19. Xu,Y.-H., Campbell,H.A., Sattler,G.L., Hendrich,S., Maronpot,R., Sato,K. and Pitot,H.C. (1990) Quantitative stereological analysis of the effects of age and sex on multistage hepatocarcinogenesis in the rat by use of four cytochemical markers. *Cancer Res.*, **50**, 472–479.
20. Campbell,H.A., Xu,Y.-H., Hanigan,M.H. and Pitot,H.C. (1986) Application of quantitative stereology to the evaluation of phenotypically heterogeneous enzyme-altered foci in the rat liver. *J. Natl. Cancer Inst.*, **76**, 751–767.
21. Steel,R.G.D. and Torrie,J.H. (1980) Enumeration data II: contingency tables, some uses of χ-square. In *Principles and Procedures of Statistics, a Biometrical Approach.* McGraw-Hill Book Company, New York, pp. 469–520.
22. Pitot,H.C., Goldsworthy,T.L., Moran,S., Kennan,W., Glauert,H.P., Maronpot,R.R. and Campbell,H.A. (1987) A method to quantitate the relative initiating and promoting potencies of hepatocarcinogenic agents in their dose–response relationships to altered hepatic foci. *Carcinogenesis*, **8**, 1491–1499.
23. Safe,S. (1983) Polychlorinated biphenyls (PCBs) and polybrominated biphenyls: biochemistry, toxicology and mechanisms. *CRC Rev. Toxicol.*, **13**, 319–325.
24. Silberhorn,E.M., Glauert,H.P. and Robertson,L.W. (1990) Carcinogenicity of polyhalogenated biphenyls: PCBs and PBBs. *Crit. Rev. Toxicol.*, **20**, 439–496.
25. Eriksson,L., Ahluwalia,M., Spiewak,J., Lee,G., Sarma,D.S.R., Roomi,M.J. and Farber,E. (1983) Distinctive biochemical pattern associated with resistance to hepatocytes in hepatocyte nodules during liver carcinogenesis. *Environ. Health Perspect.*, **49**, 171–174.
26. Dragan,Y.P., Xu,Y.-H., Hully,J.R., Bawa,N., Rizvi,T., Campbell,H.A., Maronpot,R.R. and Pitot,H.C. (19??) An initiation-promotion assay in rat liver as a potential complement to the two-year carcinogenesis bioassay. *Fund. Appl. Toxicol.*, in press.
27. Schulte-Hermann,R., Roome,N., Timmermann-Trosiener,I. and Schuppler,J. (1984) Immunocytochemical demonstration of a phenobarbital-induced cytochrome P450 in putative preneoplastic foci of rat liver. *Carcinogenesis*, **5**, 149–153.
28. Schwarz,M., Peres,G., Buchmann,A., Friedberg,T., Waxman,D.J. and Kunz,W. (1987) Phenobarbital induction of cytochrome P450 in normal and preneoplastic rat liver: comparison of enzyme and mRNA expression as detected by immunohistochemistry and *in situ* hybridization. *Carcinogenesis*, **8**, 1355–1357.
29. Forgue,S.T., Preston,B.D., Hargraves,W.A., Reich,I.L. and Allen,J.R. (1979) Direct evidence that an aerene oxide is a metabolic intermediate of 2,5,2′,5′-tetrachlorobiphenyl. *Biochem. Biophys. Res. Commun.*, **91**, 475–483.
30. Forgue,S.T. and Allen,J.R. (1982) Identification of an aerene oxide metabolite of 2,5,2′,5′-tetrachlorobiphenyl by gas chromatography–mass spectroscopy. *Chem.-Biol. Interactions*, **40**, 233–245.
31. Stadnicki,S.S., Francis,S.D.L. and Allen,J.R. (1979) DNA strand breaks caused by 2,5,2′,5′-tetrachlorobiphenyl and its metabolites. *Res. Commun. Chem. Pathol. Pharmacol.*, **24**, 313–325.
32. Preston,B.D., Miller,J.A. and Miller,E.C. (1984) Reactions of 2,2′,5,5′-tetrachlorobiphenyl 3,4-oxide with methionine, cysteine and glutathione in relation to the formation of methylthio-metabolites of 2,2′,5,5′-tetrachlorobiphenyl in the rat and mouse. *Chem.-Biol. Interactions*, **50**, 289–312.
33. Sargent,L.M., Roloff,B.D. and Meisner,L.F. (1989) *In vitro* chromosome damage due to PCB interactions. *Mutat. Res.*, **224**, 79–88.
34. Wyndhman,C., Devenish,J. and Safe.S. (1978) The *in vitro* metabolism, macromolecular binding and bacterial mutagenicity of 4-chlorobiphenyl, a model PCB substrate. *Res. Commun. Chem. Pathol. Pharmacol.*, **15**, 563–570.
35. Kawabata,T.T. and White,K.L., Jr (1989) Benzo[*a*]pyrene metabolism by murine spleen microsomes. *Cancer Res.*, **49**, 5816–5822.
36. Buchmann,A., Kunz,W., Wolf,C.R., Oesch,F. and Robertson,L.W. (1986) Polychlorinated biphenyls, classified as either phenobarbital- or 3-methylcholanthrene-type inducers of cytochrome P450, are both hepatic tumor promoters in diethylnitrosamine-initiated rats. *Cancer Lett.*, **32**, 243–253.
37. Roomi,M.W., Ho,R.K., Sarma,D.S.R. and Farber,E. (1985) A common biochemical pattern in preneoplastic hepatocyte nodules generated in four different models in the rat. *Cancer Res.*, **45**, 564–571.
38. Ghoshal,A., Gurtoo,H.L., Faletto,M.B., Koo,P., Nagi,M. and Farber,E. (1990) Molecular basis for the constitutive decrease in cytochromes P450 in putative preneoplastic hepatocytes. *Proc. Am. Assoc. Cancer Res.*, **31**, 136.
39. Goldstein,J.A., Hickman,P., Bergman,H., McKinney,J.D. and Walker, M.P.(1977) Separation of pure polychlorinated biphenyl isomers into two types of inducers on the basis of induction of P450 or P448. *Chem.-Biol. Interactions*, **17**, 69–87.
40. Cordle,F., Corneliussen,P., Jelinek,C., Hackley,B., Lehman,R., McLaughlin,J., Rhoden,R. and Shapiro,R. (1978) Human exposure to polychlorinated biphenyls and polybrominated biphenyls. *Environ. Health Perspect.*, **24**, 157–172.
41. Sherer,E., Feringa,A.W. and Emmelot,P.(1984) Initiation–promotion–initiation induction of neoplastic foci within islands of precancerous liver cells in the rat. In Börzxönyi,M., Lapi,K., Day,N. and Yamasaki,H. (eds), *Models, Mechanisms and Etiology of Tumour Promotion.* IARC Scient. Pub. 56, Lyon, pp. 57–66.
42. Pitot,H.C. (1989) Progression: the terminal stages in carcinogenesis. *Jpn. J. Cancer Res.*, **80**, 599–607.
43. Schauer,A. and Kunze,E. (1976) Tumours of the liver. In Turusov,V.S. (ed.), *Pathology of Tumours in Laboratory Animals. Vol. 1. Tumours of the Rat, Part 2.* IARC, Lyon, pp. 41–72.
44. Squire,R.A. and Levitt,M.H. (1975) Report of a workshop on classification of specific hepatocellular lesions in rats. *Cancer Res.*, **35**, 3214–3223.
45. National Research Council (1980) Histologic typing of liver tumors in the rat. *J. Natl. Cancer Inst.*, **64**, 179–206.

Received on August 20, 1990; revised on January 17, 1991; accepted on January 25, 1991

Attachment 6

CANCER MORTALITY IN WORKERS EXPOSED TO 2,3,7,8-TETRACHLORODIBENZO-*p*-DIOXIN

MARILYN A. FINGERHUT, PH.D., WILLIAM E. HALPERIN, M.D., DAVID A. MARLOW, B.S., LAURIE A. PIACITELLI, M.S., PATRICIA A. HONCHAR, PH.D., MARIE H. SWEENEY, PH.D., ALICE L. GREIFE, PH.D., PATRICIA A. DILL, A.B., KYLE STEENLAND, PH.D., AND ANTHONY J. SURUDA, M.D.

Abstract *Background.* In both animal and epidemiologic studies, exposure to dioxin (2,3,7,8-tetrachlorodibenzo-*p*-dioxin, or TCDD) has been associated with an increased risk of cancer.

Methods. We conducted a retrospective cohort study of mortality among the 5172 workers at 12 plants in the United States that produced chemicals contaminated with TCDD. Occupational exposure was documented by reviewing job descriptions and by measuring TCDD in serum from a sample of 253 workers. Causes of death were taken from death certificates.

Results. Mortality from several cancers previously associated with TCDD (stomach, liver, and nasal cancers, Hodgkin's disease, and non-Hodgkin's lymphoma) was not significantly elevated in this cohort. Mortality from soft-tissue sarcoma was increased, but not significantly (4 deaths; standardized mortality ratio [SMR], 338; 95 percent confidence interval, 92 to 865). In the subcohort of 1520 workers with ≥1 year of exposure and ≥20 years of latency, however, mortality was significantly increased for soft-tissue sarcoma (3 deaths; SMR, 922; 95 percent confidence interval, 190 to 2695) and for cancers of the respiratory system (SMR, 142; 95 percent confidence interval, 103 to 192). Mortality from all cancers combined was slightly but significantly elevated in the overall cohort (SMR, 115; 95 percent confidence interval, 102 to 130) and was higher in the subcohort with ≥1 year of exposure and ≥20 years of latency (SMR, 146; 95 percent confidence interval, 121 to 176).

Conclusions. This study of mortality among workers with occupational exposure to TCDD does not confirm the high relative risks reported for many cancers in previous studies. Conclusions about an increase in the risk of soft-tissue sarcoma are limited by small numbers and misclassification on death certificates. Excess mortality from all cancers combined, cancers of the respiratory tract, and soft-tissue sarcoma may result from exposure to TCDD, although we cannot exclude the possible contribution of factors such as smoking and occupational exposure to other chemicals. (N Engl J Med 1991; 324:212-8.)

SEVERAL epidemiologic and toxicologic studies have suggested an association between 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), or the chemicals it contaminates, and soft-tissue sarcoma,[1-4] Hodgkin's disease,[5] non-Hodgkin's lymphoma,[6-8] stomach cancer,[9,10] nasal cancer,[11] and cancer of the liver.[12,13] In other studies of these cancers, no significant associations with TCDD exposure were found.[14-19] The carcinogenicity of TCDD has been demonstrated in studies of rats, mice, and hamsters; histiocytic lymphomas, fibrosarcomas, and tumors of liver, skin, lung, thyroid, tongue, hard palate, and nasal turbinates have been found.[12,13,20] TCDD acts as a promoter[21,22] and may also initiate carcinogenesis.[12,13,20] To evaluate the effect of occupational exposure to TCDD, particularly with respect to the cancers listed above, we conducted a retrospective cohort study of mortality among U.S. chemical workers assigned to the production of substances contaminated with TCDD.

METHODS

Identification of Companies

In 1978 the National Institute for Occupational Safety and Health began an effort that would eventually identify the exposed workers at all U.S. chemical companies that had made TCDD-contaminated products between 1942 and 1984. TCDD was generated as a contaminant in the production of 2,4,5-trichlorophenol and was carried into subsequent production processes.[23] One derivative, 2,4,5-trichlorophenoxyacetic acid, was widely used in the United States to kill brush and was a constituent of defoliants such as Agent Orange. Other derivatives included the herbicides 2-(2,4,5-trichlorophenoxy)propionic acid (Silvex) and 2-(2,4,5-trichlorophenoxy)-ethyl 2,2-dichloropropionate (Erbon), the insecticide *O,O*-dimethyl *O*-(2,4,5-trichlorophenyl)phosphorothioate (Ronnel), and the bactericide 2,2′-methylene-bis[3,4,6-trichlorophenol] (hexachlorophene).

Identification of Exposed Workers

Workers from 12 companies were included in the study cohort if a personnel or payroll record documented that they had been assigned to a production or maintenance job in a process involving TCDD contamination (n = 5000), or if they had been identified in a previously published study on the basis of exposure to TCDD (n = 172).[24] Personnel records for 202 workers did not reveal the duration of their assignment to processes involving TCDD contamination; they were therefore included in the analysis of overall mortality but excluded from analyses according to duration of exposure. Sixty-seven women are not included in this report; there were 10 deaths among them, including a single death from cancer (lung cancer).

At each plant, we made a thorough review of operating conditions, job duties, and records of TCDD levels in industrial-hygiene samples, intermediate reactants, products, and wastes. This review provided clear evidence of potential daily exposure to TCDD. The production of TCDD-contaminated substances at the various plants involved similar raw materials, processes, and job duties.[25] However, there were differences between jobs and between plants in the extent of TCDD exposures. Occupational exposure to substances contaminated with TCDD was confirmed by measuring serum TCDD levels, as adjusted for lipids, in 253 surviving members of the study cohort from two plants who were also participants in a related cross-sectional medical study.[26]

Life-Table Analysis

Vital status was determined as of December 31, 1987, from records of the Social Security Administration or Internal Revenue Service, or from the National Death Index. All death certificates

From the Industrywide Studies Branch, Division of Surveillance, Hazard Evaluations, and Field Studies, National Institute for Occupational Safety and Health, Centers for Disease Control, 4676 Columbia Pky., Cincinnati, OH 45226, where reprint requests should be addressed to Dr. Fingerhut.

Supported in part by the Agency for Toxic Substances and Disease Registry.

were independently classified by two nosologists according to the rules of the revision of the *International Classification of Diseases* (ICD) in effect at the date of death.[27]

Life-table analysis was used to evaluate mortality in the cohort.[28] At each plant, the number of person-years at risk was calculated as the interval between the first systematically documented assignment to a process involving TCDD contamination and the date of death or December 31, 1987, whichever occurred first. Those whose vital status was unknown were assumed to be alive at the end of the study. Standardized mortality ratios (SMRs) were computed by dividing the observed number of deaths by the expected number and multiplying by 100, after stratification to adjust for the confounding effects of age, race, and year of death. Two-sided 95 percent confidence intervals were computed for each cause-specific SMR, with use of the Byar approximation for eight deaths or more and Fisher's exact method for fewer than eight deaths.[29] The U.S. population was used as the reference group, because the 12 plants were located in 11 states throughout the country.

Analyses According to Duration of Exposure and Employment

Duration of exposure was defined as the number of years the worker was employed in processes involving TCDD contamination and was calculated with data from personnel records. We used duration of exposure as a surrogate for cumulative exposure to TCDD on the basis of the high correlation of the logarithm of serum TCDD levels with the logarithm of the number of years assigned to processes involving TCDD contamination in our sample of 253 workers (Pearson's product-moment coefficient r = 0.72) (Fig. 1), and on the assumption that the production processes were similar in the 12 plants.[25]

Because of the concentration of person-years in the short-duration categories, duration of exposure was stratified before analysis into categories of <1, 1 to <5, 5 to <15, and ≥15 years (Table 1). Mortality was also examined according to time since first exposure (latency) in periods of 0 to <10, 10 to <20, and ≥20 years since first exposure. To examine mortality in a subgroup with substantial exposure and adequate time for cancer to develop, we identified a group of workers who had 1 year or more of exposure to processes involving TCDD contamination and at least 20 years of latency. One year was chosen as a cutoff point for this high-exposure subcohort because in the sample of workers whose serum TCDD levels were measured, 100 percent of those exposed for more than one year had serum TCDD levels higher than the mean level in the unexposed reference group (7 pg per gram of lipid). For this subcohort, the number of person-years at risk was calculated from the date the person attained both 20 years of latency and 1 year of exposure.

Most of the 12 plants were large U.S. chemical manufacturing sites that produced thousands of chemicals. Complete documentation of each worker's exposures was impossible. A separate measure called "duration of employment," defined as the total time that each worker was employed at a study plant, was therefore used. Because of the long total employment at the plants, analyses according to duration of employment were stratified into periods of <5, 5 to <10, 10 to <15, 15 to <20, 20 to <25, 25 to <30, and ≥30 years (Table 1). For these analyses, latency was defined as time since first employment.

When the SMRs showed an apparent trend associated with duration of exposure or employment and when the observed numbers of deaths were sufficiently large, we conducted internal comparisons using directly standardized rate ratios and tests for trend.[30] For the standardized rate ratios, the cause-specific mortality rate in each of the categories of longer duration was compared with the rate in the category of shortest duration, after stratification of the rates for the potential confounding effects of age, race, and calendar time.

Results

The cohort of 5172 male workers from 12 plants had 116,748 person-years of observation. Table 1 describes the vital status, race, latency, and duration of exposure and employment of the workers. Overall mortality for all causes of death was similar to national rates in the United States (1052 deaths; SMR, 99; 95 percent confidence interval, 93 to 105). Mortality from heart disease was also similar to national rates

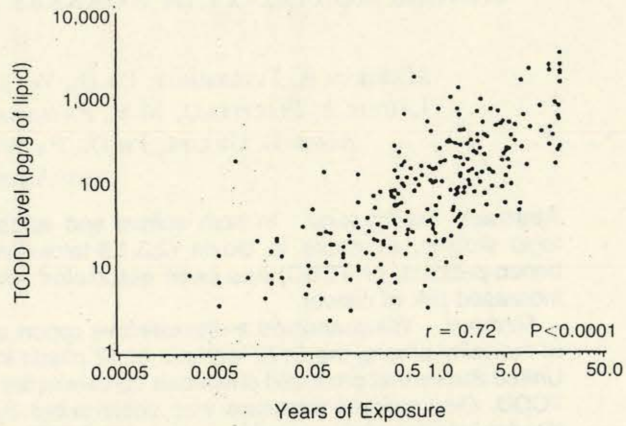


Figure 1. Serum Levels of TCDD, as Adjusted for Lipids, in 253 Workers, According to Years of Exposure.

Table 1. Vital Status and Demographic and Employment Characteristics of the Study Cohort.

Variable	Number (Percent)
Vital status*	
Alive	4043 (78)
Dead	1052 (20)
Unknown	77 (2)
Total	5172 (100)
Deaths*	
White men	985 (94)
Nonwhite men	67 (6)
Total	1052 (100)
Death certificates obtained	1037 (99)
Race	
White	4590 (89)
Nonwhite	385 (7)
Unknown	197 (4)
Total	5172 (100)
Duration of exposure (yr)†	
<1	2697 (54)
1 to <5	1427 (29)
5 to <15	639 (13)
≥15	207 (4)
Total	4970 (100)
Duration of employment (yr)†	
<5	2125 (43)
5 to <10	501 (10)
10 to <15	605 (12)
15 to <20	403 (8)
20 to <25	391 (8)
25 to <30	415 (8)
≥30	530 (11)
Total	4970 (100)
Years since first exposure (latency)†	
<10	271 (5)
10 to <20	1663 (33)
≥20	3036 (61)
Total	4970 (100)
Years since last exposure†	
<10	453 (9)
10 to <20	1789 (36)
≥20	2728 (55)
Total	4970 (100)

*As of December 31, 1987.

†Excludes 202 workers for whom duration of assignment to processes involving TCDD contamination was not available from work records.

(393 deaths; SMR, 96; 95 percent confidence interval, 87 to 106). There were significant reductions in the mortality rates for diseases of the circulatory system (67 deaths; SMR, 77; 95 percent confidence interval, 60 to 98), primarily because of fewer deaths from stroke, and for diseases of the digestive system (38 deaths; SMR, 70; 95 percent confidence interval, 49 to 96), primarily because of fewer deaths from cirrhosis. There were also significantly fewer deaths from alcoholism and personality disorders (2 deaths; SMR, 23; 95 percent confidence interval, 3 to 87). The low mortality from circulatory disease may be a reflection of the "healthy worker" effect — cohorts of workers die at lower rates than the general population, particularly of causes other than cancer.[31] The reduced number of deaths from cirrhosis and alcoholism implies that this cohort consumed less alcohol than the general population. Reduction may also have occurred simply by chance, since numerous comparisons were made between the cohort and the U.S. population. Fatal injuries were significantly more frequent in the cohort (106 deaths; SMR, 128; 95 percent confidence interval, 104 to 154), but they did not appear to be associated particularly with exposure to TCDD. Mortality from all cancers combined (265 deaths; SMR, 115; 95 percent confidence interval, 102 to 130) was significantly elevated in the cohort.

Cancers of a Priori Interest

The term "soft-tissue sarcoma" describes the group of rare malignant neoplasms arising from supporting tissue other than bone.[32] We restricted our analysis of mortality due to soft-tissue sarcoma to cases of soft-tissue sarcoma listed as the underlying cause of death

Table 2. Cancer Mortality in the Entire Cohort and in Workers with More Than 20 Years of Latency.

Site of Cancer	ICD Code*	Entire Cohort (N = 5172)†			Subcohort with ≥20 Yr of Latency (N = 3036)‡					
					<1 yr of exposure (N = 1516)§			≥1 yr of exposure (N = 1520)¶		
		deaths observed	deaths expected	SMR‖	deaths observed	deaths expected	SMR‖	deaths observed	deaths expected	SMR‖
All cancers	140–208	265	229.9	115 (102–130)**	48	46.8	102 (76–136)	114	78.0	146 (121–176)**
Buccal and pharynx	140–149	5	7.0	70 (23–166)	2	1.4	145 (18–524)	2	2.2	90 (11–325)
Pharynx	146–149	3	3.4	88 (18–259)	2	0.7	298 (36–1080)	0	1.2	0 (—)
Other parts	142–145	2	1.9	105 (13–379)	0	0.4	0 (—)	2	0.6	329 (40–1190)
Digestive organs	150–159	67	59.7	112 (87–143)	13	11.8	111 (59–189)	28	20.1	140 (93–202)
Esophagus	150	9	5.9	152 (70–290)	2	1.2	165 (20–602)	4	2.0	200 (55–513)
Stomach	151	10	9.7	103 (50–190)	3	1.7	178 (37–521)	4	2.9	138 (38–353)
Small intestine and colon	152–153	25	20.4	122 (79–181)	5	4.3	117 (38–274)	13	7.3	178 (95–304)
Rectum	154	5	5.6	89 (29–209)	1	1.0	100 (3–557)	2	1.7	115 (14–415)
Liver and biliary	155, 156	6	5.2	116 (42–252)	1	1.0	100 (3–557)	1	1.7	59 (1–327)
Pancreas	157	10	11.9	84 (40–155)	1	2.4	41 (1–232)	4	4.0	100 (27–253)
Peritoneum and unspecified	158, 159	2	1.1	184 (22–666)	0	0.2	0 (—)	0	0.4	0 (—)
Respiratory system	160–165	96	84.5	113 (92–139)	19	18.4	103 (62–161)	43	30.2	142 (103–192)
Larynx	161	7	3.3	211 (84–434)	2	0.7	297 (36–1074)	3	1.1	268 (55–783)
Trachea, bronchus, and lung	162	89	80.1	111 (89–137)	17	17.5	96 (56–155)	40	28.8	139 (99–189)
Male genital organs	185–187	17	15.3	111 (65–177)	2	3.2	63 (8–229)	9	6.0	149 (68–283)
Prostate	185	17	13.9	122 (71–195)	2	3.0	67 (8–237)	9	5.9	152 (70–290)
Urinary organs	188–189	17	11.4	148 (86–238)	3	2.4	128 (26–373)	6	4.0	149 (55–324)
Kidney	189.0–189.2	8	5.7	140 (60–275)	3	1.2	253 (52–742)	2	1.9	106 (13–384)
Bladder and other	188, 189.3–189.9	9	5.7	157 (72–298)	0	1.2	0 (—)	4	2.2	186 (51–476)
Lymphatic and hematopoietic tissue	200–208	24	22.1	109 (70–162)	4	3.9	102 (28–260)	8	6.4	125 (54–247)
Hodgkin's disease	201	3	2.5	119 (25–349)	0	0.2	0 (—)	1	0.4	276 (7–1534)
Non-Hodgkin's lymphoma††	200, 202	10	7.3	137 (66–254)	2	1.5	135 (16–488)	2	2.1	93 (11–337)
Lymphosarcoma and reticulosarcoma††	200	5	3.5	142 (46–332)	0	0.6	0 (—)	1	0.9	107 (3–594)
Other lymphatic††	202	5	3.7	133 (43–313)	2	0.9	215 (26–779)	1	1.4	71 (2–385)
Multiple myeloma††	203	5	3.0	164 (53–385)	0	0.6	0 (—)	3	1.1	262 (54–766)
Leukemia and aleukemia	204–208	6	8.9	67 (24–146)	2	1.6	126 (15–457)	2	2.6	77 (9–277)
Other sites	170–173, 190–199	39	29.6	131 (94–180)	5	5.8	87 (28–202)	18	9.0	201 (118–316)**
Skin	172, 173	4	4.9	82 (22–211)	0	0.9	0 (—)	2	1.3	155 (19–559)
Brain and nervous system	191, 192	5	7.3	68 (22–160)	0	1.3	0 (—)	2	1.9	106 (13–384)
Bone	170	2	0.9	227 (27–819)	0	0.1	0 (—)	1	0.2	521 (13–2903)
Connective tissue and soft tissue	171	4	1.2	338 (92–865)	0	0.2	0 (—)	3	0.3	922 (190–2695)**
Other and unspecified	194–199	24	14.8	162 (104–241)**	5	3.1	159 (52–372)	10	5.1	196 (94–361)

*From the *International Classification of Diseases*, 9th revision.

†Mean number of years exposed, 2.7; mean number of years employed, 12.6.

‡Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records.

§Mean number of years exposed, 0.3; mean number of years employed, 10.7; 12,299 person-years at risk.

¶Mean number of years exposed, 6.8; mean number of years employed, 19.2; 15,136 person-years at risk.

‖SMR equals deaths observed divided by deaths expected and multiplied by 100. Slight differences are due to rounding. Values in parentheses are 95 percent confidence intervals.

**P<0.05.

††Person-years at risk and observed deaths are computed from 1960; no deaths occurred before that year.

on death certificates and assigned to the ICD category "malignant neoplasms of connective and other soft tissue." In the cohort, mortality from soft-tissue sarcoma was nonsignificantly higher than in the reference population (four deaths; SMR, 338; 95 percent confidence interval, 92 to 865) (Table 2). The deaths occurred at 2 of the 12 plants, with a significant increase at 1 plant (two deaths; SMR, 1512; 95 percent confidence interval, 183 to 5462). A review of tissue specimens from the four men whose deaths were attributed to soft-tissue sarcoma showed that only two were in fact soft-tissue sarcomas (Cases 1 and 4, Table 3).[33] Mortality from soft-tissue sarcomas was increased significantly in the subcohort of 1520 workers with 1 year or more of exposure and at least 20 years of latency (the high-exposure subcohort) (three deaths; SMR, 922; 95 percent confidence interval, 190 to 2695). Two other deaths in the cohort (Cases 5 and 6) were attributed to soft-tissue sarcoma according to hospital records, and one of them (Case 5) was confirmed by review of a tissue specimen. These two deaths did not contribute to mortality due to soft-tissue sarcoma in our life-table analysis, because the deaths were assigned other ICD codes. We are aware of a seventh death from soft-tissue sarcoma, which occurred in a group of 139 workers with chloracne who were excluded from the cohort because they did not meet the entry criteria.

In the cohort, the SMRs for the other cancers of a priori interest were nonsignificantly increased (Table 2). There were no deaths from nasal cancer, although approximately one was expected. In the high-exposure subcohort, the SMRs were nonsignificantly higher for Hodgkin's disease and stomach cancer and lower for non-Hodgkin's lymphoma and cancer of the liver, biliary passages, and gallbladder (Table 2).

A Posteriori Findings

A small but significant increase in mortality due to all cancers combined was observed in the entire cohort (SMR, 115; 95 percent confidence interval, 102 to 130). In the high-exposure subcohort the SMR was 146 (95 percent confidence interval, 121 to 176) (Table 2). At 9 of the 12 plants, mortality from all cancers combined was increased; at one of these plants the increase was statistically significant. Mortality was significantly higher than expected in the category of cancers of unspecified sites, which included those of rare sites not included in a category of the life-table analysis and those for which no primary site was listed on the death certificate. Hospital records, which were obtained for 96 percent of these cancers, revealed no particular clustering according to site.

The cohort had a nonsignificant increase in mortality from cancers of the trachea, bronchus, and lung (ICD code 162; SMR, 111; 95 percent confidence interval, 89 to 137). Mortality from cancers of the respiratory system (ICD codes 160 to 165) was significantly higher than expected in the high-exposure subcohort (SMR, 142; 95 percent confidence interval, 103 to 192) (Table 2). To estimate the effect of smoking on the increase in lung cancer, the expected number of lung cancers was adjusted according to the smoking prevalence found in lifetime histories obtained in 1987 by interviewing 223 workers from two plants.[25] This adjustment increased the expected number of lung cancers in the overall cohort by 5 percent and in the high-exposure subcohort by 1 percent, which reduced the SMR in the full cohort to 105 (95 percent confidence interval, 85 to 130) and in the high-exposure subcohort to 137 (95 percent confidence interval, 98 to 187).

Analyses According to Duration of Exposure and Employment

The study cohort worked a mean of 2.7 years in processes involving TCDD contamination and 12.6 years at the plants. The high-exposure subcohort worked a mean of 6.8 years in processes involving TCDD contamination and a mean of 19.2 years in total employment at the plants.

The numbers of deaths due to the rare cancers of

Table 3. Deaths from Soft-Tissue Sarcoma among Workers in the Cohort.*

Case No.	Years Employed	Type of Exposure	Year First Exposed	Years Exposed	Year of Death	Latency (yr)†	Cause of Death: Death Certificate	Cause of Death: Hospital Records	Cause of Death: Tissue Review‡
1	1946–1978	TCP and 2,4,5-T	1950	8.8	1978	28	MFH	MFH	MFH
2	1946–1972	TCP and 2,4,5-T	1948	7.1	1972	24	Liposarcoma	Liposarcoma	Carcinoma, poorly differentiated§
3	1950–1975	TCP	1963	1.2	1975	12	Fibrosarcoma	Fibrosarcoma	Renal carcinoma§
4	1951–1982	TCP	1951	14.9	1983	32	MFH	MFH	MFH
5¶	1943–1975	TCP or 2,4,5-T	Intermittent	Unknown	1980	Unknown	Carcinomatosis§	Myxoid neurogennic sarcoma	Leiomyosarcoma
6¶	1941–1964	TCP	1949	Unknown	1965	16	Metastatic osteosarcoma§	Fibrosarcoma	Not available

*Cases 1 through 5 have been previously described.[33] For other previously described cases, records of exposure to TCDD were not available, and the cases were not included in this cohort study. Some information differs slightly from that reported earlier, since additional records were reviewed. Few details about exposure were available for Cases 5 and 6. TCP denotes 2,4,5-trichlorophenol; 2,4,5-T, 2,4,5-trichlorophenoxyacetic acid; and MFH, malignant fibrous histiocytoma.

†Time from first exposure to death.

‡Conducted at the Armed Forces Institute of Pathology.

§Not a soft-tissue sarcoma.

¶Death was not attributed to soft-tissue sarcoma in the life-table analysis.

Table 4. Mortality from All Cancers and from Cancers of the Trachea, Bronchus, and Lung, According to Latency Period and Duration of Exposure to Processes Involving TCDD Contamination.*

CAUSE/LATENCY PERIOD	DURATION OF EXPOSURE (YR)										TEST FOR TREND
	<1		1 TO <5		5 TO <15		≥15		OVERALL		
	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	
All cancers											
<10 Yr	10	68	8	71	3	71	0	0	21	70	
10 to <20 Yr	28	109	16	87	18	122	7	340†	69	113	
≥20 Yr	48	102	59	165‡	37	138	18	115	162	129‡	
Total	86	98	83	127†	58	126	25	141	252	116†	
SRR		100		127		123		129			0.3
Trachea, bronchus, and lung											
<10 Yr	3	77	3	95	1	79	0	0	7	84	
10 to <20 Yr	6	69	5	79	9	180	1	137	21	101	
≥20 Yr	17	96	17	126	14	146	9	156	57	123	
Total	26	86	25	109	24	151	10	154	85	112	
SRR		100		109		166		136			0.2

*Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records. The number of observed deaths and the SMRs therefore differ slightly from those in Table 2. SRR denotes standardized rate ratio.

†P<0.05. ‡P<0.01.

a priori interest were too small to permit meaningful analyses according to duration. For all cancers combined and for cancers of the trachea, bronchus, and lung, Table 4 shows the distribution of mortality with increasing duration of exposure to products contaminated with TCDD. The standardized rate ratios were increased in the strata of longer duration for both these categories, but significant linear trends were not found. Mortality increased with increasing latency for both these categories of cancer. Table 5 shows the distribution of mortality for the same categories with increasing duration of employment. Significant linear trends were not observed for either category with increasing length of employment, although standardized rate ratios were higher than expected in several strata of employment ≥20 years. Mortality increased with increasing latency for both categories of cancer.

Serum Levels of TCDD

The mean serum TCDD level, as adjusted for lipids, in the sample of 253 workers from two plants was 233 pg per gram of lipid (range, 2 to 3400) (Fig. 1). A mean level of 7 pg per gram was found in the comparison group of 79 unexposed persons, all of whose levels were under 20, a range found in other unexposed populations.[34] The mean for 119 workers with one year or more of exposure was 418 pg per gram. All the workers had received their last occupational exposures 15 to 37 years earlier.

Discussion

TCDD, widely known as dioxin, has acquired the reputation of a potent carcinogen. Our study, although limited in its ability to detect increased numbers of rare cancers, found little increase in mortality from the cancers associated with TCDD in previous studies in humans. The exception was an increase in soft-tissue sarcoma. The difficulties of evaluating soft-tissue sarcomas in a cohort study of mortality have been described.[33] These include variability in pathological diagnosis and misclassification on death certificates. Consequently, the interpretation of the increased mortality from soft-tissue sarcoma in our study is limited by the small number of cases and the fact that the cause of death was sometimes misclassified on the death certificates of the workers (Table 3) and in the U.S. comparison population.[35]

Several case–control studies have found significant fourfold increases in non-Hodgkin's lymphoma in persons reporting exposure to phenoxy herbicides or chlorophenols, some of which contained TCDD.[6,8] The magnitude of the increase in mortality in the cohort described here (SMR, 137; 95 percent confidence interval, 66 to 254) suggests a smaller increase in this risk, or no increase at all. Mortality was not significantly higher than expected for other cancers of a priori interest — liver and stomach cancers and Hodgkin's disease. No deaths from nasal cancer were observed. The inconsistency between the results reported here and those of earlier epidemiologic studies is accentuated by the longer and probably greater exposure of this cohort to phenoxy herbicides and chlorophenols contaminated with TCDD.

Mortality from cancers of the trachea, bronchus, and lung was nonsignificantly higher in the cohort. Among the workers with 20 years or more of latency, mortality from respiratory cancer was significantly increased in the high-exposure subcohort, which had 1 year or more of exposure (SMR, 142; 95 percent confidence interval, 103 to 192) but not in the subcohort with less than 1 year of exposure (SMR, 103; 95 percent confidence interval, 62 to 161) (Table 2). SMRs for lung cancer are known to be somewhat higher in blue-collar groups than in the general U.S. population because of more cigarette smoking in the blue-collar groups.[36] However, the increased number of lung cancers in the high-exposure subcohort was probably not due to confounding by smoking, for several reasons. First, other diseases related to smoking were not more common than expected in this subco-

Table 5. Mortality from All Cancers and from Cancers of the Trachea, Bronchus, and Lung, According to Latency Period and Duration of Employment at the Study Plants.*

Cause/Latency Period	Duration of Employment (yr)																Test for Trend
	<5		5 to <10		10 to <15		15 to <20		20 to <25		25 to <30		≥30		Overall		
	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	deaths observed	SMR	
All cancers																	
<10 Yr	10	85	1	18	0	0	0	0	0	0	0	0	0	0	11	64	
10 to <20 Yr	21	114	5	126	12	103	8	80	0	0	0	0	0	0	46	105	
≥20 Yr	40	138	15	140	6	70	15	98	34	134	31	116	54	135†	195	125‡	
Total	71	120	21	104	18	89	23	91	34	134	31	116	54	135†	252	116	
SRR		100		99		61		76		128		84		115			0.9
Trachea, bronchus, and lung																	
<10 Yr	3	103	1	74	0	0	0	0	0	0	0	0	0	0	4	94	
10 to <20 Yr	5	82	0	0	5	139	4	122	0	0	0	0	0	0	14	98	
≥20 Yr	11	102	2	51	2	65	3	55	12	133	18	180†	19	126	67	117	
Total	19	96	3	46	7	105	7	81	12	133	18	180†	19	126	85	112	
SRR		100		65		91		89		171		147		98			0.6

*Excludes 202 workers for whom the duration of assignment to processes involving TCDD contamination was not available from work records. SRR denotes standardized rate ratio.

†P<0.05. ‡P<0.01.

hort; mortality from nonmalignant respiratory disease (ICD codes 470 to 478 and 490 to 519), which is often associated with smoking, was lower than expected (15 deaths; SMR, 96; 95 percent confidence interval, 54 to 158). Second, in the exposed population with 20 years of latency, whose members presumably shared similar smoking habits, the increase was confined to the high-exposure subcohort. Third, on the basis of empirical evidence from other studies, Siemiatycki et al.[36] have shown that between a blue-collar population and the general U.S. population, confounding by smoking is unlikely to account for an excess risk of more than 10 to 20 percent. Finally, a limited adjustment in the risk of lung cancer,[37,38] based on the smoking prevalence of surviving workers at only two plants, did not substantially change our results.[25] Although confounding by smoking is unlikely to explain the higher rate of respiratory cancer in the high-exposure subcohort, it remains possible that the increase was due to confounding by occupational exposures other than TCDD. For example, asbestos may have contributed to mortality from lung cancer in the cohort, since two deaths were due to mesotheliomas.

An unexpected finding was the small but significant increase in mortality from all cancers combined. The observed increase is consistent with a carcinogenic effect of TCDD. For all cancers combined, mortality was significantly higher than expected in the entire cohort, more pronounced in the high-exposure subcohort, and increased at 9 of 12 plants. With mortality from cancers of the trachea, bronchus, and lung excluded, mortality from all remaining cancers combined was still higher than expected in the overall cohort (SMR, 117; 95 percent confidence interval, 100 to 136) and in the high-exposure subcohort (SMR, 150; 95 percent confidence interval, 118 to 189). Consequently, the increased risk for all cancers combined is not explained by smoking or by increased mortality due to cancer of the trachea, bronchus, and lung. The generation of tumors in a number of organs in animals exposed to TCDD[12,13] and the demonstration that TCDD promoted tumors in two organs[21,22] make it biologically plausible that TCDD may produce tumors in more than one organ in humans. Moreover, a significantly increased SMR for all cancers combined is unusual in occupational studies of chemical workers. Results similar to ours were observed in a study of German workers exposed to TCDD after a 2,4,5-trichlorophenol reactor accident in 1953. A subgroup of workers with chloracne (used as a surrogate for exposure) and at least 20 years of latency had an SMR of 201 (90 percent confidence interval, 122 to 315) for all cancers combined, based on 14 deaths.[39] This is the only other industrial cohort with both substantial exposure to TCDD and a long period of latency during which mortality was examined. Workers from U.S. production cohorts described in previous studies were included in the current study if they met our entry criteria.[40-42]

Two observations argue against a carcinogenic effect of TCDD. First, there was not a significant linear trend of increasing mortality with increasing duration of exposure to products contaminated with TCDD (Table 4). However, our use of duration of exposure may have misclassified the cumulative dose of some workers. In addition, a dose–response relation is generally viewed as strong evidence for an association when it is present, but as fairly weak evidence against an association when it is absent.[43] Second, our study did not directly assess the effect of exposure to TCDD alone. The workers were exposed concurrently to the chlorophenols and phenoxy herbicides that were contaminated with TCDD. In addition, they may have been exposed to numerous other chemicals while employed at the plants.

Because the exposure of our cohort was substantially higher than that of most nonoccupational populations, the estimates of effect in this study may provide an upper level of risk to be anticipated in humans. For several types of cancer previously associated with

TCDD, we found no increases above expected levels. Soft-tissue sarcoma was an exception; a ninefold increase was found among workers who were exposed for 1 year or more and who had at least 20 years of latency. Interpretation of the increased SMR is limited, however, by the small number of cases and because this cause of death was sometimes misclassified on the death certificates of the workers and in the national comparison population. Continued surveillance of the cohort may provide a firmer estimate of risk.

Mortality from all cancers combined was 15 percent higher than expected in the overall cohort. The subcohort with 1 year or more of exposure and 20 years or more of latency had a 46 percent increase in all cancers combined and a 42 percent increase in cancers of the respiratory tract. Although the study could not completely exclude the possible contribution of other occupational carcinogens or smoking, the increased mortality, especially in the subcohort with one year or more of exposure, is consistent with the status of TCDD as a carcinogen.

We are indebted to the National Institute for Occupational Safety and Health statistical clerks, Steve Green, Joyce Godfrey, and others, for their technical contributions; to representatives of the companies and unions for assistance in gathering the data for the study; to our colleagues at the Center for Environmental Health and Injury Control, Centers for Disease Control, for analysis of the serum samples; and to Lawrence Fine, David Brown, and the members of our blue-ribbon review panel for their helpful advice.

References

1. Hardell L, Sandstrom A. Case-control study; soft-tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. Br J Cancer 1979; 39:711-7.
2. Eriksson M, Hardell L, Adami HO. Exposure to dioxins as a risk factor for soft tissue sarcoma: a population-based case-control study. J Natl Cancer Inst 1990; 82:486-90.
3. Eriksson M, Hardell L, Berg N, Moller T, Axelson O. Soft-tissue sarcomas and exposure to chemical substances: a case-referent study. Br J Ind Med 1981; 38:27-33.
4. Hardell L, Eriksson M. The association between soft tissue sarcomas and exposure to phenoxyacetic acids: a new case-referent study. Cancer 1988; 62:652-6.
5. Hardell L, Bengtsson NO. Epidemiologic study of socioeconomic factors and clinical findings in Hodgkin's disease, and reanalysis of previous data regarding chemical exposure. Br J Cancer 1983; 48:217-25.
6. Hardell L, Eriksson M, Lenner P, Lundgren E. Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols and phenoxy acids: a case-control study. Br J Cancer 1981; 43:169-76.
7. Woods JS, Polissar L, Severson RK, Heuser LS, Kulander BG. Soft tissue sarcoma and non-Hodgkin's lymphoma in relation to phenoxyherbicide and chlorinated phenol exposure in western Washington. J Natl Cancer Inst 1987; 78:899-910.
8. Persson B, Dahlander A, Fredriksson M, Brage HN, Ohlson CG, Axelson O. Malignant lymphomas and occupational exposures. Br J Ind Med 1989; 46:516-20.
9. Axelson O, Sundell L, Andersson K, Edling C, Hogstedt C, Kling H. Herbicide exposure and tumor mortality: an updated epidemiologic investigation on Swedish railroad car workers. Scand J Work Environ Health 1980; 6:73-9.
10. Thiess AM, Frentzel-Beyme R, Link R. Mortality study of persons exposed to dioxin in a trichlorophenol-process accident that occurred in the BASF AG on November 17, 1953. Am J Ind Med 1982; 3:179-89.
11. Hardell L, Johansson B, Axelson O. Epidemiological study of nasal and nasopharyngeal cancer and their relation to phenoxy acid or chlorophenol exposure. Am J Ind Med 1982; 3:247-57.
12. Kociba R, Keyes D, Beyer J, et al. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. Toxicol Appl Pharmacol 1978; 46:279-303.
13. National Toxicology Program (NTP). Carcinogenesis bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin (CAS No. 1746-01-6) in Osborne-Mendel rats and B6C3F1 mice (gavage study) 1982. Washington, D.C.: Government Printing Office, 1982. (DHHS publication no. (NIH) 82-1765.)
14. Smith AH, Pearce NE, Fisher DO, Giles HJ, Teague CA, Howard JK. Soft tissue sarcoma and exposure to phenoxyherbicides and chlorophenols in New Zealand. J Natl Cancer Inst 1984; 73:1111-7.
15. Wiklund K, Holm L. Soft tissue sarcoma risk in Swedish agricultural and forestry workers. J Natl Cancer Inst 1986; 76:229-34.
16. Pearce NE, Sheppard RA, Smith AH, Teague CA. Non-Hodgkin's lymphoma and farming: an expanded case-control study. Int J Cancer 1987; 39:155-61.
17. Wiklund K, Dich J, Holm LE. Risk of malignant lymphoma in Swedish pesticide appliers. Br J Cancer 1987; 56:505-8.
18. Olsen JH, Jensen OM. Nasal cancer and chlorophenols. Lancet 1984; 2:47-8.
19. Hardell L, Bengtsson N, Jonsson V, Ericksson S, Larsson L. Aetiological aspects on primary liver cancer with special regard to alcohol, organic solvents and acute intermittent porphyria — an epidemiological investigation. Br J Cancer 1984; 50:389-97.
20. Rao MS, Subbarao V, Prasad JD, Scarpelli DG. Carcinogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the Syrian golden hamster. Carcinogenesis 1988; 9:1677-9.
21. Poland A, Palen D, Glover E. Tumour promotion by TCDD in skin of HRS/J hairless mice. Nature 1982; 300:271-3.
22. Pitot HC, Goldsworthy T, Campbell HA, Poland A. Quantitative evaluation of the promotion by 2,3,7,8-tetrachlorodibenzo-p-dioxin of hepatocarcinogenesis from diethylnitrosamine. Cancer Res 1980; 40:3616-20.
23. Esposito M, Tiernan T, Dryden F. Dioxins. 1980. Cincinnati: Industrial Environmental Research Laboratory, 1980. (EPA publication 600/2-80-197.)
24. Suskind RR, Hertzberg VS. Human health effects of 2,4,5-T and its toxic contaminants. JAMA 1984; 251:2372-80.
25. Fingerhut M, Halperin W, Marlow D, et al. Mortality among U.S. workers employed in the production of chemicals contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). NIOSH Final Report PB91125971. Springfield, Va.: National Technical Information Service, 1990.
26. Sweeney MH, Fingerhut MA, Connally LB, et al. Progress of the NIOSH cross-sectional medical study of workers occupationally exposed to chemicals contaminated with 2,3,7,8-TCDD. Chemosphere 1989; 19:973-7.
27. World Health Organization. International classification of diseases: manual of the international statistical classification of diseases, injuries, and causes of death. Geneva: World Health Organization, 1977.
28. Steenland K, Beaumont J, Spaeth S, et al. New developments in the NIOSH lifetable analysis system. J Occup Med 1990; 32:1091-8.
29. Rothman K, Boice J. Epidemiologic analysis with a programmable calculator. Washington, D.C.: Government Printing Office, 1979:30-1. (DHEW publication no. (NIH) 79-1649.)
30. Rothman KJ. Modern epidemiology. Boston: Little, Brown, 1986:229, 338-9.
31. Fox AJ, Collier PF. Low mortality rates in industrial cohort studies due to selection for work and survival in the industry. Br J Prev Soc Med 1976; 30:225-30.
32. Suit HD. Sarcoma of soft tissue. CA 1978; 28:284-95.
33. Fingerhut MA, Halperin WE, Honchar PA, Smith AB, Groth DH, Russell WO. An evaluation of reports of dioxin exposure and soft tissue sarcoma pathology among chemical workers in the United States. Scand J Work Environ Health 1984; 10:299-303.
34. Patterson DG Jr, Fingerhut MA, Roberts DR, et al. Levels of polychlorinated dibenzo-p-dioxins and dibenzofurans in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Am J Ind Med 1989; 16:135-46.
35. Percy C, Stanek E III, Gloekler L. Accuracy of cancer death certificates and its effect on cancer mortality statistics. Am J Public Health 1981; 71:242-50.
36. Siemiatycki J, Wacholder S, Dewar R, Cardis E, Greenwood C, Richardson L. Degree of confounding bias related to smoking, ethnic group, and socioeconomic status in estimates of the association between occupation and cancer. J Occup Med 1988; 30:617-25.
37. Axelson O. Aspects on confounding in occupational health epidemiology. Scand J Work Environ Health 1978; 4:98-102.
38. Steenland K, Beaumont J, Halperin W. Methods of control for smoking in occupational cohort mortality studies. Scand J Work Environ Health 1984; 10:143-9.
39. Zober A, Messerer P, Huber P. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. Int Arch Occup Environ Health 1990; 62:139-57.
40. Zack JA, Suskind R. The mortality experience of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident. J Occup Med 1980; 22:11-4.
41. Zack JA, Gaffey WR. A mortality study of workers employed at the Monsanto Company plant in Nitro, West Virginia. Environ Sci Res 1983; 26:575-91.
42. Ott MG, Olson RA, Cook RR, Bond GG. Cohort mortality study of chemical workers with potential exposure to the higher chlorinated dioxins. J Occup Med 1987; 29:422-9.
43. Monson RA. Occupational epidemiology. Boca Raton, Fla.: CRC Press, 1990:100.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE 4 February 1987

SUBJECT 2,3,7,8-TCDD in Aquatic Environments

FROM Philip M. Cook, Ph.D. PMC
Chief, Hazardous Waste Research Branch, ERL-Duluth

TO Jim Cummings
Office of the Assistant Administrator
for Solid Waste and Emergency Response

This memorandum is provided in response to your request for an update on the state of knowledge concerning 2,3,7,8-TCDD in aquatic environments. A considerable amount of new information is being generated and much will be reported during 1987. Most of the information I can provide results from our own research. I believe you have already received reprints for research results already published.

I reported bioconcentration factor (BCF) determinations for 2,3,7,8-TCDD, 1,2,3,4-TCDD, 1,3,6,8-TCDD and 1,3,7,9-TCDD at the Society for Environmental Toxicology and Chemistry meeting last November. A journal publication is in preparation. The EPA Water Quality Criteria Document presently uses a value of 5000 for the 2,3,7,8-TCDD BCF. We determined a value of 66,000 for carp and 97,000 and 159,000 for fathead minnows at two different exposure concentrations. Our BCF data for the four TCDD isomers is summarized in the attached table. We concluded from this study that ---

1. BCFs for different TCDD isomers vary greatly as expected from field monitoring data.

2. TCDD isomers other than 2,3,7,8-TCDD have lower BCFs than predicted on the basis of structure or log Kow due to more rapid rates of elimination.

3. Differences in rates of metabolism probably explain differences in TCDD rates of elimination and thus BCFs.

4. The gill uptake efficiencies for the four TCDD isomers studied appear to be similar despite structural differences and different uptake rate measurements attributed to large differences in elimination rates.

5. Approximately 90% of the TCDD in the fish exposure water was associated with particulate and dissolved organic matter. Thus, BCFs calculated on the basis of organic carbon free TCDD in the water would be ten times greater.

6. The Water Quality Criteria Document BCF value for 2,3,7,8-TCDD is very low because previously reported BCF determinations were made on the basis of very short exposure periods, inadequate depuration data, static exposure conditions, overestimates of water exposure concentrations, and other factors which lower the estimate of equilibrium fish concentrations with respect to actual water concentrations.

7. 2,3,7,8-TCDD is so toxic to fish that BCF determinations have not yet been made over long exposure periods without toxic effects and mortality occurring. No-effect levels are likely to be less than 10 ppq total 2,3,7,8-TCDD in water and possibly less than 1 ppq if only "dissolved" 2,3,7,8-TCDD is considered in the bioaccumulatable and toxic component.

8. 2,3,7,8-TCDD was lethal to carp at an accumulated dose of 2 ug/Kg. Rainbow trout appear to be a little more sensitive. This toxicity is comparable to the 1 ug/Kg LD50 found for the guinea pig, the most sensitive mammalian species known. Fathead minnows appear to be at least five times less sensitive than carp or rainbow trout.

It is likely that fish bioaccumulation of PCDDs and PCDFs is greatly influenced by food chain links to contaminated sediments and contact time of fish with sediment. Field monitoring data generally supports this premise. For example, fish collected from field surveys when analyzed for all TCDD isomers generally only have detectable amounts of 2,3,7,8-TCDD despite the presence of greater amounts of other TCDD isomers in contaminated sediments. Many of the TCDD isomers have relatively low bioaccumulation potential as seen from our BCF measurements for 1,2,3,4-TCDD and 1,3,7,9-TCDD and thus are not likely to be detected. 1,3,6,8-TCDD, however, would be expected in the fish in detectable levels if uptake from water was the major route for bioaccumulation. The lack of 1,3,6,8-TCDD in the fish is consistent with a kinetic effect involving decreasing amounts of 1,3,6,8-TCDD with respect to 2,3,7,8-TCDD in each step along the food chain to a fish and the absence of significant uptake from water.

For higher chlorinated PCDD and PCDF congeners, differences in elimination rates from fish and their food chain organisms create similar preferential bioaccumulation of 2,3,7,8-substituted planar molecules which are likely to be metabolized at a slower rate. In addition, as molecular weight and size increase with increasing degree of chlorination, it is apparent that the rate uptake from water across the gills decreases. Absorption efficiency from ingested material is also probably less for higher chlorinated congeners.

The net result of the above considerations is that many PCDDs and PCDFs found in sediments are not detectable in fish. The attached table on "Congener Dependent Bioavailability of PCDDs and PCDFs"

LB

demonstrates how this same effect occurs for laboratory exposure of fish to municipal incinerator fly ash. The effect is more extreme when the "food chain chromatography" effect is present and longer exposure times are involved (much longer time required to reach steady state) as with the fish exposed to sediment in a reservoir. The compounds included in the table are all members of the "biosignificant fraction of PCDDs and PCDFs in that they do appear to bioaccumulate, are all 2,3,7,8-substituted and thus all have significant toxic potential. We developed a simple expression called the "bioavailability index" (BI) for comparing relative bioaccumulation tendencies for different chemicals associated with different solid wastes on sediments. The BI is simply the ratio of chemicals accumulated per gram of fish lipid to the amount present per gram of organic carbon in the solid material the fish are exposed to. The BI can be normalized to a value of 1.0 for 2,3,7,8-TCDD in order to make comparison of the other PCDD and PCDF congeners BIs easier. Although the magnitudes of the fly ash and sediment BIs cannot be directly compared due to great differences in the fish exposures, the normalized BIs for both fly ash and sediment show the same trends. For both PCDDs and PCDFs the normalized BIs decrease as the degree of chlorination increases. There also appears to be a tendency for 2,3,7,8-TCDF to be less bioaccumulable than 2,3,7,8-TCDD. The penta-CDD and -CDF results for the sediment seem divergent and will be rechecked before this data is published in this form. We will soon have much more of this kind of data when results are obtained for Lake Ontario sediments and paper mill sludges.

EPA is frequently faced with the question of what fish TCDD contamination levels will result from known or projected environmental contamination levels. The use of a BCF value, no matter how accurate, for predicting fish residues has a major limitation in that environmental TCDD water concentrations can never be detected even with the most sensitive techniques. Even if water measurements could be made, it would be difficult to determine what fraction of TCDD in water is not associated with dissolved or particulate organic carbon so that a laboratory derived BCF could be applied. An alternative approach is to use expected equilibrium partitioning relationships for sediment and fish to predict maximum levels of fish contamination and rely on site-specific sediment to fish TCDD ratios to determine more realistic "approach to steady-state" relationships likely to exist between sediments and fish. This should be done on the basis of partitioning between organic carbon in sediment and lipid in fish. In theory there should be a simple 1:1 equilibrium relationship between sediment organic carbon and lipid concentrations for very hydrophobic organic compounds such as 2,3,7,8-TCDD which are very slowly metabolized and eliminated from the organism. There are data for compounds such as PCBs which indicate approximately a four-fold preference of these compounds for lipids over organic carbon in sediment. Our 2,3,7,8-TCDD BI value of .27 for sediment is 4X less than the theoretical partitioning value of 1.0 and ~~8X~~ 16X less than the lipid preference value of 4.0 at least in part because steady-state conditions were not reached when the fish were exposed to the sediment.

In many environmental situations expected steady-state relationships between fish bioaccumulation levels and sediment contamination levels will

not be reached. Kinetic models and appropriate rate constants are needed to accurately predict fish bioaccumulation levels. When an aquatic ecosystem has a constant input of TCDD so that surface sediment concentrations are relatively constant, fish concentrations will approach a steady-state level dependent on rates of uptake from water, food and contact with sediment. For Lake Ontario we are investigating sediment to fish TCDD ratios under present conditions so that remedial actions for Superfund sites and other sources of TCDD can be evaluated with respect to changes in fish residues which will result in the future. That is, if sediment TCDD levels are decreased or increased in the future through man's activities, we should be able to predict eventual changes in fish contamination levels when a new "approach to steady-state" system results. In Lake Ontario our preliminary data indicates that fish lipids have only about 5% of the TCDD concentration found in the organic carbon fraction of the surface sediments. An extensive survey of sediment and fish TCDD levels throughout Lake Ontario is scheduled for this summer.

CONGENER DEPENDENT BIOAVAILABILITY OF PCDDs AND PCDFs IN FLY ASH AND SEDIMENT

Compound	Fly Ash PG/G Carbon	Fish PG/G Lipid	BI	Normalized BI	Sediment PG/G Carbon	Fish PG/G Lipid	BI	Normalized BI
2,3,7,8-TCDD	1.3×10^5	93	7.4×10^{-4}	1.00	5450	1500	.27	1.00
2,3,4,8-TCDF	1.7×10^5	95	5.7×10^{-4}	.77	5870	300	.06	.22
1,2,3,7,8-PeCDD	1.2×10^6	540	4.3×10^{-4}	.58	1000	60	.06	.22
2,3,4,7,8-PeCDF	7.3×10^5	180	2.5×10^{-4}	.34	190	55	.28	1.04
1,2,3,6,7,8-; 1,2,3,4,7,8-H_xCDD	5.0×10^6	1300	2.6×10^{-4}	.35	5800	200	.04	.15
1,2,3,6,7,8-H_xCDF	8.2×10^5	290	3.5×10^{-4}	.47	560	~~200~~ 12	.04	.14
1,2,3,4,6,7,8-H_pCDD	1.6×10^7	1300	7.8×10^{-5}	.11	71000	540	.005	.018
1,2,3,4,6,7,8-H_pCDF	3.7×10^6	340	9.2×10^{-5}	.12	9400	31	.003	.012

Attachment 8

Environmental Toxicology and Chemistry, Vol. 7, pp. 47-62, 1988
Printed in the USA. Pergamon Journals Ltd.

555

TOXICITY AND BIOCONCENTRATION OF 2,3,7,8-TETRACHLORODIBENZODIOXIN AND 2,3,7,8-TETRACHLORODIBENZOFURAN IN RAINBOW TROUT

PAUL M. MEHRLE,* DENNY R. BUCKLER, EDWARD E. LITTLE, LARRY M. SMITH, JIM D. PETTY, PAUL H. PETERMAN and DAVID L. STALLING
National Fisheries Contaminant Research Center, U.S. Fish and Wildlife Service, Columbia, Missouri 65201

G. M. DE GRAEVE and JAMES J. COYLE
Battelle Laboratories—Columbus, Columbus, Ohio 43201

WILLIAM J. ADAMS
Monsanto, St. Louis, Missouri 63167

(*Received* 25 *March* 1987; *Accepted* 14 *July* 1987)

Abstract—Among the most toxic isomers of polychlorinated dibenzodioxins and polychlorinated dibenzofurans, two groups of toxic aromatic compounds, are 2,3,7,8-tetrachlorodibenzodioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF). We examined the chronic toxicity of these compounds to rainbow trout (*Salmo gairdneri*). The fish (0.38 ± 0.09 g) were continuously exposed in an intermittent-flow proportional diluter for 28 d to 0, 38, 79, 176, 382, and 789 pg TCDD/L (parts per quadrillion) or to 0, 0.41, 0.90, 1.79, 3.93, and 8.78 ng TCDF/L (parts per trillion); exposures to each chemical were followed by a 28-d depuration phase. TCDD had significant effects on survival, growth, and behavior during the exposure and depuration phases. The no observed effect concentration was lower than the lowest exposure concentration of 38 pg/L. The average measured BCF at 28 days was 26,707. The estimated bioconcentration factor at steady-state equilibrium was 39,000 in the lowest exposure concentration where fish were least affected. TCDF, like TCDD, induced similar effects on survival, growth and behavior. The no observed effect concentration, based on survival, was 1.79 ng/L; that based on growth was 0.41 ng/L. The measured bioconcentration factor was 6,049 in fish exposed to 0.41 ng/L, and 2,455 in fish exposed to 3.93 ng/L for 28 d.

Keywords—Dioxin Furan 2,3,7,8-tetrachlorodibenzodioxin (TCDD) Rainbow trout 2,3,7,8-tetrachlorodibenzofuran (TCDF)

INTRODUCTION

Polychlorinated dibenzofurans (PCDFs) and polychlorinated dibenzo-*p*-dioxins (PCDDs) are two groups of toxic compounds composed of 135 and 75 individual isomers, respectively. Certain of these isomers are extremely toxic, particularly those with chlorine substituents in the 2,3,7,8-positions of the aromatic rings. PCDFs occur as trace contaminants in polychlorinated biphenyls (PCBs) and are sometimes formed in significant quantities from pyrolysis or incomplete combustion of PCBs [1]. Isomer specific PCDFs and PCDDs also occur as contaminants in the manufacture and pyrolysis of certain chlorinated phenols [2]. During combustion of these formulations, PCDDs are formed primarily from thermal dimerization and conversion of chlorinated phenoxyphenols, whereas PCDFs are formed from chlorinated diphenyl ethers. PCDDs and PCDFs have also been found in fly ash of municipal waste incinerators [3].

The isomers 2,3,7,8-tetrachlorodibenzodioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF) have been reported as contaminants in fish and sediment. Both have been detected in fish from the Great Lakes [4–6], and residues have been found in resident and migratory fish, crustaceans and sediment in the Chesapeake Bay area [7] and in industrialized and heavily populated areas of the northeastern United States [8]. The concentrations of these compounds in fish vary widely from low pg/g to ng/g quantities, and those of

*To whom correspondence may be addressed.

TCDF are usually higher than those of TCDD. In certain areas of the Great Lakes and the northeastern United States (Newark Bay, Passaic River), TCDD residues in fish and crustaceans exceed the U.S. Food and Drug Administration (FDA) "levels of concern" of 25 pg/g and 50 pg/g, respectively [8,9].

The chronic toxicity and bioconcentration of TCDD and TCDF in aquatic species have not been elucidated. Helder [10,11] reported that exposing fertilized eggs of rainbow trout (*Salmo gairdneri*) for 96 h to TCDD concentrations of 0.1 ng/L significantly decreased the growth of the resulting fry, and that exposing rainbow trout fry for 96 h to 10 and 100 ng/L TCDD retarded growth, caused histological changes in tissues and delayed mortality. Miller et al. [12] reported the toxicity and pathologic changes induced by short-term exposures of guppies (*Poecilia reticulata*) and coho salmon (*Oncorhyncus kisutch*) to TCDD. Coho salmon exposed to 56 pg/L and 1,000 ng/L for 24 h exhibited delayed mortality. Cooper et al. [13] observed delayed development and decreased survival in Japanese medaka (*Oryzias latipes*) exposed to TCDD concentrations of 6 to 500 ng/L. The oral toxicity and metabolism of TCDD in rainbow trout and yellow perch (*Perca flavescens*) were recently reported by Kleeman et al. [14,15]. In rainbow trout exposed for 6 h to 107 ng/L TCDD, followed by a 139-d depuration period, Branson et al. [16] estimated the bioconcentration factor (BCF) to be 9,270 and the elimination half-life to be 58 d. Significant delayed effects were similar to those reported by Miller et al. [12]. No similar studies have been conducted to characterize the toxicity and bioconcentration of TCDF in aquatic species.

Because of the lack of chronic toxicity data involving continuous low-level exposures of fish to TCDD and TCDF, we attempted to measure the chronic toxicity of these two compounds to rainbow trout. Their effects on survival, growth, and behavior were evaluated during a 28-d continuous exposure followed by a 28-d depuration phase. Uptake and depuration kinetics and BCFs for TCDD and TCDF were also evaluated.

METHODS

Test organisms

Eyed eggs of rainbow trout obtained from the Erwin (Tennessee) National Fish Hatchery came from two-year-old spawners of the "Fish Lake" strain; they were transferred to the National Fisheries Contaminant Research Center (NFCRC), Columbia, Missouri, where they hatched on 11 April 1985. About 2,000 swim-up fry produced from the eggs were shipped by air to Battelle Laboratories, Columbus, Ohio, on 2 May 1985. Mortality associated with shipping was less than 5%.

The fish were maintained in reconstituted water in 1,200-liter fiberglass tanks until the study was begun. The fish were held at a temperature of 11°C (±1°C), and were fed Tetramin floating flake food ad libitum. Analysis of the food showed no detectable quantities of TCDD (detection limit, less than 0.06 ng/g), TCDF (detection limit, less than 0.04 ng/g) or other organochlorine compounds.

Experimental approach

A flow-through diluter was used to continuously expose rainbow trout for 28 d to five duplicated concentrations each of [^{3}H]TCDD and TCDF plus duplicated controls. After the exposure period, toxicant input to the exposure chambers was terminated and the fish were held in laboratory water under flow-through conditions in the same test chambers during the 28-d depuration period. The fish were fed Tetramin floating flake food ad libitum throughout the study.

Fifty fish (0.38 ± 0.09 g each) were stocked in each aquarium. Samples of fish for residue analyses were taken on days 7, 14, 21, and 28 of the exposure phase and on day 28 of the depuration phase. To determine initial background concentrations of TCDD and TCDF, 30 fry with no previous TCDD and TCDF exposure history were weighed, measured, frozen, and analyzed for TCDD and TCDF. Fish collected for residue analyses were frozen until the time of analysis.

Daily survival records were maintained throughout the study. In addition, we recorded daily observations of swimming behavior, feeding behavior, location and position in the exposure tank, external lesions, and deformities.

Diluter and toxicant exposure system

The diluter system used in the study was constructed at NFCRC and installed in the West Jefferson Environmental Research Laboratory, Battelle Laboratories, Columbus, Ohio. The system consisted of two separate proportional flow-through diluters in a temperature-controlled waterbath. Both the diluter and waterbath were enclosed in a vented Plexiglas structure to reduce environmental exposures resulting from volatilization of the compounds. Each diluter delivered five concentrations (50% dilutions) of each compound (plus water for controls) into duplicate tanks containing

15 liters of water. Over the course of the study the diluter cycle rate varied between 2.4 and 3.0 cycles per hour; the replacement volume was 500 ml per replicate tank per cycle. The approximate water turnover rate in the exposure tanks was 2.4 times per day. The maximum fish loading in each test tank throughout the study was about 1.3 g/L and the maximum fish loading was 0.5 g/L of water passing through the tank in 24 h. Excess food and fecal matter were removed daily. Daily records of diluter operations were maintained throughout the studies. Nominal exposure concentrations (ng/L) were 0 (control), 0.115, 0.231, 0.463, 0.925, and 1.85 for TCDD; and 0 (control), 1.3, 2.7, 5.3, 10.6, and 21.3 for TCDF. Water temperature in the exposure tanks was maintained at 12 ± 1°C.

The combined effluents from the diluter system were recycled through two columns containing activated charcoal to remove TCDD and TCDF from solution. GC-MS and radiometric analyses were used to monitor the effluent for TCDD and TCDF.

Toxicants

Monsanto Company (St. Louis, MO) supplied the TCDD and TCDF used in the studies. The [^{3}H]TCDD (99+% pure; 22% unlabeled, 42% monotritiated and 36% ditritiated) used had a specific activity of 2.81×10^5 dpm/ng (0.128 μCi/ng) as determined by radiometric and GC-MS analyses. The TCDF provided by Monsanto was originally obtained from KOR, Inc. (Cambridge, MA), and was 98+% pure as determined by GC-MS.

Preparation of stock solutions

All glassware used to prepare stock solutions was rinsed several times with reagent-grade solvents. Carrier solvent for the compounds was acetone (Baker-analyzed). The [^{3}H]TCDD was diluted with acetone to a concentration of 36 ng/L. The stock solution was analyzed by GC-MS and by liquid scintillation radiometric analysis. Toxicants were delivered by an automatic pipetting system (Micromedic) that provided 0.05 ml/L or less of acetone to each exposure concentration. The TCDF was diluted with acetone to a measured concentration of 407 ng/L. This stock solution was used throughout the study and was delivered to exposure tanks by Micromedic pipetting systems. The acetone concentration delivered to each tank was 0.05 ml/L or less.

Water chemistry

In an effort to reduce the number of instruments coming in contact with the toxicants, we performed routine water chemistry only on the control chambers of both compounds, and only once during the exposure phase and once during the depuration phase. Alkalinity was measured by potentiometric titration with 0.02 N H_2SO_4 to pH 4.5, and hardness was titrated with EDTA according to standard methods [17]. We used an Orion

Table 1. Concentration of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in exposure water as measured by radiometric and GC-MS analyses

		TCDD nominal concentration (pg/L)					
Day	Measurement	0	115	231	463	925	1,850
1	pg/L (^{3}H)[a]	1.2	31	62	130	280	527
	pg/L (GC-MS)	—[b]					—[b]
7	pg/L (^{3}H)[a]	1.4	41	78	169	359	705
	pg/L (GC-MS)	<25[c]					840
14	pg/L (^{3}H)[a]	1.1	34	69	146	298	606
	pg/L (GC-MS)	<15[c]					730
21	dpg/L (^{3}H)[a]	0.7	41	87	200	466	970
	pg/L (GC-MS)	<15[c]					1,220
28	pg/L (^{3}H)[a]	1.3	44	99	234	507	1,135
	pg/L (GC-MS)	<20[c]					1,400
$\bar{x}$ pg/L (^{3}H) ± SD		1.1	38 ± 5	79 ± 15	176 ± 42	382 ± 101	789 ± 256
$\bar{x}$ pg/L (GC-MS) ± SD		<15[c]					1,048 ± 315

[a]Measured by radiometric analyses for [^{3}H]TCDD. Conversion of dpm/L to pg/L (^{3}H) based on specific activity of 2.81×10^5 dpm ^{3}H/ng TCDD.

[b]Not determined.

[c]None detected (less than minimal detectable limits).

digital pH meter to measure pH, a Sybron/Barnstead Model pM-70CB conductivity bridge to measure conductivity and a Varian Model 3700 gas chromatograph to measure ammonia. Water chemistry determinations were as follows: hardness, 153 ppm; alkalinity, 88 ppm; pH, 7.7; conductivity, 215 μohms; un-ionized ammonia, 0.0013 mg/L; and dissolved oxygen, 65 to 85% saturation.

Analyses of exposure water

During the exposure phase of the study, samples for GC-MS analysis were extracted from the TCDD control and highest exposure concentrations and from all TCDF exposure concentrations on days 0, 7, 14, 21, and 28. On each day immediately following the date of sample collection for GC-MS, we took samples for radiometric TCDD analyses from all exposure chambers. Radiometric analyses of all water extracts were conducted at Battelle Laboratories. Water from replicate *A* was sampled on days 0, 7 and 21, and water from replicate *B* on days 1, 14, and 28. On day 7 of the depuration period, the TCDD control and highest concentrations were measured radiometrically, and the TCDF control and highest concentrations were sampled for GC-MS analysis. On day 7 of the depuration phase, only 92 pg/L TCDD was measured in water from the highest TCDD exposure chamber, and 0.56 ng/L TCDF in the highest TCDF exposure chamber. The TCDD and TCDF exposure concentrations measured throughout the exposures are shown in Tables 1 and 2.

Water samples of a volume necessary to provide an adequate amount of analyte were collected from the diluter tanks with solvent-washed glassware and transferred directly to a glass separatory funnel. The water sample was then spiked with the appropriate internal standard solution containing $[^{13}C_{12}]$2,3,7,8-TCDD and $[^{13}C_{12}]$2,3,7,8-TCDF at 4.0 pg/μl in acetonitrile. The water sample was extracted three times with 50-ml portions of methylene chloride (CH_2Cl_2) and the extracts were passed through a column (about 2 × 6 cm) of anhydrous, granular sodium sulfate to break emulsions and remove suspended water. The extract was then rotary-evaporated to a low volume and transferred with three or four portions of CH_2Cl_2 to a glass ampoule, blown to dryness with nitrogen and flame-sealed.

The sample was removed from the opened ampoule with four 1.5-ml portions of 20% CH_2Cl_2 in hexane onto a dual column arrangement of 2 × 0.5 cm 40% H_2SO_4 on silica gel (SA-SG) in the first column and 15 mg·Amoco PX-21 activated carbon dispersed in 150-mg glass fibers (CGF) [18]. The efficiency of transfer of $[^3H]$TCDD from these ampoules in the presence of solid residues was determined to exceed 99%. The SA-SG column was then discarded and the CGF column slightly pressurized to move the sample entirely onto the carbon adsorbent. We applied 15 ml CH_2Cl_2 to the CGF column at about 2 ml/min under pressure, and discarded the eluate.

The analyte, either $[^3H]$TCDD or TCDF, was recovered from the CGF by back-flushing with 15 ml toluene. The toluene was removed by rotary evaporation in a waterbath at 65 to 70°C under a 9.8-cm vacuum (sample taken just to dryness).

At this point, we added 2-(4-biphenyl)-6-phenylbenzoxazole (PBBO) to perform radiometric analyses on each sample or aliquots thereof containing $[^3H]$TCDD. The quench curve for counting efficiency was determined by the sealed tritium standard (HAV3612), corrected for decay, as the reference point, and replicate analyses of samples of $[^3H]$TCDD at various quench values. We used the equation, $dpm = cpm/0.85 \times S$, where dpm is disintegrations per minute, cpm is counts per minute and S is the quench value.

Table 2. Concentration (ng/L) of 2,3,7,8-tetrachlorodibenzofuran (TCDF) as measured by GC-MS in exposure water during a 28-d chronic toxicity study with rainbow trout

	TCDF nominal concentration (ng/L)					
Day	0	1.3	2.7	5.3	10.6	21.3
1	0.02	0.38	0.70	1.40	3.20	6.60
7	<0.06	0.33	0.91	1.98	3.84	9.04
14	<0.029	0.44	0.86	1.56	3.82	7.97
21	<0.025	0.37	0.93	1.93	4.19	10.4
28	0.017	0.52	1.10	2.10	4.60	9.9
$\bar{x} \pm$ SD	<0.02	0.41 ± 0.07	0.90 ± 0.14	1.79 ± 0.30	3.93 ± 0.52	8.78 ± 1.53

We applied the sample to alumina (Bio-Rad AG4 acid alumina, 3.5 ml = 3.65 g activated at 190°C) packed in a 5-ml graduated pipet with solvent reservoir using multiple washings of hexane totaling 5.0 ml. The column was then washed with 10 ml 5% CH_2Cl_2 in hexane (discarded) and the analyte recovered with 10 ml 20% CH_2Cl_2/hexane. The sample was evaporated just to dryness by rotary evaporation and transferred with three 1-ml portions of CH_2Cl_2 to a conical vial. The solvent was gently removed under a stream of nitrogen. The sample was then dissolved in a minimum of 5 μl *o*-xylene in preparation for GC-MS analysis.

We carried out the GC-MS analysis on a Finnigan 4023 quadrupole mass spectrometer (EI mode at 35 eV), using a 30 m × 0.25 mm DB-5 (0.25 μm) column (J&W Scientific, Inc., Rancho Cordova, CA) and helium carrier gas at about 35 cm/s. The temperature program was 120°C, hold 1 min, increase 20°C/min to 210°C, 5°C/min to 270°C and 4.5°C/min to 300°C. Selected ions monitored were m/z 304, 306, and 308 summed for 2,3,7,8-TCDF; m/z 316, 318 and 320 summed for [$^{13}C_{12}$]2,3,7,8-TCDF; m/z 320, 322, 324 and 326 summed for [^{3}H]2,3,7,8-TCDD; and m/z 332, 334, and 336 summed for [$^{13}C_{12}$]2,3,7,8-TCDD. We calibrated the internal standard solutions by preparing calibration mixtures of these standards with quantitative standards of native 2,3,7,8-TCDD and 2,3,7,8-TCDF prepared at the NFCRC and 2,3,7,8-TCDD solution as a U.S. Environmental Protection Agency (EPA) quality assurance material (Ref. No. 20603; EPA, Las Vegas, NV). We assumed equal integrated GC-MS responses for the molecular ions of native and [^{3}H]2,3,7,8-TCDD. The level of tritiation of the [^{3}H]2,3,7,8-TCDD computed from the molecular ion abundances measured by GC-MS gave a mole fraction of tritium of 27.3% and a specific activity of 2.15×10^5 dpm/ng. We calculated the specific activity, using the GC-MS–determined concentration and measured activity, to be $2.81 \pm 0.07 \times 10^5$ dpm/ng (triplicate analyses).

Collection of fish for residue analyses

Fish for whole-body TCDD and TCDF residue analyses were collected during the exposure period on days 0 (prior to exposure), 7, 14, 21, and 28, and on day 56 (after 28 d of depuration). When we removed fish from the exposure tanks for residue analyses on day 7, we removed unequal numbers from different tanks to reduce the number of fish remaining in all tanks to 42, and thus reduce the biomass and avoid potential overloading in the exposure tanks.

Fish for residue analyses were collected randomly from the exposure tanks for each toxicant. Individual weights and lengths were measured for fish collected on day 7 of the exposure and on day 28 of the depuration phase. Fish collected on other sampling days were weighed but not measured for length. All fish were blotted dry before they were weighed and were then wrapped in hexane-rinsed aluminum foil, placed in labeled screw-topped glass vials and stored at −10°C until residue analyses were begun.

GC-MS determinations of TCDD and TCDF in fish

Analyses of fish samples were performed by the method of Smith et al. [19]. The GC-MS conditions and spiking procedures were as described above for the analysis of the water samples.

Sample extracts that required radiometric analysis for [^{3}H]TCDD were rotary-evaporated and brought to 10.0-ml volumes; an appropriate aliquot (usually 1.00 ml) was then taken for scintillation counting. The quench values for the aliquots of the fish extracts were uniformly near the minimum (*S* values of 0.65), as observed for analytical standards. Negative and positive control samples were routinely included in the radiometric determinations of [^{3}H]TCDD and established so that there was no procedural background contribution in these determinations.

The internal standard procedure for GC-MS determinations of both [^{3}H]TCDD and TCDF provided internal quality control for overall accuracy of quantitation. In all reported determinations of these analytes, the criteria attained were relative GC retention time (±1 scan number in 1,160 or ±0.001 relative retention units) and correct ion abundances of the three or four molecular ion cluster members (±10% of theoretical value). The limit of quantitation was five times the signal-to-noise ratio and the limit of detection was three times the signal-to-noise ratio. The molecular ion cluster for [^{3}H]TCDD was significantly distorted from that produced by the native populations of ^{35}Cl and ^{37}Cl. Relative ion abundances of m/z 320, 324, and 326 were 24, 75, 100 and 70%, respectively. This pattern remained constant throughout the study, indicating no significant exchange of hydrogen for tritium in TCDD during the exposure. This observation also demonstrated no significant background of native 2,3,7,8-TCDD in any of the samples, because the presence of

native dioxin would have had an easily discernible effect on this pattern. Procedural background controls showed no 2,3,7,8-TCDD (limit of quantitation, less than 0.006 ng/g) by radiometric analysis and no TCDF (limit of quantitation, less than 0.06 ng/g) by GC-MS. The limit of quantitation for [^{3}H]TCDD was also less than 0.06 ng/g by GC-MS.

Analyses of fish food were carried out by the same procedure used for fish samples, and analyses of [^{3}H]TCDD and TCDF stock solutions were performed by direct dilution before analysis.

We computed percent recoveries of [^{13}C]TCDD and [^{13}C]TCDF internal standards by the less precise external standard technique, using the responses of the [^{13}C]TCDD and [^{13}C]TCDF internal standards; the recoveries of [^{13}C]TCDF and [^{13}C]TCDD, respectively, are listed here according to the various matrices: stock solutions, 71 ± 30% and 71 ± 33%; exposure water, 134 ± 55% and 109 ± 52%; fish, 101 ± 37% and 117 ± 46%; all matrices combined, 112 ± 51% and 105 ± 47%.

Determination of total concentration of [^{3}H]TCDD species in fish by biological material oxidation procedure

Determinations of total body burden of [^{3}H]TCDD residues in fish, as opposed to extractable residue, were made on homogenate aliquots of individual fish by the method of total burn, followed by liquid scintillation radiometric analysis of the combustion products. A Harvey Biological Materials Oxidizer (Model OX-100, R. J. Harvey Instrument Corp., Hillsdale, NJ) and a Harvey tritium cocktail (lot No. DC02) were used in the procedure. The combustion/trapping efficiency was 84% with triplicate analyses of a [^{14}C]PCB standard. Cryogenic traps and dry ice and methanol were used to trap the tritiated water produced in the combustion. The combustion/trapping efficiency observed for a standard of [^{3}H]TCDD was 89 ± 3% for spiked fish tissue. The scintillation counting efficiency when the tritium cocktail was used was 37%, and radioactivity was calculated from scintillation analysis using the equation, dpm = cpm/0.64 × S, after subtraction of 50 cpm background.

Samples that had previously been weighed, wrapped in filter paper and aluminum foil and stored in the freezer were transferred along with the approximately 1-cm^2 pieces of filter paper to the quartz combustion boats. Before combustion of samples, we ran a series of blanks and spikes to ensure that performance was satisfactory. Each sample was combusted twice into the cryogenic trap, which contained about 0.5 ml residual methanol. The glass elbow connecting the trap and oxidation chamber was heated with a hot air gun during the procedure to prevent loss by condensation. The condensed residue was transferred from the trap to a scintillation vial with three 5-ml portions of the cocktail. We then washed the trap thoroughly three times with methanol, leaving about 0.5 ml to aid in the next trapping. Because previous tests had indicated that carryover between sample combustions was a potential problem, blank combustions were performed after each sample and control. Scintillation analysis of the blanks showed that carryover was negligible.

Observation of fish for behavioral responses

The behavioral responses of rainbow trout were assessed daily during the TCDD and TCDF exposures. A checklist of behavioral reactions modified from Drummond et al. [20] was used to systematically document and characterize abnormal responses. The responses included coloration, activity (hyperactive, lethargic), excitability by external stimuli (hyperactive, unresponsive), location in aquaria, mode of swimming (head-up, frequent sinking and rising, swimming on side, swimming on back, free swimming), feeding, and morphological observations (bent spine, fin erosion). Observations were made each day by the same observer at the time of feeding.

An aberrant behavioral reaction was recorded when at least one fish in a given treatment responded in a manner that obviously differed from that of controls. Although no attempt was made to quantify the number of fish responding abnormally, an overall measure of the onset, duration and sequence of behavioral changes was made from the systematic daily observations.

Statistical analyses

Daily mortality was analyzed by one-way analysis of variance on the arc-sin transformed values. Differences among means were determined using Fisher's least significant difference (LSD) procedure [21].

Growth as measured by weight or length was analyzed by analysis of variance, including the effects of treatment, replicate within treatment, day, treatment × day, and replicate (treatment × day). Since the replicates, not the individual fish, were the experimental unit, replicate within treatments was used as the error term for testing the effect of treatment, and replicate (treatment × day) was used as the error term for testing the effects of day and treatment × day. We deter-

mined differences among means by calculating a t statistic, using the standard error of the difference for a split-plot design. For growth of TCDD-exposed fish during the depuration phase, we tested the control and lowest exposure concentration groups for equal population means, using a two-sample t test adjusted for unequal variance where appropriate [21].

The cumulative number of days on which fish showed abnormal behavior, from the time of induction to the day of depuration, was analyzed by simple regression against concentration, to provide an estimate of the behavioral responses to chemical exposure.

The BIOFAC computer program [22] was used to estimate the bioconcentration kinetics for TCDD and TCDF. Data from only the exposure phase in each study were used to estimate the kinetics because the number of fish residue samples available during the depuration phase was not adequate. In addition, the fish were held in their original exposure test tanks during the depuration phase, which resulted in the presence of the toxicants in the water because they desorbed from the glass aquaria. Because water concentration measurements and sufficient fish to sample during the depuration phase were not available, we were unable to use data from the depuration phase to estimate rate constants for the toxicants.

To estimate the 56-d LC50 value for TCDD, we computed a multiple-regression model to determine the relationship between percent mortality (arc-sin transformation) to concentration and time of exposure. The linear statistical model contained the effects of linear concentration (CL), days of exposure linear (DL), concentration quadratic (CQ), and day of exposure quadratic (DQ): CL * DL, CL * DQ, CQ * DL and CQ * DQ [21]. We used a quadratic function relationship to estimate the concentration of TCDD at a constant mortality (50%) and period of exposure (56 d).

RESULTS AND DISCUSSION

Mortality

TCDD induced significant mortality in rainbow trout within 14 d of exposure in the highest exposure concentration (789 pg/L), and there was a trend toward increased mortality in fish exposed to 176 and 382 pg/L (Table 3). After 28 d of exposure, significant mortality was evident in the three highest exposure concentrations; the no observed effect concentration (NOEC) was 79 pg/L. Although no mortality was observed, fish in the 38 and 79 pg/L exposure groups were obviously stressed, as judged by reduced growth and behavioral responses. Only rainbow trout in the control group and the three lowest exposure concentrations were observed during the 28-d depuration phase of the study; fish in the two highest exposure concentrations were excluded because the survivors were few and obviously stressed. Significant mortality continued to occur throughout the depuration period in fish previously exposed to 38, 79, and 176 pg/L. There was no apparent recovery in the fish during the 28-d depuration period in clean

Table 3. Cumulative mortality (%) in rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzodioxin (TCDD) for 28 d followed by a 28-d depuration period

	Mean TCDD exposure concentration (pg/L)						
Phase and day	0	38	79	176	382	789	F value
Exposure							
7	5	0	1	4	6	10	1.79
14	5	1	1	13	17	33[a]	5.48[b]
21	5	3	9	36[a]	46[a]	74[a]	28.02[b]
28	5	6	18	50[a]	73[a]	85[a]	27.51[b]
Depuration							
7	5	12	64[a]	85[a]	—[c]	—[c]	9.33[b]
14	5	22	78[a]	95[a]	—	—	30.49[b]
21	7	33	83[a]	95[a]	—	—	28.63[b]
28	7	45[a]	83[a]	95	—	—	27.72[b]

[a]Significantly different from controls by least-significant-difference multiple means comparison test ($p < 0.05$).

[b]Significant treatment effect (one-way analysis of variance; $p < 0.05$).

[c]Exposure groups not part of depuration phase.

water. The NOEC of TCDD, based on mortality throughout the exposure and depuration phases, was less than the lowest exposure concentration of 38 pg/L (parts per quadrillion).

Further insight into the NOEC was inferred from the background concentration of 1.1 pg/L of TCDD detected by radiometric analyses in the control group throughout the study. This low background was probably due to volatilization of TCDD and translocation within the diluter system. Mortality in the control group was 5% during the exposure phase and most of the depuration phase. We suggest from these observations that the NOEC was between 1.1 and 38 pg/L. However, the minimal detectable limits for TCDD in water by GC-MS were not adequate to confirm the 1.1 pg/L detected by radiometric analyses.

A 56-d LC50 of 46 pg/L was calculated from the combined mortality data for the exposure and depuration phases. The surface response curve describing the relation among daily mortality, time and exposure concentrations is shown in Figure 1. The quadratic equation describing this relation was used to derive the 56-d LC50.

Significant mortality was induced by TCDF in rainbow trout within 14 d at exposure concentrations of 3.93 and 8.78 ng/L (Table 4). No additional significant mortality occurred throughout the 28-d exposure phase. During the depuration phase, additional mortality occurred only in fish exposed to 8.78 ng/L. The NOEC throughout the exposure and depuration phases was 1.79 ng/L.

Growth

Growth as measured by the weight of the fish was significantly decreased by all TCDD concentrations after 28 d of exposure (Table 5). There were trends of decreased growth within 14 d of exposure, but significant effects in all concentrations were not observed until 28 d of exposure. During the 28-d depuration phase, growth was measured in fish from only the control and the lowest exposure concentration because of the excessive mortality in the higher TCDD exposure concentrations. There was a significant decrease in growth in the fish exposed to 38 pg/L after the 28-d depuration phase. Fish exposed to 38 pg/L TCDD did not grow during the depuration phase, whereas the weight of fish in the control group exhibited an 80% increase. The NOEC of TCDD on growth during the exposure and depuration phases was less than the lowest exposure concentration of 38 pg/L.

TCDF exposure concentrations of 1.79, 3.93 and 8.78 ng/L significantly decreased the growth of rainbow trout within 28 d of exposure (Table 6). There were trends toward decreased growth

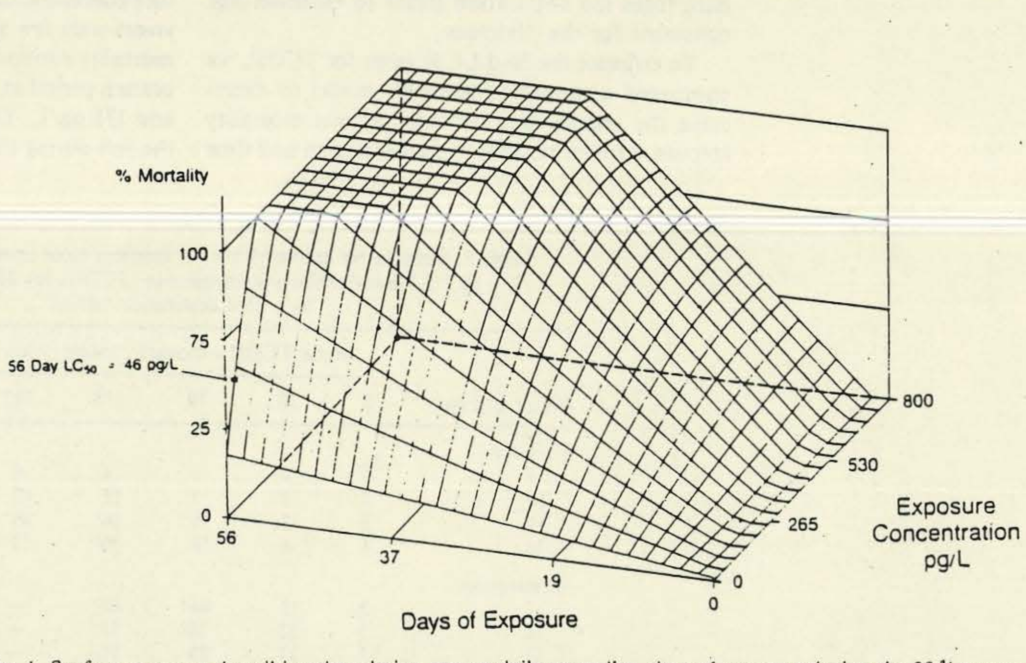


Fig. 1. Surface response describing the relation among daily mortality, time of exposure during the 28-d exposure and 28-d depuration phases, and TCDD exposure concentrations. The quadratic relation was used to derive a 56-d LC50 value of 46 pg/L TCDD for rainbow trout.

Table 4. Cumulative mortality (%) in rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d followed by a 28-d depuration period

Phase and day	Mean TCDF exposure concentration (ng/L) 0	0.41	0.90	1.79	3.93	8.78	F value
Exposure							
7	0	1	1	2	2	12	2.54
14	0	1	3	3	16[a]	22[a]	4.51[b]
21	0	2	5	3	18[a]	23[a]	3.73[b]
28	0	2	6	3	18[a]	28[a]	4.49[b]
Depuration							
7	0	2	6	3	20[a]	37[a]	6.53[b]
14	0	2	6	3	22[a]	46[a]	8.56[b]
21	0	2	6	3	22[a]	46[a]	8.56[b]
28	0	2	6	3	22[a]	46[a]	8.56[b]

[a]Significantly different from controls by least-significant-difference multiple means comparison test ($p < 0.05$).
[b]Significant treatment effect (one-way analysis of variance; $p < 0.05$).

Table 5. Weight (g) of rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzodioxin (TCDD) for 28 d followed by a 28-d depuration period

Phase and day	Mean TCDD exposure concentration (pg/L) 0	38	79	176	382	789
Exposure[a]						
7	0.37	0.36	0.38	0.33	0.36	0.33
14	0.41	0.39	0.42	0.33	0.35	0.40
21	0.48	0.35[b]	0.40	0.39	0.39	0.44
28	0.61	0.53[b]	0.47[b]	0.49[b]	0.45[b]	0.42[b]
Depuration[c]						
28	1.1	0.54[b]	—[d]	—[d]	—[d]	—[d]

Weights are expressed as the mean of 7 to 22 observations.
[a]Analysis of variance used for testing the effects of exposure concentration and time; $F = 2.43$ (time × exposure), $p < 0.03$.
[b]Significantly different from control group (t test; $p < 0.05$).
[c]Fish weight in depuration phase analyzed by t test adjusted for unequal variances.
[d]No measurements made.

after 21 d of exposure but the decrease observed was significant only in the group exposed to 3.93 ng/L. Decreased growth was evident in fish exposed to 0.90 ng/L or more after the 28-d depuration phase. The NOEC for TCDF based on growth during the exposure and depuration phases was 0.41 ng/L. This was the most sensitive response to TCDF.

Behavioral responses

Exposure to TCDD and TCDF induced behavioral impairments that became progressively worse over time and with increasing concentration. The two highest concentrations of TCDD caused behavioral changes within two weeks of exposure that included lethargic swimming, feeding inhibition, and lack of response to external stimuli, for example, waving of hand above aquaria (Fig. 2). Similar changes were evident in all groups exposed to TCDD by the end of the 28-d exposure, whereas the behavior of the controls remained normal. Although significant mortality did not occur in the two lowest exposure concentrations during 28 d of exposure, the fish were seriously stressed, as evidenced by an abnormal head-up swimming posture and confinement to the bottom of the aquar-

Table 6. Weight (g) of rainbow trout continuously exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d followed by a 28-d depuration period

	Mean TCDF exposure concentration (ng/L)					
Phase and day	0	0.41	0.90	1.79	3.93	8.78
Exposure[a]						
7	0.33	0.35	0.37	0.36	0.35	0.32
14	0.39	0.40	0.43	0.42	0.31	0.41
21	0.55	0.47	0.45	0.50	0.39[b]	0.44
28	0.59	0.59	0.53	0.48[b]	0.50[b]	0.46[b]
Depuration[c]						
28	1.1	0.91	0.85[b]	0.80[b]	0.79[b]	0.71[b]

Weights represent the mean of 8 to 24 observations.
[a]Analysis of variance used for testing the effects of exposure concentration and time; $F = 4.37$ (time × exposure), $p < 0.05$.
[b]Significantly different from controls (t test; $p < 0.05$).
[c]Analysis of variance used for testing the effect of exposure concentration; $F = 5.73$ (exposure), $p < 0.03$.

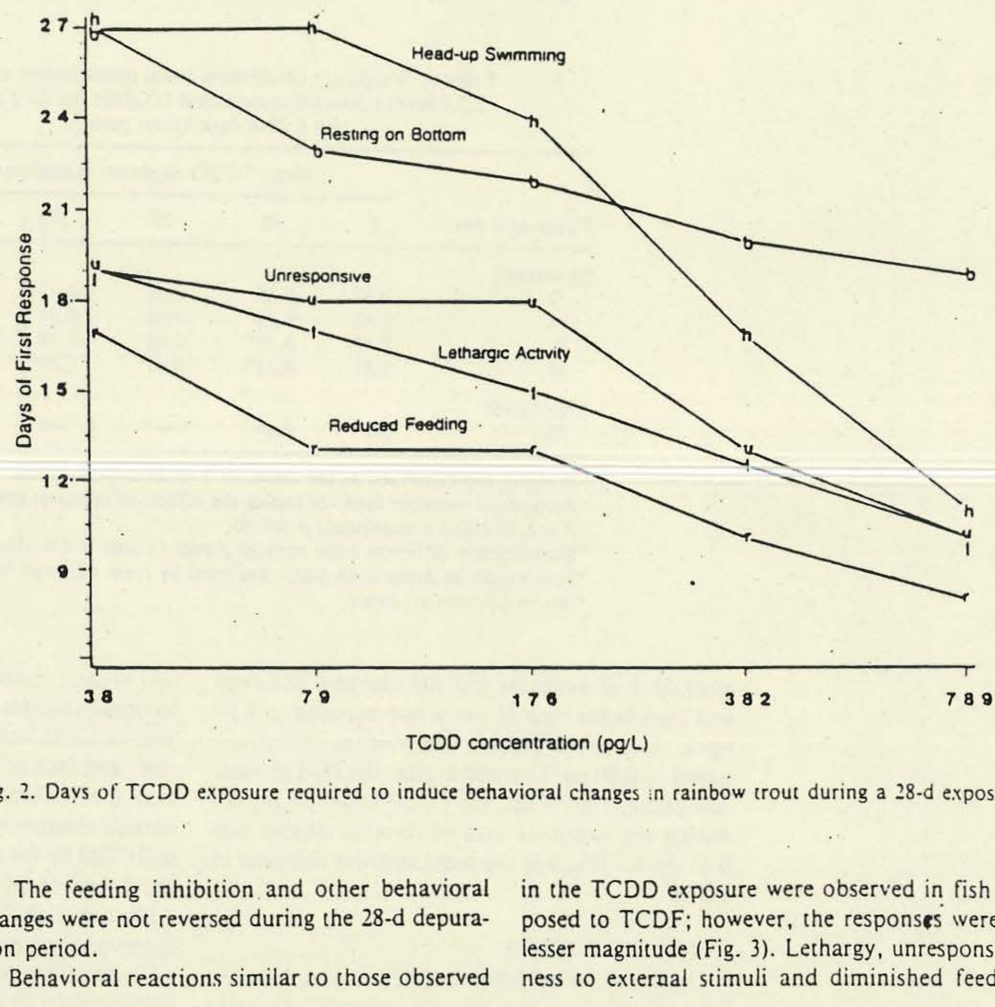


Fig. 2. Days of TCDD exposure required to induce behavioral changes in rainbow trout during a 28-d exposure.

ia. The feeding inhibition and other behavioral changes were not reversed during the 28-d depuration period.

Behavioral reactions similar to those observed in the TCDD exposure were observed in fish exposed to TCDF; however, the responses were of lesser magnitude (Fig. 3). Lethargy, unresponsiveness to external stimuli and diminished feeding

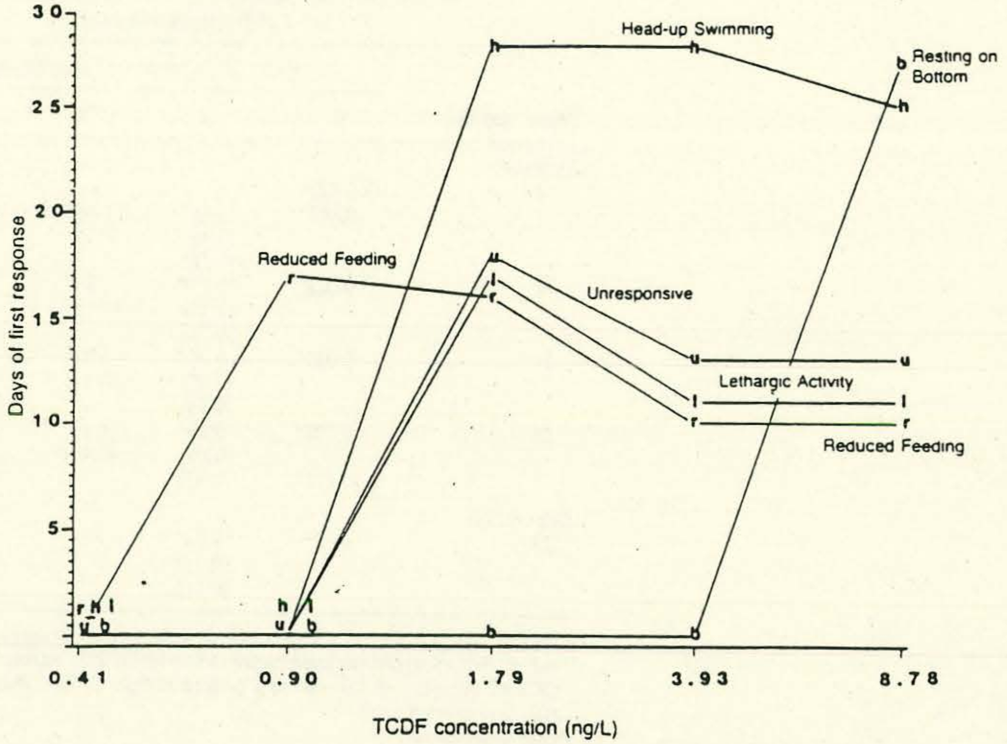


Fig. 3. Days of TCDF exposure required to induce behavioral changes in rainbow trout during a 28-d exposure.

reactions increased significantly in the three highest exposure groups. Recovery of behavioral function was evident in all but the two highest treatment groups by the end of the 28-d depuration period.

Neither TCDD nor TCDF induced observable responses in coloration or morphological characteristics such as scoliosis or lordosis; however, fin erosion was observed in fish in the lowest TCDD exposure concentration at the end of the depuration phase. In addition, exposure to both TCDD and TCDF induced observable, unique characteristics in fecal appearance. The two highest exposure concentrations of each toxicant induced long, stringy faces within the last several days of the 28-d exposure phase.

Bioconcentration

The BCFs for TCDD and TCDF differed greatly during the 28 d of continuous exposure. Whole-body residues throughout the exposure phase were in the low end of a 0.41 to 15.41 ng/g range for TCDD (Table 7). The greater the exposure concentration, the higher were the whole-body residues of TCDD during the 28-d exposures. The measured BCF for TCDD ranged from 8,558 to 28,664 during the exposure and did not appear to reach steady-state equilibrium in any of the exposure concentrations during the 28-d exposure (Table 8). The GC-MS analyses for whole-body TCDD levels agreed closely with the whole-body radiometric determinations for [^{3}H]TCDD. This similarity suggests that the ^{3}H label on the TCDD molecule was not being exchanged, and that the ^{3}H detected in the fish tissue was associated with the parent TCDD molecule. This similarity also indicates that organic extracted [^{3}H]TCDD was not being appreciably metabolized during the exposure and depuration phases. However, as judged by the results of total combustion of fish samples, it appears that about 30% of the ^{3}H label was associated with polar compounds that could have been TCDD metabolites.

Since it was apparent that a steady-state equilibrium for TCDD bioconcentration had not been reached after 28 d of exposure, we used the BIOFAC computer program [22] to estimate the bioconcentration kinetics for TCDD based only on data from the exposure phase. The estimated BCF at steady-state equilibrium was relatively consistent in fish from different exposure concentrations; the

Table 7. Whole-body residues of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout continuously exposed for 28 d followed by a 28-d depuration phase

	Mean TCDD exposure concentration (pg/L)				
Phase and day	0	38	176	382	789
Exposure					
0	[<0.02][a]				
7	0.012[a]	0.41[b] (0.05) [0.38]	1.68[b] (0.15)	3.44[b] (0.20)	6.75[b] (0.37) [6.78]
14	0.022[c]	0.77[b] (0.06) [0.71]	2.81[b] (0.18)	6.22[b] (0.67)	11.67[b] (0.68) [12.3]
21	0.023[d]	0.99[e] (0.03) [0.96]	3.87[b] (0.14)	10.10[e] (1.42) [11.3]	15.41[e] (0.86) [17.6]
28	0.027[a] [<0.02]	0.98[b] (0.05) [0.93]	4.52 (0.41)	10.95[b] (0.87) [10.8]	ND
Depuration					
28	0.22[a]	0.74[b] (0.11) [0.78]	ND	ND	ND

Values (ng/g) represent the mean (with standard deviation in parentheses) of individual fish analyzed radiometrically for [^{3}H]TCDD. Values in brackets represent GC-MS analyses performed on a pooled sample of fish, expressed as ng/g.
ND, not determined.
[a]One observation.
[b]Six observations.
[c]Two observations.
[d]Four observations.
[e]Eight observations.

Table 8. Measured bioconcentration factor (BCF)[a] for 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout exposed continuously for 28 d

	Measured TCDD exposure concentration (pg/L)			
Days of exposure	38	176	382	789
7	10,736	9,551	9,005	8,558
14	20,131	15,966	16,282	14,790
21	25,947	21,977	26,439	19,510
28	25,789	25,670	28,664	ND

[a]BCF = $(C_t/C_w) \times 1{,}000$. ND, not determined.

estimated BCF at 90% steady-state equilibrium ranged from about 37,000 to 86,000 (Table 9). Fish exposed to 382 pg/L showed somewhat different kinetics in that the estimated BCF, time to reach steady-state equilibrium and half-life were greater than in the other exposure concentrations. The relatively low K_2 value, compared with K_2 values from other exposure groups, suggested that metabolic effects may have been reducing the elimination of TCDD.

Ideally, the BCF should be estimated in fish not showing toxicity-induced responses. Inasmuch as the fish exposed to the lowest TCDD concentration of 38 pg/L showed the least toxic responses during the 28-d exposure, we suggest that the predicted BCF of 39,000 is probably the most reliable

Table 9. Estimated bioconcentration kinetics[a] of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in rainbow trout exposed to TCDD for 28 d

Kinetic parameter	TCDD exposure concentrations (pg/L)			
	38	176	382	702[b]
K_1, uptake rate constant (d^{-1})	1,852 (132)[c]	1,543 (69)	1,337 (61)	1,591 (53)
K_2, depuration rate constant (d^{-1})	0.047 (0.01)	0.041 (0.005)	0.015 (0.005)	0.043 (0.005)
BCF-K_B	39,000 (9,400)	37,560 (5,032)	86,000 (25,000)	36,637 (4,290)
Time to reach 90% steady state (d)	49 (11)	56 (7)	149 (43)	53 (6)
Elimination half-life, $t_{1/2}$ (d)	15 (3)	17 (2)	48 (13)	16 (2)

[a]Estimated kinetics using BIOFAC [22].
[b]Mean of TCDD measurements at days 1, 7, 14 and 21.
[c]Values in parentheses represent standard deviations.

estimate. The range in BCF we observed was substantially greater than the BCF of 7,000 to 9,270 previously reported in the literature [16,23,24]. Results from our study were perhaps better estimates of the equilibrium BCF because we used a continuous exposure in flowing water for a longer period at lower exposure concentrations. Based on the water solubility of 7.9 ng/L for TCDD [25], the predicted BCF would be about 467,000 if the regression equation, log BCF = 2.791 − 0.564 log S [26], were used; it would be about 1,000,000 if the regression equation, log BCF = 3.41 − 0.508 log S [27], were used.

We suggest from our experimental data that the overall bioconcentration from water to fish is probably much less than the theoretical estimation. The obvious toxicity-induced effects of TCDD, as well as potential influences on membrane transport and other metabolic functions, could account for the observed BCF being less than the theoretical predictions.

The estimated elimination half-life ($t_{1/2}$) from the BIOFAC ranged from 15 to 17 d among exposure concentrations, except for the estimated half-life of 48 d in fish exposed to 382 pg/L. Adams et al. [24] reported an elimination half-life of 15 d, and Branson et al. [16] reported a half-life of 58 d. In the fish exposed to 38 pg/L for 28 d and then held during the 28-d depuration phase, the whole-body residues did not decrease sufficiently to support an estimated half-life in the range of 15 to 17 d (Table 7). The whole-body residues decreased from 0.93 (±0.05) to 0.74 (±0.11) ng/g during the 28-d depuration phase. Excessive mortality in the other TCDD exposure concentrations precluded our obtaining experimental data on elimination in fish exposed to higher concentrations.

The uptake and depuration of TCDF were measured in fish exposed to 0.41 and 3.93 ng/L. In contrast to TCDD kinetics, TCDF uptake reached an apparent steady-state equilibrium after only 7 d of exposure (Table 10). Whole-body residues of TCDF did not increase after 7 d of exposure in fish exposed to 0.41 and 3.93 ng/L. In fish exposed for 28 d, the measured BCF was 6,049 at 0.41 ng/L and 2,455 at 3.93 ng/L (Table 11). The estimated bioconcentration kinetics of TCDF are shown in Table 12. Rainbow trout apparently were able to readily eliminate or metabolize TCDF. The whole-body residues in fish held during the 28-d depuration phase suggested a very short elimination half-life for this compound. Although TCDD and TCDF are structurally very similar, their bioconcentration kinetics and toxicities were found to be very different.

Table 10. Whole-body residues of 2,3,7,8-tetrachlorodibenzofuran (TCDF) in rainbow trout continuously exposed for 28 d followed by a 28-d depuration phase

Phase and day	Mean TCDF exposure concentration (ng/L)		
	0	0.41	3.93
Exposure			
0	<0.06		
7	0.17	1.63 (0.89)	11.9 (2.88)
14	0.12	1.80 (0.62)	9.30 (2.26)
21	0.19	1.05 (0.44)	10.7 (2.24)
28	0.22	2.48 (1.32)	9.65 (1.30)
Depuration			
28	<0.06	0.09 (0.06)	0.54 (0.08)

Values represent the mean (with standard deviation in parentheses) of four observations performed on individual fish, expressed as ng/g wet weight.

Table 11. Measured bioconcentration factors (BCF)[a] for 2,3,7,8-tetrachlorodibenzofuran (TCDF) in rainbow trout exposed continuously for 28 d

Days of exposure	TCDF exposure concentration (ng/L) 0.41	3.93
7	3,976	3,028
14	4,390	2,366
21	2,561	2,730
28	6,049	2,455

[a]BCF = $(C_t/C_w) \times 1{,}000$.

CONCLUSIONS

We conclude that TCDD and TCDF—especially TCDD—are extremely toxic to rainbow trout. A relative comparison of TCDD and TCDF chronic toxicities with those of several other organochlorine compounds demonstrated that TCDD is more than 10,000 times as toxic to fish as either endrin or toxaphene, and that TCDF is about 1,000 times more toxic than either of these insecticides (Table 13). Results from previous toxicity studies with fish by Helder [10,11], Miller et al. [12] and Adams et al. [24] demonstrated the toxicity of TCDD to be in the low ng/L range. However, we have shown that our lowest TCDD exposure concentration of 38 pg/L induced significant adverse effects on survival, growth, and behavioral responses. Results from our studies are perhaps more adequate estimates of TCDD toxicity because we used continuous exposure techniques for a longer time than had been used in previous studies. For similar reasons, we believe the BCF for TCDD derived from our studies is a more accurate estimate of the bioconcentration potential than are the estimates reported by Branson et al. [16] and Adams et al. [24]. Although we showed that TCDD was ex-

Table 12. Estimated bioconcentration kinetics[a] for TCDF in rainbow trout exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) for 28 d

Kinetic parameter	TCDF exposure concentration (ng/L) 0.41	3.93
K_1 uptake rate constant (d^{-1})	1,228 (1,191)	6,852 (8,037)
K_2 depuration rate constant (d^{-1})	0.28 (0.30)	2.60 (3.04)
BCF-K_B	4,449 (6,481)	2,640 (4,379)
Time to reach 90% steady state (d)	8 (9)	0.90 (1.04)
Elimination half-life, $t_{1/2}$ (d)	3 (3)	0.27 (3.1)

Values in parentheses represent standard deviations.
[a]Estimated kinetics using BIOFAC [22].

Table 13. Chronic no effect concentrations (μg/L) for growth and survival of freshwater fish exposed to various organochlorine chemicals

Chemical and fish species	Days of exposure	Survival	Growth[a]	Source
Aroclor 1254, brook trout	118	9.0	9.0	[28]
Chlorodecone, fathead minnows	120	>0.31	>0.31	[29]
Pentachlorophenol (ultrapure), fathead minnows	90	>139	>139	[30]
Toxaphene, brook trout	90	>0.50	0.38	[31]
Toxaphene, channel catfish	90	0.096	0.20	[32]
Endrin, bluntnose minnows	30	0.1	0.1	[33]
TCDD, rainbow trout	56	<0.000038	<0.000038	This study
TCDF, rainbow trout	56	0.00179	0.00041	This study

[a]Change in weight of fish.

tremely toxic to rainbow trout, even our lowest exposure concentration was too high to derive a NOEC.

Acknowledgement — We are grateful to the many people from the Fish and Wildlife Service (FWS), Battelle and Monsanto who assisted in conducting these studies. We especially thank Mr. Dave Zumwalt for his efforts in designing the specialized diluter exposure system, and Mr. Zumwalt and Mr. George Holroyd for their outstanding efforts in constructing and calibrating the system. We appreciate the excellent advice and assistance of Dr. Mark Ellersieck and Ms. Linda Sappington in analyzing the data, and the technical assistance of Mr. Rick Archeski in analyzing the behavioral data. We give special thanks to Dr. Paul Eschmeyer, Editorial Section, Office of Information Transfer, FWS, Fort Collins, Colorado, for his review of the manuscript and for editorial advice.

REFERENCES

1. **Olie, K., M.v.d. Berg** and **O. Hutzinger.** 1983. Formation and fate of PCDD and PCDF from combustion processes. *Chemosphere* 12:627–636.
2. **Firestone, D.** 1972. Determination of polychlorodibenzo-*p*-dioxins and related compounds in commercial chlorophenols. *J. A.O.A.C.* 55:85–92.
3. **Ballschmiter, K., W. Zoller, C. Scholz** and **A. Nottrodt.** 1983. Occurrence and absence of polychlorodibenzofurans and polychlorodibenzodioxins in fly ash from municipal incinerators. *Chemosphere* 12: 585–594.
4. **Petty, J.D., D.L. Stalling, L.M. Smith** and **J.L. Johnson.** 1983. Occurrence and potential impact of PCDF's and PCDD's in aquatic ecosystems. In D.D. Hemphill, ed., *Trace Substances in Environmental Health* – XVII. University of Missouri Press, Columbia, MO, pp. 96–102.
5. **Crummett, W.B.** 1982. Environmental chlorinated dioxins from combustion: The trace chemistries of fire hypothesis. In O. Hutzinger, R.W. Frei, E. Merian and F. Pocchiari, eds., *Chlorinated Dioxins and Related Compounds Impact on the Environment.* Pergamon Press, Elmsford, NY, p. 261.
6. **Ryan, J.J., P.-Y. Lan, J.C. Pilon** and **D. Lewis.** 1983. 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and 2,3,7, 8-tetrachlorodibenzofuran residues in Great Lakes commercial and sport fish. In G. Choudhary, L.H. Keith and C. Rappe, eds., *Chlorinated Dioxins and Dibenzofurans in the Total Environment.* Butterworth, Boston, MA, pp. 87–97.
7. **Columbia National Fisheries Research Laboratory.** 1983. Impacts of contaminants on early life stages of striped bass. In P.M. Mehrle and J.L. Ludke, eds., *Progress Report.* U.S. Fish and Wildlife Service, Columbia, MO.
8. **Belton, T.J., R. Hazen, B.E. Ruppel, K. Lockwood, R. Mueller, E. Stevenson** and **J.J. Post.** 1985. A study of dioxin contamination in select finfish, crustaceans, and sediments of New Jersey Waterways. Office of Science and Research, New Jersey Department of Environmental Protection, Trenton, NJ.
9. **U.S. Food and Drug Administration.** 1981. Correspondence from FDA Commissioner Dr. Arthur Hall Hayes, Jr., to Governor Milliken of Michigan concerning the public health significance of TCDD contaminant "levels of concern" for finfish in Great Lakes. 26 August.
10. **Helder, T.** 1980. Effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on early life stages of the pike (*Esox lucius* L.). *Sci. Total Environ.* 14:255–264.
11. **Helder, T.** 1981. Effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on early life stages of rainbow trout (*Salmo gairdneri*, Richardson). *Toxicology* 19: 101–112.
12. **Miller, R.A., A.N. Logan** and **C.L. Hawkes.** 1979. Toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in aquatic organisms. *Environ. Health Perspect.* 5: 177–186.
13. **Cooper, K.R., J. Schell, P. Kahn** and **M. Gallo.** 1986. The effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on the development and survival of the Japanese medaka (*Oryzias latipes*). *Toxicologist* 6:27 (Abstract).
14. **Kleeman, J.M., J.R. Olson, S.M. Chen** and **R.E. Peterson.** 1986. Metabolism and disposition of 2,3, 7,8-tetrachlorodibenzodioxin in rainbow trout. *Toxicol. Appl. Pharmacol.* 83:391–401.
15. **Kleeman, J.M., J.R. Olson, S.M. Chen** and **R.E. Peterson.** 1986. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin metabolism and disposition in yellow perch. *Toxicol. Appl. Pharmacol.* 83:402–411.
16. **Branson, D.R., I.T. Takahashi, W.M. Parker** and **G.E. Blau.** 1985. Bioconcentration kinetics of 2,3,7, 8-tetrachlorodibenzo-*p*-dioxin in rainbow trout. *Environ. Toxicol. Chem.* 4:779–788.
17. **American Public Health Association, American Water Works Association and Water Pollution Control Federation.** 1980. *Standard Methods for the Examination of Water and Wastewater*, 15th ed. American Public Health Association, Washington, DC.
18. **Smith, L.M.** 1981. Carbon dispersed in glass fibers as an adsorbent for contaminant enrichment and fractionation. *Anal. Chem.* 53:2152–2154.
19. **Smith, L.M., D.L. Stalling** and **J.L. Johnson.** 1984. Determination of part-per-trillion levels of dibenzofurans and dioxins in environmental samples. *Anal. Chem.* 56:1830–1842.
20. **Drummond, R.A., C.L. Russom, D.L. Geiger** and **D.L. DeFoe.** 1986. Behavioral and morphological changes in fathead minnow, *Pimephales promelas*, as diagnostic endpoints for screening chemicals according to mode of action. In *Aquatic Toxicology and Hazard Assessment: Ninth Symposium*. American Society for Testing and Materials, Philadelphia, PA, pp. 415–435.
21. **Snedecor, G.W.** and **W.C. Cochran.** 1967. *Statistical Methods*, 6th ed. Iowa State University Press, Ames, IA.
22. **Blau, G.E., W.B. Neely** and **D.R. Branson.** 1975. Ecokinetics: A study of the fate and distribution of chemicals in laboratory ecosystems. *AIChE J.* 21: 854–861.

23. **Isensee, A.R.** 1978. Bioaccumulation of 2,3,7,8-tetrachlorodibenzo-para-dioxin. *Ecol. Bull.* 27:255–262.
24. **Adams, W.J., G.M. DeGraeve, T.D. Sabourin, J.D. Cooney** and **G.M. Mosher.** 1986. Toxicity and bioconcentration of 2,3,7,8-TCDD to fathead minnows (*Pimephales promelas*). *Chemosphere* 15:1503–1511.
25. **Adams, W.J.** and **K.M. Blaine.** 1986. A water solubility determination of 2,3,7,8-TCDD. *Chemosphere* 15:1397–1400.
26. **Kenaga, E.E.** and **C.A.I. Goring.** 1980. Relationship between water solubility, soil sorption, octanol-water partitioning, and concentration of chemicals in biota. In J.G. Eaton, P.R. Parrish and A.C. Hendricks, eds., *Aquatic Toxicology*. STP 707. American Society for Testing and Materials, Philadelphia, PA, pp. 78–115.
27. **Chiou, C.T., V.H. Freed, D.H. Schmedding** and **R.L. Kohnert.** 1977. Partition coefficients and bioaccumulation of selected organic chemicals. *Environ. Sci. Technol.* 11:475–478.
28. **Mauck, W.L., P.M. Mehrle** and **F.L. Mayer.** 1978. Effects of the polychlorinated biphenyl Aroclor 1254 on growth, survival, and bone development in brook trout (*Salvelinus fontinalis*). *J. Fish. Res. Board Can.* 35:1084–1088.
29. **Buckler, D.R., A. Witt, Jr., F.L. Mayer** and **J.N. Huckins.** 1981. Acute and chronic effects of Kepone and mirex on the fathead minnow. *Trans. Am. Fish. Soc.* 110:270–280.
30. **Cleveland, L., D.R. Buckler, F.L. Mayer** and **D.R. Branson.** 1982. Toxicity of three preparations of pentachlorophenol to fathead minnows: A comparative study. *Environ. Toxicol. Chem.* 1:205–212.
31. **Mayer, F.L., P.M. Mehrle** and **W.P. Dwyer.** 1975. Toxaphene effects on reproduction, growth, and mortality of brook trout. EPA-600/3-75-013. U.S. Environmental Protection Agency, Duluth, MN.
32. **Mayer, F.L., P.M. Mehrle** and **W.P. Dwyer.** 1977. Toxaphene: Chronic toxicity to fathead minnows and channel catfish, EPA-600/3-77-069. U.S. Environmental Protection Agency, Duluth, MN.
33. **Mount, D.I.** 1962. Chronic effects of endrin on bluntnose minnows and guppies. U.S. Fish and Wildlife Service Research Report No. 58, Washington, DC.

Attachment 9

ASSESSMENT OF THE HUMAN HEALTH RISKS RELATED TO THE PRESENCE OF DIOXINS IN COLUMBIA RIVER FISH

Prepared by:

Russell E. Keenan, Ph.D.
Alan H. Parsons, Ph.D.
Ellen S. Ebert
Pamela D. Boardman, M.P.H.
Steven L. Huntley
Mary M. Sauer, M.S.P.H.

ChemRisk™
A McLaren Company
1685 Congress Street
Stroudwater Crossing
Portland, ME 04102
(207) 774-0012
(207) 774-8263

January 8, 1990

ChemRisk
A McLaren Company

An exposure pathway consists of four necessary elements: a source and mechanism of chemical release into the environment, an environmental transport medium for the released chemical, a point of potential human contact with the environmental medium, and a human exposure route (eg., inhalation, dermal contact, ingestion) at the point contact. Each pathway describes a unique potential mechanism by which a population or an individual may be exposed to a chemical. For each exposure pathway, the environmental fate and persistence of the chemical from the point of discharge to the point of human contact is an important consideration. Many factors such as adsorption onto particulates, sedimentation, and solubility influence the degree of human exposure. These factors are highly variable in the environment. Consequently, a truly valid exposure assessment can only be conducted using site-specific data. To this purpose, a study of the levels of dioxin in the edible portions of Columbia River fish has been conducted. Additionally, the rates of consumption of locally caught fish were estimated.

Columbia River fish sampling

For the purpose of determining accurate species-specific concentrations of dioxin in edible fish fillets, a variety of species of fish were collected from six different sites along the Columbia River system by an independent laboratory and consultant. A total of 680 individual fish were sampled at the six sites. Species collected included top and bottom feeders as well as resident and anadromous populations. Migratory fish sampled included coho salmon, fall chinook salmon (upriver and tule) and summer steelhead trout. Resident species sampled included white sturgeon, largescale sucker, and carp. Results of sampling data are reported below[1].

Fillet TCDD Levels in Columbia River Fish (ppt)

Species	Sampling Site					
	1	2	3	4	5	6
Coho salmon	0.08	0.10	NS	NS	NS	NS
Fall chinook salmon (Upriver)	0.08	0.09	NS	NS	NS	NS
Fall chinook salmon (Tule)	0.31	0.18	NS	NS	NS	NS
Summer steelhead trout	0.07	0.07	NS	NS	NS	NS
White sturgeon	0.09	0.12	1.09	0.88	1.68	0.55
Largescale sucker	0.32	NS	0.39	0.19	0.22	0.26
Carp	0.79	NS	1.06	1.35	1.46	0.76

At Sites 1 and 2, located downstream of NWPPA pulp and paper mills, the geometric mean concentrations of TCDD in salmon ranged from 0.08 to 0.31 parts per trillion (ppt) and steelhead trout averaged 0.07 ppt. Sturgeon, sucker, and carp collected from sites 1, 2, 3, and 4 had fillet TCDD levels averaging

[1] Note: 80% of the anadromous and 45% of all species sampled had nondetectable levels of TCDD. Nondetectable samples were assigned a value equal to one half the limit of detection per EPA protocol. This results in a more conservative estimation of tissue TCDD levels because actual values could equal zero.

DRAFT Attachment 10

ANALYSIS OF THE POTENTIAL POPULATIONS AT RISK FROM THE CONSUMPTION OF FRESHWATER FISH CAUGHT NEAR PAPER MILLS

Craig McCormack
Office of Policy Planning and Evaluation

David Cleverly 202-382-7891 (D.C)
Office of Research and Development

April 23, 1990

INTRODUCTION:

OTS, OSW, and OW have conducted a detailed human and ecological risk assessment of environmental loadings of dioxin from bleached pulp and paper mills. In that analysis only maximum lifetime cancer risk and average lifetime cancer risk to the hypothetically exposed individual was estimated for various exposure scenarios. No estimation of potential population risk, especially to sensitive subgroups, was provided in the analysis. Since draft publication of these results, we have identified populations of Asians, and tribal Native Americans that reside along the banks of the Columbia River in Oregon. The State government indicates that there are eight bleached pulp and paper mills that directly discharge to the Columbia River. The State also indicates that freshwater fish caught from the Columbia river are the main source of animal protein for these people. They consume an average of 100 to 150 grams of fish flesh each day over the course of the year. These individuals are much more likely to catch and consume fish that has been contaminated with dioxin from the effluent discharged from the mills than other populations in the area. The Native Americans number about 15,000, and the Asians number about 30,000 people.

In addition to these subpopulations exposed by diet to dioxin, we have estimated that approximately 610,000 people living in the vicinity of pulp and paper mills have family incomes at or below the poverty level. These individuals are also expected to derive a significant portion of animal protein from both subsistence and sports fishing in rivers near paper mills. Subsistence fishermen consume about 100 grams of fish per day/1, and sports fishermen consume about 69 grams fish per day/2.

For purposes of the assessment of potential cancer risk, we have employed monitoring data of dioxin contamination in fresh water fish caught in the vicinity of bleached pulp and paper mills. This was developed by the Environmental Research Laboratory in Duluth Minnesota as part of the National Bioaccumulation Study of freshwater fish in the U.S. The range of detected TCDD equivalent concentration in the edible fish fillet was from 0.1 ppt - 24 ppt. The weighted

average fillet concentration was 6.5 ppt (6.5 pg/gm). For purposes of estimating incremental lifetime cancer risk to the most exposed individual, a fillet concentration of 24 ppt was used. The weighted average dioxin concentration in the fillet of 6.5 ppt was used to derive the approximate average lifetime risk to subsistence and sports fishermen. The average exposure and average lifetime risk was used to estimate the annual cancer incidence in these sensitive subpopulations. In addition a human body weight of 70 kilograms was assumed to compute estimates of excess cancer risk.

CONCLUSIONS:

It is currently not possible to directly measure the association between the chronic dietary intake of dioxin contaminated freshwater fish, and the occurrence of specific forms of cancer in the exposed populations. The epidemiologic studies of these populations with a high dependency for subsistence fishing as a source of dietary animal protein have not been conducted. Therefore we have mathematically estimated lifetime excess cancer risk to the population residing near the Columbia River, as well as to low-income populations living in the vicinity of other mills in the U.S. This analysis is not intended to replace any previous risk assessments involving the human consumption of fish that has been contaminated with dioxin from the effluent discharged from paper mills, but is merely to illustrate that methodologies can be developed to estimate total populations at risk in the U.S.

The following are the results:

	Pop.	MIR(a)	AVG Risk(b)	Cancer Inc.(c)
Native Americans	**15,000. . . .**	**8.6 X 10^{-3}**	**1.5 X 10^{-3}**	**0.33**
Asian Americans	**30,000**	**8.6 X 10^{-3}**	**1.5 X 10^{-3}**	**0.67**
Total Risk	**45,000**	**8.6 X10^{-3}**	**1.5X 10^{-3}**	**1.0**
Low income families	**610,000**	**5.4X 10^{-3}**	**1.0 X 10^{-3}**	**9.3**

(a) MIR is the maximum individual risk, and is associated with the highest fish consumption rate and the highest dioxin concentration in fish caught near paper mills.

(b) Average lifetime cancer risk is the excess cancer risk based on the average fish consumption rate for subsistence and sports fishermen, and the weighted average dioxin concentration in fish caught near paper mills.

(c)Cancer incidence is the estimated number of cancer cases per year within the

defined exposed population. This was computed using average lifetime risk.

1/ U.S. Environmental Protection Agency (1988). Risk Assessment for Dioxin Contamination Midland, Michigan. Region 5. EPA-905/4-88-005.

2/Estimated consumption by the U.S. Food and Drug Administration, assuming substitution of average U.S. population daily consumption of red meat with fish.

Calculations of Risk

1. Native Americans

Assumptions:

a. MEI consumes 150 gms fish/day.
b. Average consumption is 100 grms fish/day.
c. 70 kilogram person.
d. Lifetime exposure.
e. Max. dioxin concentration in fish fillet = 24 pg/gm.
f. Weighted average dioxin in fish fillet = 6.5 pg/gm.
g. Population of 15,000.
h. Risk Specific Dose of Dioxin = lifetime cancer risk of one in a million is: 0.006 pg/kg/day.

Max. Daily Dose= (150 gms/day X 24 pg/gm) / 70 kg person
= 51.43 pg dioxin/kg/day

MIR ={(51.43 pg/kg/day) / (0.006 pg/kg/day)} X 10^{-6}
MIR = 8.6 X 10^{-3}

Avg. Daily Dose= (100 gms/day X 6.5 pg/gm)/ 70 kg person
= 9.28 pg dioxin/kg/ day

Avg. lifetime risk = {(9.28 pg/day)/(0.006 pg/kg/day)} X 10-6
= 1.5 X 10^{-3}

Annual Cancer Incidence = (Avg risk * population)/ 70 year lifespan
= (1.5 X 10^{-3} * 15,000)/ 70 yrs
= 0.33

2. Asian Americans

Assumptions are the same as with Native Americans. The population size is

MEI = maximally exposed individual

30,000.

Max. Daily Dose = 51.43 pg dioxin/kg/day.
MIR = 8.6 X 10-3

Avg. Daily Dose = 9.28 pg dioxin/kg/day
Avg. lifetime risk = 1.5×10^{-3}

Annual Cancer Incidence = (1.5×10^{-3} * 30,000)/70 yr lifespan
= 0.67

3. Low income families.

Assumptions:

a. MEI consumes 100 gms fish/day.
b. Average consumption is 69grms fish/day.
c. 70 kilogram person.
d. Lifetime exposure.
e. Max. dioxin concentration in fish fillet = 24 pg/gm.
f. Weighted average dioxin in fish fillet = 6.5 pg/gm.
g. Population of 610,000.
h. Risk Specific Dose of Dioxin = lifetime cancer risk of one in a million is: 0.006 pg/kg/day.

Max Daily Dose = (100 gms/day) X (24 pg dioxin/gm)/ 70 kg person
= 34.28 pg dioxin/kg/day

MIR = {(34.28 pg/kg/dy)/(0.006 pg/kg/dy)} X 10^{-6}
= 5.7×10^{-3}

Avg. Daily Dose = (69 gms/day) X (6.5 pg/gm)/70 kg person
= 6.41 pg dioxin/kg/day

Avg. lifetime risk = { (6.41 pg/kg/dy)/(0.006 pg/kg/dy)} X 10-6
= 1.0×10^{-3}

Annual Cancer Incidence ={ (1.0×10^{-3}) * (610,000)}/ 70 year lifespan
=9.3

The Bottom Line:

• The "Forest through the trees" is that the environmental loadings of dioxin from the mills may result in high levels of risk to humans.

• The analysis of the regulatory options suggests that this particular industrial source category fits the mold for a regulatory pollution prevention initiative through use of the CWA, TSCA, and RCRA.

* could require substantial reduction in the overall use of chlorine
* BACT seems to be oxygen delignification

OREGON

INSIDER

A BIWEEKLY DIGEST OF ENVIRONMENTAL NEWS

Inside the Dioxin Standard: Is it Defensible?

■ The Environmental Quality Commission (EQC) will decide Nov. 2 whether to hold public hearings on a complex proposal to update the state's water quality standards. The proposal covers an enormous number of topics including a new "anti-degradation standard" to protect pristine waterways, a new "wetlands" definition, and new standards for dissolved oxygen, bacteria, toxic pollutants, particulate matter and bacteria (see Issue 20).

Tucked somewhere in the middle of the package, the Department of Environmental Quality (DEQ) has proposed to keep unchanged the current and seemingly incomprehensible water quality standard for dioxin: 0.013 parts per quadrillion (ppq). In addition, the agency has for the first time proposed a standard limiting the amount of dioxin that can accumulate in fish tissue. Both proposals are sure to draw the attention of the pulp and paper industry and environmentalists.

Industry representatives have long questioned the scientific underpinnings of the dioxin standard. They have even challenged the assertion that dioxin poses any threat to human health or the environment, comparing it to broccoli in one study. On the other hand, environmentalists see a standard that leaves completely unregulated hundreds of closely related toxic organo-chlorine compounds that are discharged from bleach kraft pulp mills every day. Based only on protecting human populations from cancer, they also see a standard that ignores documented impacts on fish and wildlife and fails to address non-cancerous affects on human health such as reproductive interference and immune system suppression.

Each side contends that the standard for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) -- the only compound regulated by DEQ's dioxin standard -- should be changed in some way. For now, DEQ has decided to keep the standard as it is.

The standard "answers" a very narrow question for DEQ and the public: How much 2,3,7,8-TCDD can exist in the water column without creating more than a 1-in-a-million cancer risk?

The standard does not regulate the amount of dioxin in river bottom sediments, where a seemingly significant percentage of these insoluble compounds settle. It does not take into account the natural loss, or "attenuation," of dioxin through breakdown and binding with particles suspended in the water column. And, since compliance with the standard is measured down river at the edge of the "mixing zone," it isn't even used to directly regulate the amount of dioxin coming out of pulp mill discharge pipes.

There are significant gaps in the scientific understanding of this toxin and in the regulatory mechanism by which it is controlled. While it is impossible to resolve the many questions surrounding dioxin, it is not particularly difficult to understand the guts of the standard and how the federal government came up with the result of 0.013 parts per quadrillion.

CONTENTS

An Understandable Formula

For all the rhetoric, battling experts, and discussions of "linearized multistage models," "LD_{50} values" and all the rest, the standard is surprisingly understandable. The Environmental Protection Agency developed the dioxin standard using a relatively simple formula that includes six factors:

$$\text{Dioxin Standard} = \frac{\text{RISK} \times \text{WT}}{[\text{WCR} + (\text{BCF} \times \text{FCR}) \times \text{CPF}]}$$

The Six Factors

RISK: The cancer risk society is willing to tolerate from dioxin.

WT: The weight of the average adult.

WCR: The amount of water ingested by the average person each day — called the water consumption rate.

BCF: The extent to which fish concentrate dioxin in their tissues by swimming in contaminated water — called the bio-concentration factor.

FCR: The amount of fish ingested by the average person each day — called the fish consumption rate.

CPF: The chemical's cancer potency, a measure of how harmful the toxin really is — called the cancer potency factor.

The Overall Debate

Agency officials, industry representatives and environmentalists seem to agree that the formula itself is scientifically defensible. The debate rages over what numbers go into the formula and to many broader issues surrounding dioxin regulation.

EPA/DEQ Numbers

Through laboratory tests and simple assumptions, EPA assigned values to each of these factors, plugged them into a formula, and came up with the dioxin standard. DEQ adopted all of EPA's recommended values. With estimates of potential compliance costs running in the hundreds of millions of dollars and predictions of disastrous human health and environmental impacts, there is a surprisingly high degree of "play" in the numbers used to calculate the final standard. As a result, experts on both sides have been free to tweak the

THE EPA/DEQ NUMBERS:

RISK	1-in-a-million
WT	70 kilograms*
WCR	2 liters/day
BCF	5,000
FCR	6.5 grams/day*
CPF	156,000

* 6.5 grams per day is about ¼ of an ounce of fish. 70 kgs is about 155 pounds.

OREGON INSIDER (ISSN 1043-7142) is published biweekly (twenty-four times a year) as a news service of the Oregon Environmental Foundation, 2637 SW Water Avenue, Portland, Oregon 97201 (503) 222-2252. The Foundation is a non-profit corporation dedicated to education and research. Executive Editor: Peter A. Ravella, OSB No. 86264, Staff Writers: Jeff Bernstein & Sarah McCoy. Business Manager: Greg Tozian. Advisory Board Members: Roy Hemmingway, Consultant; Margaret Kirkpatrick, Attorney, Stoel, Rives, Boley, Jones & Grey; Judy Roumpf, Publisher, Resource Recycling magazine; Connie Taylor, Associate, HartCrowser; Dan Saltzman, President, Environmental Management Solutions and Diane Dimon Snow, Assistant to Earl Blumenauer. Subscription Rates: $245 per year including first-class delivery, $135 for private, non-profit 501(c)(3) organizations. Multiple subscription rates available. Letters to the Editor and comments welcome at above address.

numbers to better fit their view of the relative risks and benefits of dioxin regulation.

Three of the six factors are generally accepted and attract little attention. These are the water consumption rate, body weight, and the acceptable risk (RISK) determination.

THE "ACCEPTED" NUMBERS

WCR - 2 liters/day

Water Consumption Rate (WCR). Because of how the formula works, this factor has virtually no affect on the final standard and consequently draws little attention. If DEQ were to eliminate drinking water as a route of dioxin exposure altogether -- and plug in a "0" for the WCF -- the final standard would not change.

WT - 70 kilograms

Body Weight Factor (WT). EPA used 70 kilograms for the body "weight" factor. At about 155 pounds, this seems to be a pretty good approximation of the average adult's weight. The dioxin standard would be stricter if the agency plugged in a smaller number for body weight. For example, had EPA used 50 kilograms -- about 110 pounds -- the final dioxin standard would be .009 PPQ instead of .013 PPQ.

All else being equal, people weighing less than 155 pounds, such as children and women would, on average, face a slightly greater risk of cancer than their heavier counterparts under the .013 PPQ standard.

RISK - 1-in-a-million

Acceptable Cancer Risk (RISK). There is no magic behind DEQ's decision to base the state's dioxin standard on a 1-in-a-million cancer risk. It is not mandated by federal or state law; it is a policy decision. According to Lydia Taylor, administrator of the Water Quality Division, all DEQ water quality standards have been based on this risk level since 1987.

1-in-10-million?

Reasonable people differ whether it would be appropriate to set environmental regulatory policy on a less demanding cancer risk limit. John Bonine, a professor of environmental law at the University of Oregon, questioned whether the general population should be subjected to any greater cancer risk for the sake of industry profits. "EPA has developed guidance for dioxin based on a 1-in-10-million cancer risk. Oregon is free to adopt it but hasn't," he said.

A standard based on a 1-in-10-million cancer risk would be ten times tougher than the current one, or .0013 PPQ.

1-in-10,000?

According to Doug Morrison, environmental counsel for the Northwest Pulp & Paper Association, using a 1-in-a-million cancer risk level can be overly protective. Morrison said it would be statistically sound to accept cancer risks as high as 1-in-100,000 or 1-in-10,000 for certain sub-populations -- such as Native Americans, Asians and recreational fisherman who eat more river fish -- because there are fewer than 1 million in the group. "You can allow a higher risk factor for these smaller groups and still not cause any additional cancers," he said.

Other States Vary

At least one other state has decided to accept greater risks. Maryland's dioxin standard is based on a 1-in-100,000 cancer risk and is 1.2 PPQ, about 100 times less stringent than Oregon's.

DEQ Uses 1-in-a-million

Because DEQ's Water Quality Division has uniformly set its standards based on a 1-in-a-million cancer risk, it seems unlikely that the state would follow Maryland's lead. The EQC has made it an agency-wide goal to apply a uniform risk level to all regulatory programs, but that level has not been defined, (see DEQ 1990 "Strategic Plan."

THE "CONTROVERSIAL" NUMBERS

The remaining three factors -- fish consumption (FCR), cancer potency (CPF), and bio-concentration (BCF) -- have attracted the most debate for a couple of reasons. Not only do these factors have the greatest impact on the final standard, but the information on them is less developed. The bio-concentration and cancer potency numbers are based on laboratory studies that remain open to interpretation in the scientific community. Definitive surveys on consumption of Columbia River fish have not been done.

FCR: Who Does the Standard Protect?

Fish Consumption Rate (FCR). The debate over this factor is not complicated. Because different people eat different amounts and kinds of fish, a simple question arises: What single number best represents the public's average fish consumption? The answer may be, "There isn't one."

EPA's Number

In adopting the dioxin standard, DEQ accepted EPA's estimate that the average person consumes 6½ grams of freshwater or estuarine fish per day. That's a little less than one-quarter of an ounce per day, or about 5 pounds of fish and shellfish per year. According to Gene Foster, DEQ's expert on the dioxin standard, EPA based its estimate on a limited nationwide market survey of consumer buying habits.

Complete Data is Unavailable

"Complete fish consumption data has not been compiled specifically for the Columbia River system -- where the pulp mills discharge their effluent -- or for the fish most commonly consumed," said Foster. With the help of the Columbia River Intertribal Fish Commission, EPA is studying the diets of Native Americans along the river. Results could be available by year's end.

Accounting for Sub-Groups

Foster said differences between identifiable sub-groups cannot be overlooked when compiling fish consumption data. Native Americans -- particularly those living along the river -- Asians, commercial and recreational fisherman, and low-income subsistence fisherman all eat more fish than the general population.

FCR Range: 6.5 to 150 g/day

According to a preliminary risk assessment done by EPA this Summer, members of some sub-groups along the Columbia consume as much as 100 to 150 grams or about 3½ to 5¼ ounces of fish per day. "These rates are not off the wall," added Foster.

Industry says 13 - 16 g/day

Even the Northwest Pulp and Paper Association (NWPPA) -- an industry trade group -- acknowledges that EPA's 6.5 g/day figure is too low. The NWPPA estimates that recreational fisherman and Native Americans eat a little more than 13 and 16 grams of fish per day, respectively.

Most Agree 6.5 g/day is Low

The table at right shows how the dioxin standard would change if higher fish consumption numbers were plugged into the formula. No one claims that the average fish consumption rate in the Northwest is less than the 6.5 g/day. While

HOW MUCH FISH DO YOU EAT?

Grams Per Day	No. of 6 oz. Meals / Wk.	New Standard*
6.5	.2	0.013
10	.4	0.089
25	1.0	0.0035
50	2.0	0.0017
75	3.0	0.0012
100	4.0	0.0009
150	6.0	0.0006

* This is how the standard would change if DEQ used a higher FCR.

individuals may consume as much as 150 g/day, the overall average for the population would be lower.

BCF: Inadequate Science

Bio-concentration Factor (BCF). Dioxin in the environment tends to concentrate in living organisms, but in different ways and in different amounts. This factor quantifies the amount of dioxin fish concentrate in their tissues by swimming in contaminated water. Surprisingly, it does not take into account dioxin entering the fish through the food chain, just absorption through the skin.

Simplistic Studies

Based on simplistic laboratory experiments, EPA concluded that some fish concentrate 5,000 times as much dioxin in their tissues as is found in the water column. As with all other factors, DEQ adopted EPA's conclusion rather than conduct its own experiments.

Food Chain Ignored

Environmentalists argue a BCF of 5,000 grossly underestimates the amount of dioxin in fish tissue and therefore, the amount ingested by humans. "This is a significant oversight in the standard," said Bonine. "Scientists have documented dioxin accumulation in fish through the food change -- called "bio-accumulation" -- and it is a more important route of exposure than absorption through the skin," he said.

BCF Could Go Higher

Agency officials, industry representatives, and environmentalists generally agree that the BCF should be higher. The debate is over how much higher. Studies conducted for the NW Pulp & Paper Association indicate the BCF for sturgeon ought to be 10,600, over twice as high as the number EPA plugged into the formula.

BCF for Non-Resident Fish at Issue

"We acknowledge that our effluent is responsible for elevated dioxin levels in local, resident fish populations near our discharge pipes, said Llewellyn Matthews, executive director of the NWPPA. "We are not convinced that pulp mill effluent contributes to dioxin levels found in non-resident fish such as salmon. There are other sources of dioxin," she said.

HOW MUCH DIOXIN DO FISH ACCUMULATE?

BCF Values	New Standard*
10,000	0.0069
25,000	0.0027
50,000	0.0013
75,000	0.0009
100,000	0.0006
150,000	0.0004

* This is how the standard would change if DEQ used a higher BCF.

BCF Range: 5,000 to 150,000

According to Bill Diamond, director of EPA's Water Quality Criteria and Standards Division, EPA studies suggest the bio-concentration factor could range as high as 159,000.

Environmentalists have even argued the BCF could be as high as 500,000 for some species, if contamination of the food chain is taken into account.

DEQ Leans to 50,000

DEQ seems to be leaning toward a moderate increase in the bio-concentration factor. "The conclusions on this factor are very crude at this point," said Foster. "My guess is it will settle in somewhere around 50,000 to 60,000." The table at right shows how the dioxin standard would change if a higher bio-concentration factors were used. According to Foster, DEQ is planning to conduct field studies to develop a more accurate BCF for Columbia River fish.

CPF: How Toxic is Dioxin?

Cancer Potency Factor. Most of the debate has focused on this factor, which indicates dioxin's human cancer-causing potential. All arguments by industry and the environmental community regarding dioxin's dangerousness are subsumed in this factor. A closer look at this factor reveals that even if the industry's lowest cancer potency number is plugged into the formula, the dioxin

standard is still less than 1 part per quadrillion.

EPA selected a CPF of 156,000 mg/kg/day. The higher the CPF, the more dangerous the chemical, and the lower the water quality standard.

The Kociba Study . . .

The federal agency based its CPF on a single, two-year rat liver study completed in 1978 by Dr. R.J. Kociba. Since then, industry representatives and some members of the scientific community have challenged the Kociba study. Critics point out that the model used to develop the CPF is too simplistic. They argue Dr. Kociba improperly counted "precancerous liver tumors," failed to incorporate a "no observable affect level" in the test, and made other errors.

Under Attack

Dr. Robert Squire, a John Hopkins researcher and participant in the original study, recently reevaluated Dr. Kociba's data and concluded that the CPF was too high, possibly by a factor of 10 or more. EPA and DEQ acknowledge that legitimate questions surround the Kociba study but they are not prepared to change the CPF yet.

Other Agencies Use Lower CPFs

Other federal agencies use cancer potency factors much lower than EPA's. The U.S. Food and Drug Administration uses a CPF of 17,500 and the federal Center for Disease Control uses 36,000. According to Lydia Taylor, the administrator of DEQ's Water Quality Division, it would not be appropriate for DEQ to regulate dioxins based strictly on these cancer potency factors. "FDA is required to take economics into account when developing their cancer potency factor and we are not," she said.

Industry Wants State Review

The NWPPA has repeatedly urged DEQ to conduct its own review of dioxin's cancer potency. "The upshot is we believe they have over estimated the cancer potency of dioxin and that the states should do their own independent analysis of this factor," said Matthews.

The Washington Department of Health — with help from University of Washington researchers — has undertaken its own study of dioxin's cancer potency. EPA also has a study underway but Oregon does not.

DEQ May Respond

"We will be looking at the cancer potency factor when the new data is available from EPA, but for now we are satisfied with the value we are using," said DEQ's Foster.

CPF Range: 6,700 to 250,000

The range of CPF values seems to be between 6,700 and 250,000. The NWPPA says 6,700 to 9,700 is justified based on the Squire re-analysis and other studies. Environmentalists have challenged the objectivity of the Squire re-analysis and argue that there is no compelling reason to lower the CPF. They also assert that the CPF could be as high as 250,000.

HOW POTENT IS DIOXIN?

CPF Values	New Standard*
6,700	0.321
9,700	0.222
17,500	0.123
36,000	0.059
250,000	0.008

* This is how the standard would change if DEQ used a lower CPF.

DEQ Leans to 15,000

According to Foster, some studies suggest that the CPF could be as low as 15,000. If such a CPF were used, the dioxin standard would be about 0.12 PPQ, or about 10 times less strict than the current standard.

The table at right shows how the dioxin standard would change if lower CPF values were plugged into the formula. None of the new standards exceeds a single part per quadrillion.

PULLING IT TOGETHER

How Does the Standard Change?

The large table on page 8 shows how the dioxin standard changes as the various parameters are "tweaked" one at a time. It also shows what happens if the controversial factors were all changed at the same time, rather than independently of each other. With the help of industry, the environmental community and DEQ, four new dioxin standards were developed — two "NWPPA Numbers," the "Bonine Numbers" and the "DEQ Lean To."

Industry's Scenario

NWPPA Numbers. These numbers were provided by Doug Morrison, an attorney for the NW Pulp and Paper Association. If DEQ were to assume a fish consumption rate of 13.4 grams per day, a bio-concentration factor of 10,600 and a cancer potency factor of 6,700, the final dioxin standard would be .073 PPQ, about 5 times less strict than the current standard but still less than 1 PPQ. If the CPF were 9,700 — the NWPPA's upper end estimate — the final standard would be .050 PPQ.

Environmentalists' Scenario

Bonine Numbers. As an "exercise in number crunching," John Bonine agreed to provided his estimates for the factors: a fish consumption rate of 100 grams per day to protect Native Americans; a body weight of 50 kilograms — about 110 pounds — to better protect women and children; a risk factor of 1-in-10-million; and a bio-concentration factor of 50,000. Based on these assumptions, the dioxin standard would be 0.0000021 PPQ or 0.0021 parts per quintillion.

Bonine is actively engaged in the dioxin debate, representing the Northwest Coalition for Alternatives to Pesticides (NCAP) in litigation over DEQ's dioxin regulations.

FOUR POSSIBLE STANDARDS

Source of Values	New Standard*
NWPPA Numbers	.050
NWPPA Numbers	.073
Bonine Numbers	.0000021
DEQ 'Lean To'	.0037

* This is how the standard would change if EPA used the unofficial values provided by industry, environmentalists and DEQ.

DEQ's 'Lean To' Scenario

DEQ 'Lean To'. This scenario was developed with DEQ's help but does not reflect the agency's position on the dioxin standard. These numbers used are values the agency may "lean to" if the standard is eventually reviewed. The values are a fish consumption rate of 25 grams per day (about 1 fish meal per week), a bio-concentration factor of 50,000, and a cancer potency factor of 15,000 (over 10 times smaller than EPA's current CPF of 156,000, and smaller than any CPF employed by other federal agencies). Based on these assumptions, the final dioxin standard would be .0037 PPQ, or about 3½ times more strict than the current standard.

CONCLUSION

No Silver Bullets

All parties to the controversy acknowledge that the .013 PPQ dioxin standard is based on rough guesses and uncertain science.

Whether DEQ's dioxin standard is too strict, or not strict enough, depends on each individual's personal sense of comfort with levels of acceptable risk, and the economics of reaching the standard. As Dr. Donald Barnes, Director of the

TWEEKING THE NUMBERS: A LOOK AT HOW THE STANDARD CHANGES

	Fish Consumpt (FCR)	Water Consumpt (WCR)	Body Weight (WT)	Accepted Risk (RISK)*	Bioconcentration (BCF)	Cancer Potency (CPF)*	Final Standard
DEQ's Standard	6.5 (g/day)	2 (l/day)	70 (kg)	1.00E-06	5,000	156,000 (mg/kg/day)	.013 PPQ
	10	2	70	1.00E-06	5,000	156,000	.0089 PPQ
Tweeking	25	2	70	1.00E-06	5,000	156,000	.0035 PPQ
the	50	2	70	1.00E-06	5,000	156,000	.0017 PPQ
FCR	75	2	70	1.00E-06	5,000	156,000	.0012 PPQ
	100	2	70	1.00E-06	5,000	156,000	.0009 PPQ
	150	2	70	1.00E-06	5,000	156,000	.0006 PPQ
	6.5	2	70	1.00E-06	10,000	156,000	.0069 PPQ
Tweeking	6.5	2	70	1.00E-06	25,000	156,000	.0034 PPQ
the	6.5	2	70	1.00E-06	50,000	156,000	.0013 PPQ
BCF	6.5	2	70	1.00E-06	75,000	156,000	.0009 PPQ
	6.5	2	70	1.00E-06	100,000	156,000	.0006 PPQ
	6.5	2	70	1.00E-06	150,000	156,000	.0004 PPQ
	6.5	2	70	1.00E-06	5,000	6,700	.321 PPQ
Tweeking	6.5	2	70	1.00E-06	5,000	9,700	.222 PPQ
the	6.5	2	70	1.00E-06	5,000	17,500	.123 PPQ
CPF	6.5	2	70	1.00E-06	5,000	36,000	.059 PPQ
	6.5	2	70	1.00E-06	5,000	250,000	.008 PPQ
NWPPA Numbers	13.4	2	70	1.00E-06	10,600	9,700	.050 PPQ
	13.4	2	70	1.00E-06	10,600	6,700	.073 PPQ
Bonine Numbers	100	2	50	1.00E-07	150,000	156,000	.0000021
DEQ's 'Lean To'	25	2	70	1.00E-06	50,000	15,000	.0037 PPQ

*NOTE: The RISK FACTOR is expressed in Lotus 1-2-3 scientific notation. A 1.00E-06 notation means a 1-in-a-million risk and 1.00E-07 means 1-in-10-million.

EPA's Science Advisory Board, told the EQC this summer, "When it comes to dioxin, there are a lot of uncertainties; there are no silver bullet answers."

Standard Unlikely to Exceed 1 PPQ

Whatever else is decided, a few conclusions can be drawn. First, no single factor will be changed in isolation. Both DEQ and EPA are committed to a full review all the factors, not just the just the cancer potency, bio-concentration, or fish consumption numbers. Second, even if adjustments are made, it appears the final standard will remain below a single part per quadrillion, far below the detectable limits of today's instruments. Third, under all the scenarios presented, it appears the Columbia River will remain "water quality limited," forcing the mills to make expensive improvements to control dioxin.

Status & References

If approved by the EQC Nov. 1, eight public hearings on DEQ's entire water quality regulatory package, including the dioxin standard, will be held between Jan. 14 and Jan. 22 (watch *OI Calendar* for details). For more information, contact Eugene Foster (DEQ) at 229-6982. References: ORS 468.735, OAR 340-41 Table 20 (proposed water quality standards for toxic substances).

AIR QUALITY

Advisory Committee to Recommend Few Changes to Protect Wilderness Area Visibility

■ After some 18 months of work, it appears a Department of Environmental Quality (DEQ) advisory committee will recommended few if any significant changes in the way the agency protects visibility and other "air quality related values" in wilderness areas. Even though the group will recommend adding some new wilderness areas to the program, it will be years before that occurs.

Low Priority

"This is a slow moving process — it's not on the front burner," said John Core, visibility program coordinator and liaison to the advisory committee.

The recommendations are being developed as part of a federally-mandated review of the state "Visibility Protection Program." The VPP is supposed to protect air quality related values such as scenic vistas, air chemistry, aquatic biology and even sensitive plants in certain designated wilderness areas.

Triennial Review Underway

First completed in 1986, the VPP was approved by the Environmental Protection Agency in 1987. The program is unique because it requires air pollution control measures even where air quality is generally very high. The idea is to "preserve, protect, and enhance" the pristine air quality often found in wilderness areas, national parks, national seashores and similar areas.

DEQ appointed a 15-member Visibility Protection Advisory Committee last April to help review the program. The group includes representatives of the public, federal land management agencies, timber and agricultural industries, environmentalists and the tourism industry.

Field & Slash Burning at Issue

The primary threat to air quality in these areas is smoke from grass seed industry field burning, forest industry slash burning, and natural forest fires. The VPP restricts field and slash burning during certain months so smoke does not interfere with recreational uses.

Twelve Areas Protected Now

Some of Oregon's most noteworthy attractions are among the 12 wilderness areas currently protected under the program. These include Crater Lake National Park, Mt. Hood Wilderness Area, and popular wilderness areas near Bend. Designated "Class I," these areas receive the greatest air quality protection under the Clean Air Act and DEQ regulations.

Two Questions

There are two general questions before the committee. First, should DEQ expand the VPP to include areas set aside as wilderness since 1977? Second, should DEQ change the way visibility and other related values are protected?

DIOXINS, FURANS AND PCBs: THE TRUE STORY

Dioxins, furans and PCBs have become some of the most controversial chemicals of modern society. Dioxin in particular has been labelled the most toxic chemical ever produced by man. More than $1 billion has been spent so far on dioxin research[1], yet at the same time, industry and government officials insist that not enough evidence on the toxicity exists to justify elimination of the sources.

This paper explores some of the myths and facts surrounding these environmentally dangerous chemicals and explains why the scientific debate has become of an increasing political nature.

What Are 'Dioxins'

The term 'dioxins' usually refers to a whole chemical family with 75 individual members, which more correctly should be termed chlorinated dibenzo-p-dioxins. The most toxic member of this family is 2,3,7,8-Tetra-Chloro-Dibenzo-p-Dioxin, often abbreviated as 2,3,7,8-TCDD.

Often, the term 'dioxins' also includes a closely related chemical family called chlorinated dibenzofurans. The most toxic among the 135 known furans is 2,3,7,8-Tetra-Chloro-Dibenzo-Furan (TCDF), which is one tenth as toxic as the corresponding dioxin, TCDD.

Of the 210 dioxins and furans, twelve are extremely toxic and are commonly referred to as the 'Dirty Dozen'. Their individual toxicity is ranked by comparing them to 2,3,7,8-TCDD via internationally agreed upon Toxic Equivalence Factors (TEFs). Box 1 (next page) shows the chemical structures of dioxins and furans, and their toxicity ranking.

PCBs are another chemical family closely related to dioxins. Due to their similar chemical structure, some PCBs can act through exactly the same pathways in organisms as dioxins, but are much less potent. However, due to their chemical nature, PCBs are inevitably contaminated with furans and dioxins, and will form these more toxic chemicals during fires.

How Toxic Are Dioxins [2]

a) Extreme Ability to Kill

Dioxin TCDD is the most toxic man-made chemical ever tested on laboratory animals. Acutely lethal doses are measured in micro-grams per kilogram animal weight, in the parts per billion range. [2e] Though the lethal dose varies considerably from species to species, dioxin has been found to be extraordinarily toxic to all species tested.

Characteristic of lethal dioxin exposure is the 'wasting syndrome': animals seem to waste away, and eventually die, without displaying any overt pathological symptoms. The exact reason why dioxin can cause death in these minute quantities is not yet known.[2e]

b) Extremely Bio-Accumulative

Dioxins are some of the most persistent and bio-accumulative man-made chemicals released into the environment. While dioxins can be broken down under certain conditions, in particular when exposed to intensive sunlight, they cannot be broken down once absorbed by soil or dust. When they enter the food-chain, they will bio-magnify, often to levels many thousands of times higher than their surroundings.[2d,3]

It is this combination of dioxin's extreme toxicity and its bio-magnification in the environment that makes Greenpeace believe that there can be no safe level of dioxin emissions.

Conclusions and Greenpeace Demands

Enough research exists to prove that dioxin is extremely toxic and persistent, and that levels in our environment and in human milk are increasing. Given that many health effects occur from exposure to even minute quantities over time, and that widespread contamination of our environment and the build-up of these chemicals in the food chain has already led to dangerously high levels in human milk and in marine mammals, all energy must be devoted toward preventing any further releases of dioxins into the environment.

The elimination of man-made dioxin sources would go hand-in-hand with the elimination of a much larger group of environmentally dangerous organochlorines, which would be extremely desirable from an overall environmental point of view. Elimination of all dioxin sources would mark a turning point in our dealings with pollution control, since a holistic approach would have to include the phase-out of an entire class of anthropogenic chemicals presently discharged in large quantities into the environment.

In 1983, after two years of research, the Ministers' Expert Advisory Committee on Dioxins stated that [15]:

"Regardless of arguments about the significance of species differences in sensitivity, the validity of risk assessments, and other uncertainties which may take years to resolve, it is quite clear that dioxins are very unpleasant things to have in our environment and the less we have of them the better. It is, in fact, imperative to reduce dioxin exposure to the absolute possible minimum."

Despite these recommendations, the Canadian government has failed to eliminate even such outstanding dioxin sources as pentachlorophenol, but has instead actually added new dioxin sources to the Canadian environment by building further municipal and hazardous waste incinerators.

Greenpeace demands that the Canadian government follow the leadership provided by forward thinking European governments, and:

establish a five-year plan to eliminate all known industrial dioxin sources,

and in particular:

- **ban import and use of chlorophenols immediately;**
- **establish an indefinite moratorium on construction of new municipal and hazardous waste incinerators;**
- **phase out disposable products made of PVC or PVDC;**
- **phase out PVC coating of copper wire;**
- **phase out chlorinated solvents;**
- **eliminate the use of chlorine in the pulp and paper industry and metallurgical industry;**
- **establish a mass-balance of chlorine and organochlorines in Canada; i.e. determine the amount of chlorine gas and organochlorines produced, and their fate in the environment. This mass balance should extend to other halogens and organohalogens;**
- **commission a feasibility study on phase-out of all production and use of organochlorines.**
- **Fund research to find clean production technologies and alternatives to chlorinated products, as well as safe methods of destroying the existing piles of dioxin and other chlorinated waste.**

This paper was researched and written by Renate Kroesa, M.Sc., Toxic Project Co-ordinator.

REFERENCES

1) Report from Conferences, the 5th Int'l Dioxin Symposium, Bayreuth, 1985; Chemosphere, 1986, 15, N1-2.

2) This entire section is based on the following five overview reports/books published on the toxicology of dioxin. All reports/books give an excellent overview and provide many detailed references to the interested reader.
   a) 'Human Health Aspects of Exposure to PCDDs and PCDFs'; UAREP, Bethesda, Maryland, June 1988 (funded by the American Paper Institute).
   b) 'The Chemical Scythe', by Alistair Hay; Plenum Press 1982.
   c) 'A Cancer Risk-Specific Dose Estimate for 2,3,7,8-TCDD'; US-EPA/600/6-88/007Ab, June 1988, plus Appendices A-F.
   d) 'Dioxins in the Environment' by the UK Dept of the Environment; Pollution Paper No. 27, 1989 .
   e) S.A. Skene et al, Human Toxicol, 1989, 8, 173-203.

3) P.M. Mehrle et al, Environmental Toxicology and Chemistry, 1988, 7, 47-62.

4) F. Rohleder, Presentation to the 9th Int'l Dioxin Symposium, Toronto, 1989.

5) T. Sinks, Presentation to the 7th Int'l Symposium on Epidemiology in Occupational Health, Tokyo, 1989.

6) a) R.E. Bowman et al, Neurotoxicology, 1986, 7, 637-650.
   b) J.R. Allen et al, Toxicology and Applied Pharmacology, 1979, 48, A180.
   c) J.R. Allen et al, Bulletin of Environmental Contamination and Toxicology, 1979, 21, 463-469.

7) 'Who do you believe?', Jock Ferguson; Chemosphere, 1985, 14 791-796.

8) PCBs, PCDDs and PCDFs in Breast Milk: Assessment of Health Risks; WHO, Regional Office for Europe; EH 29 (1988).

9) W.R. Swain; Aquatic Toxicology, 1988, 11, 357-377.

10) Monitor 1988, Sweden's Marine Environment - Ecosystems Under Pressure; National Swedish Environmental Protection Board.

11) a) R.R. Bumb et al (Dow Chemical), Science, 1980, 210, 385.
   b) Nestrick et al (Dow Chemical), Chemosphere, 1983, 12, 617-626.

12) J.M. Czuczwa, R.A. Hites, Chemosphere, 1986, 15, 1417-1420.

13) a) A. Schector et al, Chemosphere, 1988, 17, 627.
   b) A. Schector et al, poster at the 9th Int'l Dioxin Symposium, Toronto, 1989.

14) W.V. Ligon et al (General Electric), Environ. Sci. Technol. 1989, 23, 1286-1290.

15) Report of the Joint Health and Welfare Canada/ Environment Canada Advisory Committee on Dioxins, November 1983.

GREENPEACE

Founded in Canada, 1971
Fondé au Canada, 1971

Vancouver

1726 Commercial Drive,
Vancouver
British Columbia
Canada V5N 4A3
✆ 604 253-7701
FAX 604 253-0114

Toronto

578 Bloor Street West
Toronto, Ontario
Canada M6G 1K1
✆ 416 538-6470
Fax 416 538-6479

Montréal

2444 Notre-Dame Ouest
Montréal (Québec)
Canada H3J 1N5
✆ 514 933--0021
Fax 514 933-1017

Press Gang Printers - a feminist worker-controlled collective

STATE OF OREGON

DEPARTMENT OF ENVIRONMENTAL QUALITY INTEROFFICE MEMORANDUM

DATE: June 7, 1991

TO: Environmental Quality Commission

FROM: Fred Hansen, Director

SUBJECT: Petition for Rule Amendment: Water Quality Standard 2,3,7,8 - TCDD

The Department would recommend to the Commission that the petition for rule making regarding the water quality standard for 2,3,7,8 - TCDD be denied. The denial at this time is based on several factors including:

1. The Department is in the process of completing the triennial review of the state's water quality standards. The standard for 2,3,7,8-TCDD was evaluated during this process. The Department, after careful review of the criteria, recommends to retain the standard as adopted in 1987.

   The Department reviewed all of the factors used to derive the criteria with special attention to three of the factors. These three factors were cancer potency, bioconcentration, and fish consumption. Various numbers have been forwarded for revision of all three of the factors. Review of the published literature indicated that the 0.013 pg/l water quality standard was an appropriate standard. When considering the possible changes to the cancer potency factor, the bioconcentration factor, and the fish consumption rate the 0.013 pg/l standard is an appropriate standard.

2. Since the Department's review of the water quality standard during the fall of 1990 the USEPA has announced that they will be conducting a review of the criteria. The USEPA expects to complete the review in one to two years. The agency expects to address wildlife, aquatic life, and human health issues related to the criteria. The agency is expected to review carcinogenic and reproductive effects to humans, wildlife and aquatic life; the rate of bioaccumulation; and, fish consumption rates.

3. Any review of the 2,3,7,8-TCDD standard which addresses wildlife and aquatic life risks could well result in a criteria value lower than the present Oregon standard. It should be noted that piscivorous wildlife have an increased risk of cancer mortality and reproductive

effects than humans when applying the Oregon water quality standard. In addition, a No Observed Adverse Effect Level (NOEL) has not been established for 2,3,7,8-TCDD. The lowest concentration studied of 38 ppq has resulted in 45% mortality of the trout exposed during the test.

4. According to the most recent USEPA memo to the Department (April 24, 1990) concerning the tracking of state water quality criteria for 2,3,7,8-TCDD there are 25 states with adopted dioxin criteria. Fourteen of the states have adopted standards at or below and 11 above the USEPA criteria level.

5. EPA's Office of Research and Development(ORD) is currently developing a review strategy which we expect to be released on or around June 14, 1991 (attachment 1). The strategy is expected to include greater detail on the scope and timing of the EPA review. This could shed additional light on the national review and the type of information it will develop. This would be very germane to a decision on the petition and the type of review to be conducted by the state.

6. There has not been new peer reviewed published information within the last five to six months since the Department has reviewed the standard, that would cause the Department to recommend a change to the standard. An epidemiological study has been published in The New England Journal of Medicine which links occupational exposure of 2,3,7,8-TCDD to an increase in the rate of mortality due to cancer (Fingerhut 1991). A new method to estimate the bioaccumulation factor has been forwarded to the Department but this method does not appear to be suitable for use in water quality criteria development. The Department is involved in projects or aware of projects which should provide specific information on bioaccumualtion in riverine systems as well as fish consumption rates of Native Americans along the Columbia River.

7. William Riley, Administrator EPA, stated in a memo dated April 10, 1991 announcing the review of the 2,3,7,8-TCDD criteria that regulatory actions concerning 2,3,7,8-TCDD should go forward.

8. On-going litigation based on the current standard is not expected to be resolved soon.

Based on the above information it would not be the best use of limited state resources to duplicate the present USEPA effort. State resources should be spent in other areas of toxin control such as the development of a comprehensive standard for all biologically and toxicologically active dioxins, furans and PCBs, technology based standards for the control of dioxins and furans in the pulp and paper industry and wood treating industry.

When the USEPA has completed their review of the 2,3,7,8-TCDD criteria, the Department would propose to immediately undertake a review of the standard if it is warranted.

If the Commission does not accept the Department's recommendation, we recommend, in accepting the petition for rule making, that a very specific statement be made regarding current regulatory actions, the items to be considered during the review and the time frame for the review. This would include:

1. The Department would continue all current regulatory activities using the current standards until such time as a new standard was adopted.

2. The re-evaluation of the state standard would be opened at this time, but the review would not be closed until the USEPA had completed its review.

3. The re-evaluation of the 2,3,7,8-TCDD water quality standard would include the review of criteria derivation for the other biologically available dioxins, furans, and co-planar PCBs to address as one standard the pollutants with similar biological/toxicological properties.

4. The Department would move forward to establish technology based standards for the control of dioxins and furans in the pulp and paper industry and wood treating industry.

ENVIRONMENT WEEK

By The Editors Of The Energy Daily And New Technology Week

KING COMMUNICATIONS GROUP, INC. • 627 NATIONAL PRESS BUILDING • WASHINGTON, D.C. 20045 • 202/638-4260

Thursday, May 2, 1991 Volume 4, Number 18

Congressmen Implore Swift Panel To Enact Interstate Waste Rules

The long-simmering congressional debate on interstate transportation of solid and hazardous waste boiled to the surface during a House Energy and Commerce subcommittee hearing on Tuesday.

BY DENNIS WAMSTED

Currently, states are essentially precluded by the Commerce Clause of the Constitution from regulating the flow of out-of-state wastes. Worried that this could turn their districts into national dumping grounds, lawmakers from waste importing states have introduced a rash of proposals to give state or municipal governments the right to regulate interstate flows of both hazardous and solid waste.

At the same time, officials from the major exporting states urge caution, saying that legislative curbs on interstate waste trade could slow the development of national recycling markets, and that in many cases the exports are driven by other environmental concerns, such as a desire to protect groundwater resources. Although disagreeing with each other, both sides, as well as several members of the Energy and Commerce subcommittee on Transportation and Hazardous Materials, criticized the Environmental Protection Agency for its listless leadership on this issue over the past 10 years.

The criticism began at the top, with subcommittee chair Rep. Al Swift (D-Wash.) voicing his dis-

(Continued on page 7)

Waxman: EPA Clean Air Act Permit Plan 'Clearly Illegal'

BY CATHERINE COONEY

Rep. Henry Waxman (D-Calif.), chairman of the House Energy and Commerce subcommittee on health and the environment, blasted Vice President Dan Quayle, head of the White House Council on Competitiveness, at a hearing on Wednesday for interfering with the Environmental Protection Agency's proposed Clean Air Act permit rule. "White House officials, spearheaded by Vice President

(Continued on next page)

ORD DRAFTS DIOXIN REASSESSMENT

BY CATHERINE COONEY

The Environmental Protection Agency's Office of Research and Development (ORD) is nearing completion of its plan for reevaluating the agency's risk assessment model for dioxin, and should send the 10-page strategy to Environmental Protection Agency chief William Reilly sometime this week, according to Peter Preuss, one of the ORD officials coordinating the review effort.

Reilly ordered the agency to reevaluate the risk assessment model in an April 8 memo sent to ORD Assistant Administrator Erich Bretthauer. Reilly's reevaluation order was based on the significant amount of new scientific data that has been published recently on the ubiquitous chemical and its impact on human health.

The reevaluation will focus on the "thinking" developed at an international conference held last fall at the Banbury Center at Cold Spring Harbor Laboratory, said Preuss. At the conference, dioxin experts developed a new approach regarding how dioxin reacts in cells: called the receptor-mediated model, it basically recognizes that dioxin must first bind to and then activate a receptor cell before it can become carcinogenic in humans. While many who attended the conference say the new approach implies that there is a level at which dioxin exposure will no longer be considered carcinogenic, Preuss said it is much too soon to predict this. "It would be speculation to say," Preuss said about the implications of the new approach.

The reassessment will look at a variety of the health effects of dioxin, such as cancer and human developmental problems. The agency plans to look at the views on dioxin from "all of the leading scientists" and will evaluate most of the literature, Preuss said. They will also review current laboratory data on how dioxin effects a cell, as well as develop new data on this. Because EPA believes that some of the data on health effects is insufficient, it will use its Health Effects Research Laboratory in Research Triangle Park, N.C. to develop new data on immunotoxicity and some early biological effects that can be measured. EPA will also look at health data at other U.S. and European labs. "But there are no new contracts now," he added.

Lastly, the agency will have to gather new data on the ecological impact of dioxin, such as its affect on aquatic life, which is still not fully understood.

After Reilly approves ORD's plan, the group will begin directing the research to prepare for its written review. This reevaluation will be written with the help of scientists outside the agency, and should be ready for peer review in a year. Within two years, the final document discussing the receptor-model risk approach will be ready for public comment.

The group will work under ORD's Bretthauer, and includes: Preuss; William Frank, who will oversee the research; and Linda Birnbaum, director of the environmental toxicity division at Research Triangle Park who will oversee the data development. True to Reilly's announced commitment that the process be open, Preuss said all of the documents concerning the reassessment will be available to the public.

NORTHWEST ENVIRONMENTAL ADVOCATES

June 10, 1991

Fred Hansen, Director
Oregon Department
of Environmental Quality
811 S.W. Sixth
Portland, OR 97204

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 10 1991
OFFICE OF THE DIRECTOR

Bill Hutchinson, Chair
Oregon Environmental Quality
Commission
Tooze, Shenker Holloway, & Duden
333 SW Taylor St.
Portland, OR 97204

Re: Notice of Consideration of Petition for Rule Amendment
(Water Quality Standard for 2,3,7,8-TCDD)

Dear Fred and Bill:

I am writing to urge the Commission to deny the pulp and paper industry's petition to change the criterion in the water quality standard for dioxin. There are numerous reasons for the Commission not to take up this issue, not the least of which is the fact that the Department recently reevaluated this standard in its most recent "triennial review." In addition, as I am sure you are aware, U.S. EPA is reexamining the criterion.

It would be redundant for the State of Oregon to reevaluate the very same issue that EPA is currently reviewing, and Oregon is certainly less well equipped to do so. It is also premature to second guess the outcome of that evaluation. In fact, EPA Administrator Reilly has urged that regulatory actions based on the existing dioxin criterion proceed as scheduled.

For as many reasons as the pulp and paper industry can come up with to argue for an increase in the allowable limits for dioxin, there are at least an equal number of arguments that the existing standard is not conservative enough. For example, the current criterion is based on a bioconcentration factor of 5,000. Yet studies show that the bioconcentration factor in fish can range up to 156,000. The existing dioxin standard does not take into account the other media by which dioxin contaminates human beings, i.e. inhalation, eating food other than fish. General human background exposure to dioxin compounds (1 to 10 parts per kilogram (equivalent to part per quadrillion) in toxicity equivalent units for all dioxins) is known to already exceed the acceptable daily intake set by EPA for protection against reproductive effects (1 part per quadrillion). In addition there are the synergistic and

408 Southwest Second Avenue, Governor Bldg. Suite 406, Portland, Oregon 97204 Telephone (503) 295-0490

additive effects caused by exposure to dioxin in tandem with other toxic pollutants.

Industry is fond of pointing out that the risk to humans from dioxin is far less than to lab rats, for which dioxin is clearly a hazard. Presumably industry would include other 'lower life forms' in its assessment of the hazards of dioxin. This is relevant to the Commission's decision because, whether or not the existing criterion for dioxin adequately protects human beings, it certainly does not take into account the increased effects dioxin has on wildlife. These effects are increased due to the lower body weight and greater consumption of contaminated aquatic life (e.g. fish) by eagles, mink, otter, and other pisciverous wildlife. States' water quality standards are supposed to protect the most sensitive beneficial uses. The Commission should not even consider this or any other petition to change the dioxin standard unless petitioners can demonstrate that a higher level of dioxin contamination will not result in a lower level of protection for the most sensitive uses.

It is an old ploy of industry's to seek to have the rules changed when it doesn't want to meet them. It is inexcusable when government accedes to this. The Commission should enforce the standards it has adopted, not bend them when the going gets tough for a segment of industry which has had the benefit of over-polluting public waters for many years.

Sincerely,

Eugene Rosolie for

Nina Bell
Executive Director

cc: Emery N. Castle
Henry Lorenzen
Carol Whipple
William W. Wessinger

VICTOR M. SHER (WSB# 16853)
TODD D. TRUE (WSB# 12864)
REBECCA E. TODD (WSB# pending)
Sierra Club Legal Defense Fund
216 First Avenue S., Suite 330
Seattle, Washington 98104
(206) 343-7340

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 10 1991
OFFICE OF THE DIRECTOR

BEFORE THE ENVIRONMENTAL QUALITY COMMISSION
OF THE STATE OF OREGON

In the Matter of the Petition of James River II, Inc. and Boise Cascade Corporation to Amend Subparagraph (2)(p)(B) of Oregon Administrative Rules Chapter 340, Division 41, Sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965.

MEMORANDUM IN OPPOSITION TO THE PETITION FOR RULE AMENDMENT

I. Introduction

This Memorandum in Opposition to the Petition for Rule Amendment is submitted by the Sierra Club Legal Defense Fund, Inc. on behalf of the American Oceans Campaign, the Campaign for Puget Sound, the Dioxin/Organochlorine Center, Friends of the Earth, National Audubon Society, Puget Sound Alliance, the Washington Environmental Council, and the Washington Toxics Coalition.[1] These organizations are non-profit environmental groups dedicated to and actively working toward the preservation and protection of water resources and all life dependent on them.

[1] American Oceans Campaign, 4007 Latona Avenue NE Seattle, WA 98105; Campaign for Puget Sound, P.O. Box 2807 Seattle, WA 98111-2807; Dioxin/Organochlorine Center, 1247 Willamette Street Eugene OR 97401; Friends of the Earth, 4512 University Way NE Seattle WA 98105; National Audubon Society, P.O. Box 462 Olympia, WA 98502; Puget Sound Alliance, 4516 University Way NE Seattle WA 98105; Washington Environmental Council, 5200 University Way NE Seattle WA 98105; and the Washington Toxics Coalition, 4516 University Way NE Seattle WA 98105.

In specific, the organizations seek to reduce and eliminate entirely the discharge of toxic organochlorines to the waters of the Pacific Northwest, including 2,3,7,8 tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD), commonly known as dioxin.[2]

We strongly oppose the Petition for Rule Amendment and urge the Environmental Quality Commission to deny the Petition. We are a group of national, regional, and Washington State environmental groups concerned about the water quality of the Pacific Northwest, Oregon, and the water resources shared by Oregon, Washington, and Idaho. The Columbia River receives much of the region's pulp and paper mill organochlorine discharge and for many hundreds of miles is a shared resource and border for Oregon and Washington.[3] The ambient water quality standard for 2,3,7,8-TCDD in Oregon necessarily affects these shared ecosystems and the livelihood and recreation of those living in both states. We are also concerned with the precedential implications that the Petition for Rule Amendment may have nationwide and for the Pacific Northwest.

---

[2] "Dioxin" as it refers to 2,3,7,8-TCDD is actually a misnomer. Dioxins are a family of approximately 75 separate chlorinated organic compounds, each of which is characterized by the existence of two oxygen atoms connecting two chlorinated benzene rings.

[3] The interdependence of the Pacific Northwest states with regard to the Columbia River has been recognized by the formation by Oregon and Washington of the Bistate Commission for the Columbia River, and the basin-wide protection strategies for the River established by the Environmental Protection Agency [EPA], including the establishment of Total Maximum Daily Loadings and Individual Control Strategies pursuant to the Federal Water Pollution Control Act, 33 U.S.C. §§ 1313(d) and 1314(l), respectively.

2,3,7,8-TCDD is a known human carcinogen, teratogen, and immunosuppressant.[4] Other types of damage caused by 2,3,7,8-TCDD include skin disorders, reproductive disorders, hormonal and metabolic effects, developmental defects, damage to the liver, kidney and thymus, wasting syndrome, neurobehavioural effects, and learning disabilities.[5] Furthermore, 2,3,7,8-TCDD is

---

[4] Some pertinent papers regarding this include:

Fingerhut, Marilyn A., William E. Halperin, David A. Marlow, Laurie A. Piacitelli, Patricia A. Honchar, Marie H. Sweeney, Alice L. Greife, Patricia A. Dill, Kyle Steenland, and Anthony J. Suruda, Cancer Mortality in Workers Exposed to 2,3,7,8 Tetrachlorodibenzo-p-dioxin, The New England Journal of Medicine 324: 212-218 (1991).

Schwartz, E., A Proportionate Mortality Ratio Analysis of Pulp and Paper Mill Workers in New Hampshire, British Journal of Industrial Medicine 45:234-238 (1988).

Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 (1989).

Skene, S.A., I.C. Dewhurst, and M. Greenberg, Polychlorinated Dibenzo-p-dioxins and Polychlorinated Dibenzofurans: The Risks to Human Health: A Review, Human Toxicology 8:173-203 (1989).

[5] Some pertinent papers regarding this include:

Bowman, R.E., S.L. Schantz, M.L. Gross, and S.A. Ferguson, Behavioral Effects in Monkeys Exposed to 2,3,7,8-TCDD Transmitted Maternally During Gestation and for Four Months of Nursing, Chemosphere 18:235-242 (1989).

Fish and Wildlife Service, Dioxin Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review, Biological Report 85, May 1986.

Jacobson, Joseph L., Sandra W. Jacobson, and Harold E.B. Humphrey, Effects of In Utero Exposure to Polychlorinated Biphenyls and Related Contaminants on Cognitive Functioning in Young Children, Journal of Pediatrics 116:38-45 (1990).

Larsson, Ake, T. Andersson, L. Forlin, and J. Hardig, Physiological Disturbances in Fish Exposed to Bleached Kraft Mill Effluents, Wat. Sci. Tech. 20:67-76, 1988.

McCormack, Craig and David Cleverly, United States Environmental Protection Agency, Analysis of the Potential Populations at Risk From the Consumption of Freshwater Fish Caught Near Paper Mills, Draft Report, April 23, 1990.

Schantz, Susan L., and Robert E. Bowman, Learning in Monkeys Exposed Perinatally to 2,3,7,8 Tetrachlorodibenzo-p-dioxin (TCDD), Neurotoxicology and Teratology 11:13-19, 1989.

bioaccumulative, bioconcentrative, and persistent.[6]

Moreover, while 2,3,7,8-TCDD is the most toxic substance ever identified, and hence the most toxic of the organochlorines, chlorine bleaching pulp and paper production generates tons of chlorinated organics which are toxicologically equivalent to 2,3,7,8-TCDD. In other words, these other organochlorines act within the body and the environment in virtually the same toxicological manner as 2,3,7,8-TCDD. For example, in issuing a recent Fish Consumption Advisory for Lake Roosevelt, the Washington State Department of Health recognized that 90% of the dioxin toxicity is due to 2,3,7,8 tetrachlorodibenzofuran.[7] As one of the leading scientific experts has written,

---

Svensson, Bengt-Goran, Anita Nilsson, Marianne Hansson, Christopher Rappe, Bjorn Akesson, and Staffan Skerving, Exposure to Dioxins and Dibenzofurans Through the Consumption of Fish, The New England Journal of Medicine 116:8-12 (1991).

Swain, Wayland R., Human Health Consequences of Consumption of Fish Contaminated with Organochlorine Compounds, Aquatic Toxicology 11:357-377 (1988).

Tanabe, S., N. Kannan, An. Subramanian, S. Watanabe, and R. Tatsukawa, Highly Toxic Coplanar PCBs: Occurrence, Source, Persistency and Toxic Implications to Wildlife and Humans, Environmental Pollution 47:147-163 (1987).

[6] The toxicokinetic half-life of 2,3,7,8-TCDD in human tissue has been predicted to be approximately 5 to 8 years and the half-life in sediments is even longer. See, Bowman, R.E., S.L. Schantz, N.C.A. Weerasinghe, M.L. Gross, and D.A. Barsotti, Chronic Dietary Intake of 2,3,7,8 Tetrachlorodibenzo-p-dioxin (TCDD) at 5 or 25 Parts Per Trillion in the Monkey: TCDD Kinetics and Dose-Effect Estimate of Reproductive Toxicity, Chemosphere 18:243-252 at 250 (1989), and Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 at 458 (1989).

[7] Washington Department of Ecology, First Progress Report on Ecology's Dioxin/Furan Survey in Lake Roosevelt, Memorandum from Art Johnson, Dave Serdar, and Stuart Magoon to Carl Nuechterlein, August 8, 1990.

it is misleading to consider dioxin as a single entity, and the potential health risks are properly evaluated by taking into account exposures to mixtures of the hundreds of isomers and related compounds in this group.[8]

An approach, therefore, which focuses on the cancer risks from 2,3,7,8-TCDD necessarily underestimates cancer risks from pulp and paper mill effluent[9] and also ignores other arguably more important organismic and ecosystem level impacts from 2,3,7,8-TCDD such as adverse reproductive, developmental, and wildlife effects.

//

//

//

//

//

---

[8] Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 at 456 (1989).

[9] EPA itself recognizes that its cancer risk and attendant water quality standard of .013 ppq vastly underestimate the actual cancer risk suffered by certain sensitive populations. EPA estimates that a Native American adult consuming Columbia River Basin fish in an amount average for Native Americans per day contaminated with 6.5 parts per trillion (ppt) 2,3,7,8-TCDD equivalents exceeds the EPA threshold of concern for reproductive effects by over nine times. See, McCormack, Craig and David Cleverly, United States Environmental Protection Agency, Analysis of the Potential Populations at Risk From the Consumption of Freshwater Fish Caught Near Paper Mills, Draft Report, April 23, 1990.

Furthermore, in calculating the cancer risk and water quality standard for 2,3,7,8-TCDD, EPA assumed a fish consumption rate of only 6.5 grams per day, while actual fish consumption rates are approximately five times higher than this, and Native American fish consumption rates are approximately fifteen times higher. More realistic fish consumption rates, therefore, would make the cancer risk standards five to fifteen times higher, respectively. Id.

II. The Environmental Quality Commission Should Deny the Petition for Rule Amendment.

We strongly urge the Commission to deny the Petition for Rule Amendment filed by James River II and the Boise Cascade Corporation on May 23, 1991. A new rulemaking effort makes little sense in light of the limited resources of the State of Oregon. Indeed, Oregon initially adopted the .013 ppq standard established by EPA's Quality Criteria for Water 1986 with the express realization that the State had insufficient resources to undertake adequately a separate analysis of the health risks of 2,3,7,8-TCDD. As the State continues to suffer from limited resources, it continues to be ill-advisable for the State to undertake the complex analysis of human and environmental health risks from 2,3,7,8-TCDD necessary in deciding the water quality standard.

The adoption of a water quality criterion or standard is a significant task. EPA regulations mandate that every water quality criteria

> must be based on sound scientific rational and must contain sufficient parameters or constituents to protect the designated use. For waters with multiple use designations, the criteria shall support the most sensitive use.

40 C.F.R. § 131.11(b)(1)(1990). To adopt a new water quality standard requires that the rulemaking body employ "scientifically defensible methods" in assuring that the most sensitive uses are protected. 40 C.F.R. § 1313.11(b)(1)(1990) Establishing a new water quality standard for 2,3,7,8-TCDD would be extremely resource intensive, consuming the kind of time and energy that the State of Oregon has already recognized that it lacks.

Furthermore, the issue of the proper water quality standard for 2,3,7,8-TCDD will be debated shortly in another forum. EPA established the Total Maximum Daily Loadings [TMDL] for the Columbia River on February 25, 1991, regarding the total allowable discharge of 2,3,7,8-TCDD into the Basin. We anticipate legal challenges to the TMDL asserting that the .013 ppq standard is inadequate to protect human health and wildlife. In this connection, we believe that the appropriate water quality standard for 2,3,7,8-TCDD is zero, as detailed in Section III below.

Furthermore, from an ecosystem perspective it is nonsensical to allow mills in Oregon to discharge bioaccumulative and persistent organochlorines into the Columbia River Basin at 2.3 ppq, while Idaho and Washington mills comply with the applicable .013 ppq state standards, a difference of orders of magnitude. Fish, endangered Bald Eagles feeding on them, mink, otter, other wildlife, as well as sensitive human populations such as Native Americans, Asian Americans, and subsistence and sport fishers cannot differentiate among the 2,3,7,8-TCDD contamination from Oregon and that from other states. With regard to these especially sensitive groups, the State of Oregon has a duty to protect all of the people that compose the population of the State. While the .013 ppq standard is not adequately protective of either humans and wildlife, the suggested 2.3 ppq standard is even less so.

//

//

At this time and given the limited resources of the State, the most logical and protective course of action for the Commission is to deny the Petition for Rule Amendment.

III. Alternatively, If the Environmental Quality Commission Revisits the Rulemaking Procedure, the Proper Water Quality Standard for 2,3,7,8-TCDD is Zero.

The chlorine bleaching pulp and paper mills insist that new data indicate that the ambient water quality standard for 2,3,7,8-TCDD should be loosened. It is our position, and the position of the best scientific experts in the field, that available data militate for a <u>more</u> <u>stringent</u> <u>and</u> <u>protective</u> standard. These data include human reproductive and developmental effects, the effects on wildlife reliant on contaminated ecosystems, and the bioaccumulation, bioconcentration, and persistence of 2,3,7,8-TCDD in animal tissue and sediments. If the Petition for Rule Amendment is granted, we expect that the Commission will find itself in the midst of an extremely involved and complex dispute, with both sides presenting evidence and expert opinion regarding the proper water quality standard for 2,3,7,8-TCDD.

If the Commission does indeed elect to reopen rulemaking, we anticipate arguing that the standard for 2,3,7,8-TCDD is properly zero, that is, that the Commission should allow no discharges of 2,3,7,8-TCDD at all.

//

//

//

We are not the first to suggest to the State of Oregon that the water quality standard for 2,3,7,8-TCDD should be zero. Over the past several years, the United States Fish and Wildlife Service has consistently advised that because of the long-term health effects on wildlife that 2,3,7,8-TCDD discharges be reduced and eliminated:

> We recommend that the DEQ consider limiting the [pulp and paper mills' National Discharge Elimination System, or NPDES] permit[s] to a discharge of no dioxins...

Letter from the United States Fish and Wildlife Service to the Oregon Department of Environmental Quality dated July 10, 1989. Six months later the Fish and Wildlife reiterated that

> we believe it is appropriate for DEQ to develop a long-term goal that decreases and eventually eliminates the production of dioxin and other chlorinated byproducts.

Letter from the United States Fish and Wildlife Service to the Oregon Department of Environmental Quality dated January 19, 1990.

In recognition of the severity of the organochlorine contamination in the Columbia River Basin, the Fish and Wildlife Service most recently explained that

> considering the longevity of organochlorine compounds and the potential impact of small quantities of dioxins on fish, waterfowl, and endangered species, we recommend that the EPA strive towards limiting NPDES permits to zero discharge of dioxins to the Columbia River Basin.

Letter from the United States Fish and Wildlife Service to Region 10 EPA dated November 21, 1990. The zero discharge standard is the only standard for 2,3,7,8-TCDD that will adequately protect human, wildlife, and environmental health.

There are many technologies available and in use worldwide that reduce and eliminate the use of chlorine or chlorine compounds that are the necessary precursors for all chlorinated organic compounds. Without chlorine or chlorine compounds present in the production process, organochlorines cannot be formed and discharged to the environment. Many European mills and some North American mills currently employ chlorine-free technology in their pulp and paper production. Many if not all the mills in the United States are at the very least exploring ways in which they can reduce their use of chlorine and the subsequent discharge of toxic organochlorines.

Furthermore, the public is becoming increasingly aware of the human and environmental health risks associated with chlorine bleaching and is demanding chlorine-free pulp and paper products. The mill in Lyons Falls, New York is one example of a mill that has converted to a chlorine-free technology and has subsequently experienced an increase in its market share. As consumers increasingly demand chlorine-free paper products, those mills that can supply them are enjoying competitive success in the marketplace.

As has been long recognized elsewhere, there are no functional uses of pulp and paper products that demand the super bright whiteness normally achievable with chlorine bleaching processes. Non-chlorine bleaching renders pulp and paper products that are nearly as bright white as chlorine bleached products. These chlorine-free products are suitable for every use to which pulp and paper products are put today.

Because of the availability of chlorine-free technologies, the complete lack of need for chlorine bleached pulp and paper, and the serious and persistent risks to human and environmental health, if the Commission grants the Petition for Rule Amendment, we anticipate returning to urge the Commission to promulgate an ambient water quality standard of zero for 2,3,7,8-TCDD.

IV. Conclusion

On behalf of the organizations listed above, we offer this Memorandum in Opposition to the Petition for Rule Amendment. We will gladly provide the Commission with any of the data discussed above. As we have not had the opportunity to view all the information submitted by the mills, we are unable to respond directly to their particular scientific or other assertions. Should the Commission like us to provide a more detailed response to their specific claims, we will arrange to procure the mills' lengthy submission and provide a detailed scientific analysis for the Commission's review. That being said, however, we believe that the wisest, most protective, and most efficient course of

//

//

//

//

//

//

//

//

action for the Commission is to deny the Petition for Rule Amendment and we urge the Commission to do so.

Dated this 10th day of June, 1991.

Respectfully submitted,

Victor M. Sher / RET

VICTOR M. SHER

Todd D. True / RET

TODD D. TRUE

Rebecca E. Todd

REBECCA E. TODD

Sierra Club Legal Defense Fund, Inc.
216 First Avenue S. Suite 330
Seattle, WA 98014
(206) 343-7340

Attorneys for American Oceans Campaign, Campaign for Puget Sound, Dioxin/Organochlorine Center, Friends of the Earth, National Audubon Society, Puget Sound Alliance, Washington Environmental Council, and Washington Toxics Coalition.

Sent by telecopy to:

Chair William P. Hutchison, Jr.	(503) 223-5550
Vice Chair Emery N. Castle	(503) 737-1574
Commissioner Henry Lorenzen	(503) 276-3148
Commissioner Carol A. Whipple	(503) 584-2129
Commissioner William W. Wessinger	(503) 229-4689
Director Fred Hansen	(503) 229-6124

cc: Mr. Larry Edelman
Ms. Dana Rasmussen
Mr. Rick Albright
Ms. Adrianne Allen

U.S. EPA Region 10
Water Division

FAX: (206) 553-0165
FTS 399-0165

To Confirm Your FAX Call:
(206) 553-6913
FTS 399-6913

TO: Fred Hansen

Phone No:

City, State/Region:

FAX NUMBER: 513 229-6124

FROM: Bob Burd

1200 Sixth Avenue, WD- 131 Seattle, WA 98101

Phone No: 206 553-6415

TOTAL PAGES: 6
(Including this cover sheet)

COMMENTS:

United States
Environmental Protection
Agency

Region 10
1200 Sixth Avenue
Seattle WA 98101

Alaska
Idaho
Oregon
Washington

EPA

Reply to
Attn of: WD-139

Fred Hansen, Director
Oregon Department of Environmental Quality
Executive Building
811 SW Sixth Avenue
Portland, Oregon 97204

RE: Comments on Petition to Amend Oregon's Standard for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)

Dear Mr. Hansen:

The Environmental Protection Agency (EPA) Region 10 believes it is premature for the State of Oregon to revise its dioxin standard at this time in response to the petition referenced above, and recommends that the Environmental Quality Commission deny the petition.

As you are aware, EPA is currently reassessing the toxicity of TCDD. EPA expects to complete development of a new model for predicting TCDD toxicity by the spring of 1992. Following its development, the new model will undergo extensive peer review. EPA has committed considerable resources to collect additional data on endpoints other than cancer effects to help support this model. These other endpoints, which include reproductive and immunological responses, are of concern as they may be more sensitive to TCDD exposure than the development of cancerous tumors. Consequently, it is impossible to predict at this time whether EPA's criterion will become more or less stringent as a result of the reassessment.

As a final note, I would like to add that the technology-based controls being required of pulp and paper mills in Oregon will require controls adequate to meet Oregon's current TCDD standard. Thus, the mills should not incur any irretrievable expenditures during the coming y[illegible] [illegible]ile EPA completes its TCDD reassessment.

These comments are discussed in greater detail in the enclosure to this letter. Should you have any questions regarding our comments, please call me at (206) 553-5810. Thank you for the opportunity to comment on this petition.

Sincerely,

Dana A Rasmussen

Dana A. Rasmussen
Regional Administrator

Enclosure

ENVIRONMENTAL PROTECTION AGENCY
REGION 10

COMMENTS ON PETITION TO REVISE
OREGON'S TCDD STANDARD

June 10, 1991

This document provides the Environmental Protection Agency (EPA) Region 10 comments on the May 23, 1991, petition by James River II, Inc., and Boise Cascade Corporation to amend Oregon's water quality standard for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The petitioners propose a standard of 2.3 parts per quadrillion (ppq) in place of the current standard of .013 ppq. For the reasons discussed below, EPA believes it is premature for the State of Oregon to revise its dioxin standard at this time, and recommends that the Environmental Quality Commission deny the petition.

As you are aware, EPA is currently reassessing the toxicity of TCDD. This reassessment is in response to a growing understanding of the mechanism by which TCDD acts and on newer information on its carcinogenicity. EPA will attempt to develop a new model for predicting harmful levels of TCDD exposure based on this more recent information. EPA expects to complete development of the model by the spring of 1992. Following its development, the model will undergo extensive peer review. Because the model will consider a number of toxicological endpoints, it will not focus solely on cancer effects, as the model used to develop EPA's current water quality criterion for TCDD does.

While the standard proposed in the petition is based on a model similar to that which EPA is currently evaluating, EPA believes that use of the model to revise the standard is premature for the following reasons:

1. EPA has only begun to develop this model. While there appears to be general agreement on the mechanism by which TCDD causes toxicity, development of a predictive model relies on a number of assumptions, few of which have undergone any kind of rigorous testing or peer review. Due to its extreme toxicity, it seems inappropriate to substantially elevate the TCDD standard without more critical review of model assumptions.

2. The new model being developed by EPA relies on multiple toxic endpoints. Little information exists for many endpoints of concern. Therefore, EPA has committed considerable resources to collect additional data on other endpoints such as reproductive and immunological responses. The scant information available to date

suggests that these other endpoints may be more sensitive to TCDD exposure than the development of cancerous tumors. EPA's scientists are uncertain at present whether the new model, when combined with the new toxicological information being generated, will cause EPA's criterion to become more or less stringent. To increase the TCDD standard by over two orders of magnitude in light of this information appears inappropriate.

3. A number of other chemicals endemic in the environment appear to cause toxicity via a similar mechanism. It is possible, therefore, that chemicals such as PCBs, PAHs, DDT, furans, and dioxins other than TCDD may exacerbate the effects of exposure to TCDD. Part of the additional data being generated by EPA during the coming year is aimed at addressing this issue.

4. Current information on the effects of TCDD on aquatic organisms and wildlife has been inadequate for EPA to develop a criterion for their protection. However, both fish and wildlife have proven to be extremely sensitive to TCDD. In addition, concern has been raised over the potential effects of TCDD on threatened and endangered species, particularly bald eagles, in the Columbia River basin. To address this inadequacy, EPA is also collecting the information necessary for development of a TCDD criterion for the protection of aquatic life.

Because of the extreme toxicity of dioxin to aquatic life and laboratory animals, and because EPA is in the process of collecting a vast amount of additional information on the toxicity of TCDD, it would seem premature for Oregon to revise its TCDD standard at this time.

Region 10 does not believe that Oregon's current TCDD standard will cause any irretrievable expenditures by companies in the Pacific Northwest. All companies likely to be affected by the current standard are faced with making process changes to meet existing or proposed technology-based requirements. These technology-based requirements are expected to achieve, or come very close to achieving, TCDD limits based on the current standard of .013 ppq. In fact, Region 10 does not expect the appeals of their NPDES permits by the petitioners to be completed until after EPA concludes its TCDD reassessment next spring.

In conclusion, EPA believes that it would be premature for Oregon to consider revising its TCDD standard until EPA completes its reassessment. However, should the Environmental Quality Commission decide that a rulemaking to revise the standard is appropriate at this time, EPA suggests that the following be considered:

1. The proposed rule should consider the similar mechanisms of effect of other dioxin congeners, furans, PCBs, and other similar chemicals;

2. Other chlorinated organic compounds, such as chloroform and resin acids, which are often produced in association with TCDD and which are generally controlled by the same processes which control TCDD, should also be considered for rulemaking; and,

3. Aquatic life and wildlife effects should be considered in setting a new TCDD standard.

CHARLES R. "CHUCK" NORRIS
UMATILLA COUNTY
DISTRICT 57

REPLY TO ADDRESS INDICATED:
✔ House of Representatives
Salem, Oregon 97310-1347
P.O. 121, 725 E. Highland Ave.
Hermiston, Oregon 97838

378-8050

HOUSE OF REPRESENTATIVES
SALEM, OREGON
97310-1347

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 12 1991
OFFICE OF THE DIRECTOR

June 11, 1991

William P. Hutchison, Jr., Chair
Environmental Quality Commission
c/o Department of Environmental Quality
811 SW Sixth
Portland, OR 97204

Dear Mr. Hutchison:

I understand that the EQC is in receipt of petitions to reconsider the permissible ambient level of 2,3,7,8 TCDD (dioxin) in Oregon's water. You may recall that I had previously shared some concerns on this issue, basically questioning a criterion of .013 ppq. A copy of some relevant correspondence under date of March 19, 1990 is enclosed.

A lot has happened in this matter since my letter of March 19, most notably Dr. Robert A. Squire's letter of the same date refuting the research which led to the .013 ppq criterion. I'm sure you are aware of and have seen that letter, but I enclose a copy for your convenient reference.

While I am certainly committed to avoiding realistic biological risk, I remain concerned that we do not label certain bodies of water, especially the Columbia River John Day and McNary Pools, unsafe based on other than credible scientific evidence and principles.

As stated earlier, eventually the west end of Umatilla County must rely on the Columbia as a major source of water for a variety of uses, and it would be extremely unfortunate to have such use denied because of alleged contamination based on flawed criteria. No doubt you are aware that certain other states, in concert with the EPA, have adopted standards far less stringent then .013 ppq.

Your attention in this matter will be appreciated.

Sincerely,

C.R. "Chuck" Norris

2 enclosures: As stated above.

cc: Henry Lorenzen, Member, EQC
Fred Hansen, Director, DEQ

UMATILLA COUNTY
DISTRICT 57

REPLY TO ADDRESS INDICATED:
[ ] House of Representatives
Salem, Oregon 97310-1347
[✓] P.O. 121, 725 E. Highland Ave.
Hermiston, Oregon 97838

HOUSE OF REPRESENTATIVES
SALEM, OREGON
97310-1347

567-8638, ofc

March 19, 1990

SUBJECT: Dioxin in the Columbia River

TO: Fred Hansen, Director, Department of Environmental Quality
811 SW Sixth, Portland, OR 97204

Dear Fred:

During my comments to the Environmental Quality Commission on March 1 in Pendleton I raised two basic issues regarding dioxin in the Columbia.

1. Is there a scientific basis for the limiting standard of .013 parts per quadrillion? My best recollection is that I was informed that the standard was set by the EPA.

2. I commented that the water future of parts of District 57 (primarily the west end of Umatilla County) will rest on tapping the Columbia River to replace our current dependence on deep wells. I expressed the hope that we wouldn't get there just in time to learn that dioxin contamination above McNary Dam precluded our use of that source. My best recollection is that there was no response suggesting that there is or is likely to be such a problem. My thoughts and comments at the time are reported with reasonable accuracy in the enclosed article from the Hermiston Herald. (See Enclosure 1.)

Several days after the EQC meeting I read with dismay the enclosed article from the East Oregonian of March 12. It jarred me on two counts. (See Enclosure 2.)

1. It reported that the McNary pool was already badly contaminated.

2. It reported that the Oregon (DEQ) standard is .013 parts per quadrillion but that the Federal (EPA) standard is "only" .07 parts per trillion and the Federal FDA acceptable level is more lenient yet at 25 parts per trillion--the Oregon standard being more stern by factors of 5,000 and 35,000, respectively. (I have made no effort to check the math on those factors.)

I am confused and concerned and request a clear statement on acceptable levels of dioxin in the Columbia River (or any other water source) and whether or not the interagency disparity suggested in Enclosure 2 does in fact exist. I repeat my question and concern of March 1 regarding acceptable levels--scientific or arbitrary?

Your attention in this matter will be appreciated.

2 encl: As ~~stated above~~. Not included

Sincerely,

Chuck

C.R. "Chuck" Norris

cc: Wm. P. Hutchison, JR, Chair, EQC
Henry Lorenzen, Member, EQC

ROBERT A. SQUIRE ASSOCIATES, INC.
1515 LABELLE AVENUE
RUXTON, MARYLAND 21204
301-821-0054

March 19, 1990

Robert A. Michaels, Ph.D., Chairperson
Maine Scientific Advisory Panel
RAM TRAC Corporation
931 Northumberland Drive
Schenectady, N.Y. 12309

Dear Dr. Michaels:

I enclose a copy of the independent Pathology Working Group (PWG) Report on 2,3,7,8-Tetrachlorodibenzo-P-Dioxin conducted by Pathco, Inc. This report constitutes an objective reevaluation of the female rat liver lesions, by recognized experts, based upon current pathological criteria. I am certain the other observers of the PWG, Dr. Moch from FDA and Dr.'s Singh and Chiu from EPA, would agree with me that the review was conducted in a balanced, unbiased manner by highly qualified pathologists.

The conclusions reached by the PWG are consistent with my recent findings, as reported to you in my letter of January 8, 1990. A recalculation of potential human risk, based upon these new data, is clearly necessary. One of the most important statements in the report is that the morphological findings indicate that TCDD had only a weak oncogenic effect in female rat livers. This is in contrast to the view often expressed that TCDD is a potent animal carcinogen.

The Maine Scientific Panel should be commended for raising this issue and seeking an objective review based upon current scientific evidence. Without your request, it would have been difficult to obtain the slides for reevaluation and, more importantly, there would have been little impetus to conduct the review.

Please contact me if I may be of further assistance.

Sincerely,

Robert A. Squire

Robert A. Squire, D.V.M., Ph.D.

RAS:fts

cc:Dr. Robert Frakes

MAY 04 1990

(503) 229-5502
FAX (503) 226-1355
TDD-Nonvoice (503) 229-5497

Oregon
DEPARTMENT OF HUMAN RESOURCES
Health Division

June 11, 1991

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 12 1991
OFFICE OF THE DIRECTOR

Environmental Quality Commission
Director's Office
Dept. of Environmental Quality
811 SW 6th Avenue
Portland, Oregon 97204

Dear Commissioners:

I am writing as the spokesperson for the Oregon Health Division to recommend that the Environmental Quality Commission deny James River II, Inc. and Boise Cascade's petition to amend Oregon's ambient water quality standard for TCDD. Increasing the ambient water quality criteria for TCDD could potentially undermine the future protection of public health in the State of Oregon.

As the Public Health Toxicologist for the Oregon Health Division (OHD), I am very familiar with scientific information regarding the health effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). A substantial amount of scientific data exists to support a receptor-based mechanism of toxicity for this chemical. Empirical as well as epidemiologic information provide support that animal to man inferences, and high to low dose theoretical extrapolation models have not accurately estimated TCDD's true human toxicity.

The OHD is currently monitoring the scientific debates and developments regarding the assessment of human health effects of TCDD. We are also in the process of developing a public health policy regarding dioxin and furan contaminated media of public health concern in the State of Oregon. This policy is not expected to be finalized before the end of the year.

The OHD policy will provide information about whether or not human health effects would be expected from a certain type of dioxin or furan exposure. The policy will address pre-existing environmental contamination, and provide the mechanism to initiate appropriate public health protection activities.

The OHD approach will not be unlike other agency's "acceptable daily intake" estimates which identify a dose that is not expected to result in adverse health effects. However, such estimates are not useful for developing pollution prevention or antidegradation environmental protection policies. To be protective of public health,

BARBARA ROBERTS
Governor

1400 SW 5th Avenue
Portland, OR 97201
(503) 229-5599 Emergency
(503) 252-7978 TDD
Emergency

FAX

Cover Sheet

Office of Environment and Health Systems

Oregon Health Division

Fill in shaded boxes

Date: 6/11/91

From: Dr Roseanne Lorenzana

Office of Environmental and Health Systems, Oregon Health Division

Number of pages (including this cover sheet): 3

To: Fred Hansen, Director

Company: Dept of Env. Quality Phone: 229-5300

Subject:

Comments:

Note: If any of these FAX copies are illegible or you did not receive the number of pages stated above, please contact OEHS immediately at 503 / 229-6300.

Incoming FAX: 226-1355.

LIZ VanLEEUWEN
LINN COUNTY
DISTRICT 37

REPLY TO ADDRESS INDICATED:
☑ House of Representatives
Salem, OR 97310-1347
Capitol Message 378-8772

☐ 27070 Irish Bend Loop
Halsey, Oregon 97348
Home Phone 369-2544

HOUSE OF REPRESENTATIVES
SALEM, OREGON
97310-1347

COMMITTEES
Chairman:
Intergovernmental Affairs
Vice-Chairman:
Agriculture, Forestry, and Natural Resources
Member:
Enviroment and Energy

June 11, 1991

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 13 1991
OFFICE OF THE DIRECTOR

Mr. William P. Hutchison
Chairman, Environmental Quality Commission
811 S.W. Sixth Avenue
Portland, OR 97204

Dear Mr. Hutchison:

I am writing to support the James River Corporation and Boise Cascade petition to review Oregon's water quality standard for dioxin.

Oregon's current water quality standard of .0013 parts per quadrillion (ppq) may be more restrictive than necessary to protect human health. Recently, the EPA approved water quality standards in other states that are 100 times less stringent than the original EPA guideline criterion which Oregon adopted. Now EPA has called for a review of the science on dioxin. However, if Oregon awaits the outcome of the EPA study before reviewing its own dioxin standard, the two pulp and paper companies listed above will be bound by state law to invest millions of dollars in what may prove to be unnecessary environmental controls. That is why we need rule-making now.

James River will spend close to $20 million in the next three years to further reduce the discharge of dioxin from its Wauna pulp and paper mill on the Columbia River. If the Wauna mill were located in Maryland, Virginia or elsewhere in the Southeast, the mill already would be in compliance with EPA-approved standards, and the expenditures would not be necessary.

<u>We must establish a scientifically-based water quality standard for dioxin that protects Oregonians, but at the same time does not overwhelmingly disadvantage Oregon industry.</u> I urge you and other commission members to accept the petition to review Oregon'' water quality standard for dioxin when you meet June 14.

Sincerely,

Liz VanLeeuwen

Liz VanLeeuwen
State Representative
District 37

IF YOU THINK WHITER IS BETTER...

AGAIN.

This paper is whiter. It was bleached with chlorine.

A SMALL DIFFERENCE TO YOU...

...MAKES A BIG DIFFERENCE TO OTHERS.

Chlorine-bleached pulp is bad for the environment. There can be no doubt about that. Studies have shown again and again that effluents from kraft or sulphite mills using chlorine technology lead to reduced reproductivity in fish, suppressed immune systems, impaired metabolism, and a multitude of other long-term effects. Chlorine-bleached paper is also bad for you. Many of the chlorinated poisons discharged by the mills will also be found in paper - like the page you are now holding in your hand. Even dioxin, one of the most toxic chemicals ever produced, is likely to be present in this chlorine-bleached paper. Dioxin has been proven to leach from bleached paper products, such as milk cartons and coffee filters. Yet, dioxin is only the tip of the iceberg when it comes to organochlorine pollution from pulp and paper mills. Up to 1,000 different chemicals can be found in the effluent of mills employing chlorine-bleaching. Many of these cause cancer or genetic damage

and are persistent and accumulate in the environment. On average, pulp mills discharge around 35 tons of toxic organochlorines every single day. Even those mills that already have up-

graded their process to reduce formation of the most notorius organochlorine, dioxin, will still discharge between 10 and 20 tons of other chlorinated poisons every single day. These discharges must stop now. The page you are now reading was printed on sulphite pulp bleached with oxygen-based agents. Such chlorine-free bleaching technology is readily available and must be employed immediately by mills using the sulphite process. Chlorine-free bleaching technology available for kraft mills will yield a cream-colored pulp. That brightness is entirely sufficient for most purposes, particulary since kraft pulp is mainly used in paper products that need to be strong, not white, such as packaging, stationery or envelopes.

THINK TWICE BEFORE YOU BUY WHITE, AND SUPPORT GREENPEACE IN ITS DEMANDS FOR

- Complete elimination of all chlorine-based bleaching chemicals.
- Use of the right fiber for the right product, i.e. the use of off-white kraft and off-white sulphite pulp, or completely unbleached pulp whenever possible.

CHLORINE-FREE BY 1993!

For more information about different pulp and paper making technologies and their impact on the environment, please ask us for the Greenpeace Guide to Paper.

EQC File

Oregon

DEPARTMENT OF
ENVIRONMENTAL
QUALITY

July 15, 1991

John W. Gould
Lane Powell Spears Lubersky
800 Pacific Building
520 S. W. Yamhill Street
Portland, Oregon 97204

Richard Baxendale
506 National Building
108 Western Avenue
Seattle, Washington 98104

Enclosed is an ORDER affirming the June 14, 1991, action of the Environmental Quality Commission on the petition of James River II, Inc., and Boise Cascade Corporation to amend subparagraph (2)(p)(B) of Oregon Administrative Rules Chapter 340, Division 41, Sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965.

Sincerely,

Harold L. Sawyer

Harold L. Sawyer
Inter/Intra Program Coordinator

HLS:l

enclosure

811 SW Sixth Avenue
Portland, OR 97204-1390
(503) 229-5696

Before the Environmental Quality Commission
of the State of Oregon

In the Matter of the Petition of James River II, Inc., and Boise Cascade Corporation to Amend Subparagraph (2)(p)(B) of Oregon Administrative Rules Chapter 340, Division 41, Sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965.	)	ORDER

1. James River II, Inc., and Boise Cascade Corporation filed a petition on May 23, 1991, to amend Oregon's ambient water quality standard for 2,3,7,8-tetrachloro-dibenzo-p-dioxin (TCDD). Specifically, the petition proposed a standard of 2.3 parts per quadrillion (ppq) in place of the current standard of 0.013 ppq. The petitioners stated that supporters included the Associated Oregon Industries, the Northwest Pulp & Paper Association, the Association of Western Pulp and Paper Workers, Local 1, and the United Paper Workers International, Local 1097. Petitioners requested opportunity to make an oral presentation to the Commission regarding the petition.

2. Petitioners identified persons (and their attorneys) believed to be interested in the proposed rule change as follows: City of St. Helens, Northwest Coalition for Alternatives to Pesticides, Columbia River United, Pope and Talbot, Inc., UA Local 290, Plumbers and Steamfitters, and Mike Jerkiewicz. Petitioners provided a copy of their petition and supporting documentation to the attorneys for those believed to be interested in the proposed rule change.

3. The Environmental Quality Commission (Commission) gave notice dated May 28, 1991, that it would consider, and could act upon, this petition at its regularly scheduled meeting on June 14, 1991. This meeting was held in Room 3A of the Department of Environmental Quality offices at 811 S. W. 6th Avenue, Portland, Oregon, beginning at 8:30 a.m. The item was listed on the regular agenda as an action item to be considered at 10:00 a.m.

4. Interested persons were given the opportunity to submit written memoranda on the petition by filing six (6) copies of all written materials at the Director's Office, Department of Environmental Quality, 811 S. W. 6th Avenue, Portland, Oregon 97204 by no later than 4:00 p.m. on June 7, 1991, or in the alternative, by serving individual copies upon each Commission member and the Director by no later than 4:00 p.m. on June 10, 1991.

5. Written materials were submitted as follows:

Date	Date Received	Item Description
June 2, 1991	June 4, 1991	Letter from **Roger and Mary Thompson**
June 4, 1991	June 7, 1991	Letter from **Robert J. Thompson**
June 6, 1991	June 7, 1991	Letter from **Northwest Pulp & Paper**
June 6, 1991	June 7, 1991	Letter from **Oregon Salmon Commission**
June 7, 1991	June 10, 1991	Letter and attachments from **Greenpeace**
June 7, 1991	June 11, 1991	Memorandum from the **Department of Environmental Quality**
June 10, 1991	June 10, 1991	Letter from **Northwest Environmental Advocates**
June 10, 1991	June 10, 1991	Memorandum from **Sierra Club Legal Defense Fund**
Undated	June 11, 1991	Letter from **Environmental Protection Agency**
June 11, 1991	June 12, 1991	Letter from **Representative Norris**
June 11, 1991	June 12, 1991	Letter from **Oregon Health Division**
June 11, 1991	June 13, 1991	Letter from **Representative Van Leeuwen**
June 14, 1991	June 13, 1991	Statement from **Oregon State Public Interest Research Group**

6. The Commission received oral presentations at the June 14, 1991, meeting from persons who signed up to present testimony. Presenters were asked to limit testimony to a maximum of 5 minutes on the issue of whether the Commission should:

(a) accept the petition and initiate a rulemaking proceeding as requested in the petition, or

(b) deny the petition.

7. The following presented oral testimony to the Commission or responded to questions from the Commission:

Name	Representing
John Gould	James River II, Inc., and Boise Cascade Corporation
Dr. Russell Keenan	James River II, Inc., and Boise Cascade Corporation
Donald L. Kallberg	City of St. Helens
John Gorley	United Paper Workers International Union, Local 1097, Wauna, Oregon
Billy Taylor	United Paper Workers International Union, Local 1097, Wauna, Oregon
Linda Res	Association of Western Pulp and Paper Workers, Local 1
Tom Donaca	Associated Oregon Industries
Kenneth Brooks	U. S. Environmental Protection Agency
Greg deBruler	Columbia River Defense Project; and Columbia River United
Nina Bell	Northwest Environmental Advocates
Larry Edelman	Assistant Attorney General, Oregon Department of Justice
Lydia Taylor	Department of Environmental Quality, Water Quality Division
Neil Mullane	Department of Environmental Quality, Water Quality Division
Gene Foster	Department of Environmental Quality, Water Quality Division

8. The Commission evaluated materials and testimony presented, and voted unanimously (with four members present) to deny the petition for rulemaking.

9. Reasons cited by the Commission for denying the petition include but are not limited to the following:

- The Department recently reviewed available new information regarding 2,3,7,8-TCDD (dioxin) in connection with the triennial review of water quality standards. The Department further indicated that no new peer-reviewed information had come forward since the Department completed this evaluation. The Department concluded that the current dioxin standard continues to be appropriate.

- Following the Department review as part of the triennial review process, EPA announced they would undertake a review of their recommended criteria for dioxin. The Oregon standard for dioxin was adopted based on the EPA recommended criteria. EPA expects this review to take 1-2 years to complete. The EPA review will address all of the issues raised by the petitioners. EPA has recommended that regulatory actions proceed based on existing criteria pending completion of its review of the present dioxin criteria.

- The EPA review could result in a criteria value lower than the present Oregon standard in order to protect wildlife and aquatic life.

- While there may be consensus among some of the leading scientists that a different theoretical way of looking at risks associated with dioxin should be used, there does not appear to be consensus with respect to the risk implications of the different theoretical approach.

- Concern was expressed about the Department's ability and resources to analyze a particularly complex question, particularly in light of the EPA's indication that, with all of its expertise and resources, one to two years will be required to evaluate the new information and arrive at a comprehensive determination.

- Studies on dioxin will go on, and new information will be forthcoming. When EPA has completed their review of the dioxin criteria, the Department will undertake a review of the current standard if it is warranted.

ORDER

It is hereby ordered that the Petition of James River II, Inc., and Boise Cascade Corporation to Amend Subparagraph (2)(p)(B) of Oregon Administrative Rules Chapter 340, Division 41, Sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965 be denied.

Dated this 15 day of July, 1991.

On behalf of the Commission

Fred Hansen

Fred Hansen, Director
Department of Environmental Quality

Before the Environmental Quality Commission
of the State of Oregon

In the Matter of the Petition of James River II, Inc., and Boise Cascade Corporation to Amend Subparagraph (2)(p)(B) of Oregon Administrative Rules Chapter 340, Division 41, Sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965.	)	NOTICE OF CONSIDERATION OF PETITION FOR RULE AMENDMENT

1. James River II, Inc., and Boise Cascade Corporation have filed a petition as noted above to amend Oregon's ambient water quality standard for 2,3,7,8-tetrachloro-dibenzo-p-dioxin (TCDD). Specifically, the petition proposes a standard of 2.3 parts per quadrillion (ppq) in place of the current standard of 0.013 ppq. The petitioners state that supporters include the Associated Oregon Industries, the Northwest Pulp & Paper Association, the Association of Western Pulp and Paper Workers, Local 1, and the United Paper Workers International, Local 1097. Petitioners requested opportunity to make an oral presentation to the Commission regarding the petition.

2. Petitioners have identified persons (and their attorneys) believed to be interested in the proposed rule change as follows: City of St. Helens, Northwest Coalition for Alternatives to Pesticides, Columbia River United, Pope and Talbot, Inc., UA Local 290, Plumbers and Steamfitters, and Mike Jerkiewicz. Petitioners have provided a copy of their petition and supporting documentation to the attorneys for those believed to be interested in the proposed rule change.

3. The Environmental Quality Commission (EQC) will consider, and may act upon, this petition at its regularly scheduled meeting on June 14, 1991. The item will be listed on the regular agenda as an action item. This meeting will be held in Room 3A of the DEQ offices at 811 S. W. 6th Avenue, Portland, Oregon, beginning at 8:30 a.m. Persons interested in this item should be present when the meeting begins.

4. Interested persons may submit written memoranda on the petition provided either that six (6) copies of all written materials are received by the Director's Office, Department of Environmental Quality, 811 S. W. 6th Avenue, Portland, Oregon 97204 of DEQ by no later than 4:00 p.m. on June 7, 1991, or in the alternative, that individual copies are served upon each Commission member and the Director by no later than 4:00 p.m. on June 10, 1991.

5. The EQC will allow limited oral presentations, not to exceed 5 minutes, addressed to the issue of whether the Commission should:

   (a) accept the petition and initiate a rulemaking proceeding as requested in the petition, or

   (b) deny the petition.

   Oral presentations should summarize written materials submitted.

6. Questions relating to this matter should be directed to the DEQ Directors Office at 229-5300.

Dated this 29 day of May, 1991.

William P. Hutchison, Jr.

William P. Hutchison, Jr., Chair
Environmental Quality Commission

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
MAY 23 1991
OFFICE OF THE DIRECTOR

May 23, 1991

HAND DELIVERED

Mr. Fred Hansen, Director
Oregon Department of Environmental Quality
811 S.W. Sixth Avenue
Portland, Oregon 97204

Re: Petition for Rule Amendment

Dear Mr. Hansen:

Enclosed is a petition to amend Oregon's ambient water quality criterion for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The petitioners are James River II, Inc., and Boise Cascade Corporation. Also supporting the petition are the Associated Oregon Industries, the Northwest Pulp & Paper Association[1], the City of St. Helens, the Association of Western Pulp and Paper Workers, Local 1, and the United Paper Workers International Union, Local 1097.

As you know, Oregon's present ambient water quality criterion for TCDD is 0.013 parts per quadrillion (ppq). The Environmental Quality Commission adopted this criterion in 1987 from an EPA guidance criterion developed in 1984. Since the criterion's adoption, and particularly within the last several months, a substantial body of new scientific evidence has shown that the assumptions upon which EPA relied in developing its guidance criterion were incorrect and that EPA's guidance criterion enormously overstated the risks posed by TCDD. The new evidence prompted EPA Administrator William Reilly in April of this year to order a complete reevaluation of the risks posed by TCDD and of EPA's TCDD-related programs.

The supporting documents appended to the petition describe in detail the latest scientific information concerning the risks posed by TCDD, as well as information concerning environmental exposures to TCDD in Oregon. Based on this information, the petition proposes an Oregon water quality criterion for TCDD of 2.3 ppq.

---

1 Pope & Talbot, Inc., is a member of the Northwest Pulp & Paper Association but takes no position on the petition.

mrcpay24 15760/133

In submitting this petition, the petitioners are mindful of the Department's triennial review recommendation to retain the existing water quality criterion of 0.013 ppq. It is the petitioners' understanding, however, that the Department's recommendation was made without the benefit of the very recent scientific information that prompted EPA Administrator Reilly's April decision to reevaluate the risks posed by TCDD. This information includes the reassessment of the animal studies on which EPA relied in developing its guidance criterion for TCDD, the results of the Banbury Conference on TCDD risks, and recently published epidemiologic studies of workers and others exposed to TCDD.

The petitioners are also mindful of the limited resources of the Commission and the Department and their extensive obligations with respect to other matters. Given these constraints, the Commission may be tempted not to take any action until EPA has undertaken the lengthy process of revising its guidance criterion for TCDD. Unfortunately, by the time that EPA has acted, Oregon's existing TCDD criterion may have resulted in tens of millions of dollars of additional pollution control expenditures that the latest scientific information shows will produce no environmental benefit. Maryland and Virginia have recently averted this wasteful result by adopting, with EPA approval, water quality criteria for TCDD that are nearly 100 times less stringent than EPA's now outdated 1984 guidance criterion.

By granting the petition, the Commission will not, of course, have committed itself to revising the TCDD criterion. The petitioners ask only for an opportunity to present the latest scientific evidence on TCDD to the Commission and the public in the open forum provided by the Commission's procedures for rulemaking. In presenting this evidence, the petitioners would make available to the Commission, as well as the public, national experts in the risks posed by TCDD, including Dr. Robert Squire, whose evaluation of the tissues of rats fed TCDD was the primary basis for EPA's present guidance criterion. The petitioners are confident that this evidence will convincingly demonstrate that a TCDD criterion of 2.3 ppq

will fully protect human health and all designated beneficial uses of the waters of the state.

Very truly yours,

John W. Gould
Lane Powell Spears Lubersky
800 Pacific Building
520 S.W. Yamhill Street
Portland, Oregon 97204
(503) 226-6151
Of Attorneys for
Petitioner James River II, Inc.

Richard Baxendale by MRC
Richard Baxendale
506 National Building
1008 Western Avenue
Seattle, Washington 98104
(206) 623-2848
Of Attorneys for
Petitioner Boise Cascade
Corporation

cc: Chair William P. Hutchison, Jr.
Commissioner Emery N. Castle
Commissioner Henry Lorenzen
Commissioner Carol A. Whipple
Commissioner William W. Wessinger
Mr. John E. Bonine
Mr. Larry Edelman
Mr. Michael Huston
Mr. Peter Linden
Ms. Lydia Taylor
Ms. Linda K. Williams
Mr. Jay T. Waldron
Mr. James M. Whitty, Associated Oregon Industries
Ms. Llewellyn Matthews, Northwest Pulp & Paper Association
Mr. William Taylor, United Paper Workers International Union, Local 1097
Mr. Gordon Simpson, Association of Western Pulp and Paper Workers, Local 1

mrcpay24 15760/133

Before the Environmental Quality Commission
of the State of Oregon

In the Matter of the Petition of James River II, Inc., and Boise Cascade Corporation to Amend Subparagraph (2)(p)(B) of Oregon Administrative Rules Chapter 340, Division 41, Sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965.	)	NOTICE OF CONSIDERATION OF PETITION FOR RULE AMENDMENT

1. James River II, Inc., and Boise Cascade Corporation have filed a petition as noted above to amend Oregon's ambient water quality standard for 2,3,7,8-tetrachloro-dibenzo-p-dioxin (TCDD). Specifically, the petition proposes a standard of 2.3 parts per quadrillion (ppq) in place of the current standard of 0.013 ppq. The petitioners state that supporters include the Associated Oregon Industries, the Northwest Pulp & Paper Association, the Association of Western Pulp and Paper Workers, Local 1, and the United Paper Workers International, Local 1097. Petitioners requested opportunity to make an oral presentation to the Commission regarding the petition.

2. Petitioners have identified persons (and their attorneys) believed to be interested in the proposed rule change as follows: City of St. Helens, Northwest Coalition for Alternatives to Pesticides, Columbia River United, Pope and Talbot, Inc., UA Local 290, Plumbers and Steamfitters, and Mike Jerkiewicz. Petitioners have provided a copy of their petition and supporting documentation to the attorneys for those believed to be interested in the proposed rule change.

3. The Environmental Quality Commission (EQC) will consider, and may act upon, this petition at its regularly scheduled meeting on June 14, 1991. The item will be listed on the regular agenda as an action item. This meeting will be held in Room 3A of the DEQ offices at 811 S. W. 6th Avenue, Portland, Oregon, beginning at 8:30 a.m. Persons interested in this item should be present when the meeting begins.

4. Interested persons may submit written memoranda on the petition provided either that six (6) copies of all written materials are received by the Director's Office, Department of Environmental Quality, 811 S. W. 6th Avenue, Portland, Oregon 97204 of DEQ by no later than 4:00 p.m. on June 7, 1991, or in the alternative, that individual copies are served upon each Commission member and the Director by no later than 4:00 p.m. on June 10, 1991.

5. The EQC will allow limited oral presentations, not to exceed 5 minutes, addressed to the issue of whether the Commission should:

   (a) accept the petition and initiate a rulemaking proceeding as requested in the petition, or

   (b) deny the petition.

   Oral presentations should summarize written materials submitted.

6. Questions relating to this matter should be directed to the DEQ Directors Office at 229-5300.

Dated this 29 day of May, 1991.

William P. Hutchison, Jr.

William P. Hutchison, Jr., Chair
Environmental Quality Commission

United States
Environmental Protection
Agency

Region 10
1200 Sixth Avenue
Seattle WA 98101

Alaska
Idaho
Oregon
Washington

EPA

JUN 11 1991

Reply to
Attn of: WD-139

Fred Hansen, Director
Oregon Department of Environmental Quality
Executive Building
811 SW Sixth Avenue
Portland, Oregon 97204

RE: Comments on Petition to Amend Oregon's Standard for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)

Dear Mr. Hansen:

The Environmental Protection Agency (EPA) Region 10 believes it is premature for the State of Oregon to revise its dioxin standard at this time in response to the petition referenced above, and recommends that the Environmental Quality Commission deny the petition.

As you are aware, EPA is currently reassessing the toxicity of TCDD. EPA expects to complete development of a new model for predicting TCDD toxicity by the spring of 1992. Following its development, the new model will undergo extensive peer review. EPA has committed considerable resources to collect additional data on endpoints other than cancer effects to help support this model. These other endpoints, which include reproductive and immunological responses, are of concern as they may be more sensitive to TCDD exposure than the development of cancerous tumors. Consequently, it is impossible to predict at this time whether EPA's criterion will become more or less stringent as a result of the reassessment.

As a final note, I would like to add that the technology-based controls being required of pulp and paper mills in Oregon will require controls adequate to meet Oregon's current TCDD standard. Thus, the mills should not incur any irretrievable expenditures during the coming year while EPA completes its TCDD reassessment.

These comments are discussed in greater detail in the enclosure to this letter. Should you have any questions regarding our comments, please call me at (206) 553-5810. Thank you for the opportunity to comment on this petition.

Sincerely,

Dana A Rasmussen

Dana A. Rasmussen
Regional Administrator

Enclosure

ENVIRONMENTAL PROTECTION AGENCY
REGION 10

COMMENTS ON PETITION TO REVISE OREGON'S TCDD STANDARD

June 10, 1991

This document provides the Environmental Protection Agency (EPA) Region 10 comments on the May 23, 1991, petition by James River II, Inc., and Boise Cascade Corporation to amend Oregon's water quality standard for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The petitioners propose a standard of 2.3 parts per quadrillion (ppq) in place of the current standard of .013 ppq. For the reasons discussed below, EPA believes it is premature for the State of Oregon to revise its dioxin standard at this time, and recommends that the Environmental Quality Commission deny the petition.

As you are aware, EPA is currently reassessing the toxicity of TCDD. This reassessment is in response to a growing understanding of the mechanism by which TCDD acts and on newer information on its carcinogenicity. EPA will attempt to develop a new model for predicting harmful levels of TCDD exposure based on this more recent information. EPA expects to complete development of the model by the spring of 1992. Following its development, the model will undergo extensive peer review. Because the model will consider a number of toxicological endpoints, it will not focus solely on cancer effects, as the model used to develop EPA's current water quality criterion for TCDD does.

While the standard proposed in the petition is based on a model similar to that which EPA is currently evaluating, EPA believes that use of the model to revise the standard is premature for the following reasons:

1. EPA has only begun to develop this model. While there appears to be general agreement on the mechanism by which TCDD causes toxicity, development of a predictive model relies on a number of assumptions, few of which have undergone any kind of rigorous testing or peer review. Due to its extreme toxicity, it seems inappropriate to substantially elevate the TCDD standard without more critical review of model assumptions.

2. The new model being developed by EPA relies on multiple toxic endpoints. Little information exists for many endpoints of concern. Therefore, EPA has committed considerable resources to collect additional data on other endpoints such as reproductive and immunological responses. The scant information available to date

suggests that these other endpoints may be more sensitive to TCDD exposure than the development of cancerous tumors. EPA's scientists are uncertain at present whether the new model, when combined with the new toxicological information being generated, will cause EPA's criterion to become more or less stringent. To increase the TCDD standard by over two orders of magnitude in light of this information appears inappropriate.

3. A number of other chemicals endemic in the environment appear to cause toxicity via a similar mechanism. It is possible, therefore, that chemicals such as PCBs, PAHs, DDT, furans, and dioxins other than TCDD may exacerbate the effects of exposure to TCDD. Part of the additional data being generated by EPA during the coming year is aimed at addressing this issue.

4. Current information on the effects of TCDD on aquatic organisms and wildlife has been inadequate for EPA to develop a criterion for their protection. However, both fish and wildlife have proven to be extremely sensitive to TCDD. In addition, concern has been raised over the potential effects of TCDD on threatened and endangered species, particularly bald eagles, in the Columbia River basin. To address this inadequacy, EPA is also collecting the information necessary for development of a TCDD criterion for the protection of aquatic life.

Because of the extreme toxicity of dioxin to aquatic life and laboratory animals, and because EPA is in the process of collecting a vast amount of additional information on the toxicity of TCDD, it would seem premature for Oregon to revise its TCDD standard at this time.

Region 10 does not believe that Oregon's current TCDD standard will cause any irretrievable expenditures by companies in the Pacific Northwest. All companies likely to be affected by the current standard are faced with making process changes to meet existing or proposed technology-based requirements. These technology-based requirements are expected to achieve, or come very close to achieving, TCDD limits based on the current standard of .013 ppq. In fact, Region 10 does not expect the appeals of their NPDES permits by the petitioners to be completed until after EPA concludes its TCDD reassessment next spring.

In conclusion, EPA believes that it would be premature for Oregon to consider revising its TCDD standard until EPA completes its reassessment. However, should the Environmental Quality Commission decide that a rulemaking to revise the standard is appropriate at this time, EPA suggests that the following be considered:

1. The proposed rule should consider the similar mechanisms of effect of other dioxin congeners, furans, PCBs, and other similar chemicals;

2. Other chlorinated organic compounds, such as chloroform and resin acids, which are often produced in association with TCDD and which are generally controlled by the same processes which control TCDD, should also be considered for rulemaking; and,

3. Aquatic life and wildlife effects should be considered in setting a new TCDD standard.

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
MAY 23 1991
OFFICE OF THE DIRECTOR

May 23, 1991

HAND DELIVERED

Mr. Fred Hansen, Director
Oregon Department of Environmental Quality
811 S.W. Sixth Avenue
Portland, Oregon 97204

Re: Petition for Rule Amendment

Dear Mr. Hansen:

Enclosed is a petition to amend Oregon's ambient water quality criterion for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The petitioners are James River II, Inc., and Boise Cascade Corporation. Also supporting the petition are the Associated Oregon Industries, the Northwest Pulp & Paper Association[1], the City of St. Helens, the Association of Western Pulp and Paper Workers, Local 1, and the United Paper Workers International Union, Local 1097.

As you know, Oregon's present ambient water quality criterion for TCDD is 0.013 parts per quadrillion (ppq). The Environmental Quality Commission adopted this criterion in 1987 from an EPA guidance criterion developed in 1984. Since the criterion's adoption, and particularly within the last several months, a substantial body of new scientific evidence has shown that the assumptions upon which EPA relied in developing its guidance criterion were incorrect and that EPA's guidance criterion enormously overstated the risks posed by TCDD. The new evidence prompted EPA Administrator William Reilly in April of this year to order a complete reevaluation of the risks posed by TCDD and of EPA's TCDD-related programs.

The supporting documents appended to the petition describe in detail the latest scientific information concerning the risks posed by TCDD, as well as information concerning environmental exposures to TCDD in Oregon. Based on this information, the petition proposes an Oregon water quality criterion for TCDD of 2.3 ppq.

---

[1] Pope & Talbot, Inc., is a member of the Northwest Pulp & Paper Association but takes no position on the petition.

mrcpay24 15760/133

In submitting this petition, the petitioners are mindful of the Department's triennial review recommendation to retain the existing water quality criterion of 0.013 ppq. It is the petitioners' understanding, however, that the Department's recommendation was made without the benefit of the very recent scientific information that prompted EPA Administrator Reilly's April decision to reevaluate the risks posed by TCDD. This information includes the reassessment of the animal studies on which EPA relied in developing its guidance criterion for TCDD, the results of the Banbury Conference on TCDD risks, and recently published epidemiologic studies of workers and others exposed to TCDD.

The petitioners are also mindful of the limited resources of the Commission and the Department and their extensive obligations with respect to other matters. Given these constraints, the Commission may be tempted not to take any action until EPA has undertaken the lengthy process of revising its guidance criterion for TCDD. Unfortunately, by the time that EPA has acted, Oregon's existing TCDD criterion may have resulted in tens of millions of dollars of additional pollution control expenditures that the latest scientific information shows will produce no environmental benefit. Maryland and Virginia have recently averted this wasteful result by adopting, with EPA approval, water quality criteria for TCDD that are nearly 100 times less stringent than EPA's now outdated 1984 guidance criterion.

By granting the petition, the Commission will not, of course, have committed itself to revising the TCDD criterion. The petitioners ask only for an opportunity to present the latest scientific evidence on TCDD to the Commission and the public in the open forum provided by the Commission's procedures for rulemaking. In presenting this evidence, the petitioners would make available to the Commission, as well as the public, national experts in the risks posed by TCDD, including Dr. Robert Squire, whose evaluation of the tissues of rats fed TCDD was the primary basis for EPA's present guidance criterion. The petitioners are confident that this evidence will convincingly demonstrate that a TCDD criterion of 2.3 ppq

will fully protect human health and all designated beneficial uses of the waters of the state.

Very truly yours,

John W. Gould

John W. Gould
Lane Powell Spears Lubersky
800 Pacific Building
520 S.W. Yamhill Street
Portland, Oregon 97204
(503) 226-6151
Of Attorneys for
Petitioner James River II, Inc.

Richard Baxendale by MRC

Richard Baxendale
506 National Building
1008 Western Avenue
Seattle, Washington 98104
(206) 623-2848
Of Attorneys for
Petitioner Boise Cascade
Corporation

cc: Chair William P. Hutchison, Jr.
Commissioner Emery N. Castle
Commissioner Henry Lorenzen
Commissioner Carol A. Whipple
Commissioner William W. Wessinger
Mr. John E. Bonine
Mr. Larry Edelman
Mr. Michael Huston
Mr. Peter Linden
Ms. Lydia Taylor
Ms. Linda K. Williams
Mr. Jay T. Waldron
Mr. James M. Whitty, Associated Oregon Industries
Ms. Llewellyn Matthews, Northwest Pulp & Paper Association
Mr. William Taylor, United Paper Workers International Union, Local 1097
Mr. Gordon Simpson, Association of Western Pulp and Paper Workers, Local 1

mrcpay24 15760/133

BEFORE THE ENVIRONMENTAL QUALITY COMMISSION
OF THE STATE OF OREGON

In the matter of the petition of James River II, Inc., and Boise Cascade Corporation to amend subparagraph (2)(p)(B) of Oregon Administrative Rules chapter 340, division 41, sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965.	PETITION FOR RULE AMENDMENT (ORAL PRESENTATION REQUESTED)

May 23, 1991

I. INTRODUCTION

James River II, Inc. (James River) and Boise Cascade Corporation (Boise Cascade) petition the Commission to amend subparagraph (2)(p)(B) of OAR chapter 340, division 41, sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965. Supporting the Petition are the Associated Oregon Industries, the Northwest Pulp & Paper Association[1], the City of St. Helens, the Association of Western Pulp and Paper Workers, Local 1, and the United Paper Workers International Union, Local 1097.

The sections of the Oregon Administrative Rules listed above establish water quality criteria for all of Oregon's water basins. Subparagraph (2)(p)(B) of each section is identical:

> Levels of toxic substances shall not exceed the most recent criteria values for organic and inorganic pollutants established by EPA [the U.S. Environmental Protection Agency] and published in **Quality Criteria for Water** (1986). A list of the criteria is presented in Table 20.

The most stringent of EPA's published criteria for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), as set forth in Table 20, is 0.000013 nanograms per liter, or 0.013 parts per quadrillion (ppq), for the protection of human health.

---

[1] Pope & Talbot, Inc., is a member of the Northwest Pulp & Paper Association but takes no position on the Petition.

A substantial body of new scientific evidence concerning the toxicity of TCDD has become available since EPA published its guideline TCDD criteria in 1984.[2] This new evidence overwhelmingly shows that TCDD is far less harmful than was originally assumed and that EPA's TCDD criterion of 0.013 ppq for the protection of human health is no longer scientifically defensible. The new evidence, together with evidence concerning TCDD that is specific to Oregon, is discussed in the "Supporting Document for the Establishment of an Ambient Water Quality Criterion for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin in the State of Oregon," attached as Appendix A, and in "An Assessment of Potential Carcinogenic Risk from 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)," attached as Appendix B. In accordance with the recommendations set forth in Appendix A, the Petitioners request that the Commission initiate rulemaking proceedings to amend subparagraph (2)(p)(B) of the sections listed above to provide that concentrations of TCDD shall not exceed 2.3 ppq in Oregon waters.

The Petitioners submit this Petition for Rule Amendment pursuant to ORS 183.390, OAR 340-11-046, and OAR 137-01-070. As provided in OAR 137-01-070(3)(b), the Petitioners

---

[2] EPA's Quality Criteria for Water 1986, EPA 440/5-86-001, was published in 1986, but EPA's criteria for TCDD were published in 1984, 49 Fed. Reg. 5831 (Feb. 15, 1984).

[redacted]

II. PETITIONERS

Petitioner James River owns and operates a bleached kraft pulp and paper mill at Wauna, Oregon. The mill discharges process wastewater into the Columbia River pursuant to a National Pollutant Discharge Elimination System (NPDES) permit issued by the Oregon Department of Environmental Quality (DEQ). On November 14, 1990, DEQ issued a renewed NPDES permit for the mill which contained effluent limits for TCDD. James River subsequently requested a contested case hearing on the TCDD effluent limits and other conditions of the renewed permit. The contested case is now pending before the Commission. James River's address is:

James River II, Inc.
Wauna Mill
Route 2, Box 2185
Clatskanie, Oregon 97016

Boise Cascade owns and operates a bleached kraft pulp and paper mill at St. Helens, Oregon. The mill discharges process wastewater into a publicly owned treatment works operated by the City of St. Helens. The treatment works discharges effluent into the Columbia River pursuant to an NPDES permit issued by DEQ. On November 14, 1990, DEQ issued a renewed NPDES permit for the City which contained effluent limits for TCDD and which required the City to limit TCDD

discharges from the mill into its treatment works. The City subsequently requested a contested case hearing on the TCDD effluent limits and other conditions of its renewed permit. Boise Cascade is a party to that contested case. The contested case has been consolidated with the contested case concerning James River's renewed NPDES permit and is now pending before the Commission. Boise Cascade's address is:

Boise Cascade Corporation
1600 S.W. Fourth Avenue
Portland, Oregon 97201

All correspondence concerning this petition should be directed to

John W. Gould
Lane Powell Spears Lubersky
800 Pacific Building
520 S.W. Yamhill Street
Portland, Oregon 97204

and

Richard Baxendale
506 National Building
1008 Western Avenue
Seattle, Washington 98104

III. OTHER INTERESTED PARTIES

The Petitioners believe that the other parties to the contested cases described above may be interested in the petition. In addition to DEQ, those parties and their attorneys are:

City of St. Helens

Represented by: Peter M. Linden
City Attorney
City of St. Helens
P.O. Box 278
St. Helens, Oregon 97051

Northwest Coalition for Alternatives to Pesticides
Columbia River United

Represented by: John E. Bonine
Western Environmental Law Clinic
School of Law
University of Oregon
Eugene, Oregon 97403

Pope and Talbot, Inc.

Represented by: Jay T. Waldron
David F. Bartz, Jr.
Schwabe, Williamson & Wyatt
1600-1950 Pacwest Center
1211 S.W. Fifth Avenue
Portland, Oregon 97204

UA Local 290, Plumbers and Steamfitters
Mike Jerkiewicz

Represented by: Linda K. Williams
1744 N.E. Clackamas Street
Portland, Oregon 97232

IV. RULE TO BE AMENDED

The Petitioners request that the Commission amend subparagraph (2)(p)(B) in each of the following sections of Oregon Administrative Rules chapter 340, division 41: 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965. Subparagraph (2)(p)(B) of each of these sections is identical:

> Levels of toxic substances shall not exceed the most recent criteria values for organic and inorganic pollutants

> established by EPA and published in **Quality Criteria for Water** (1986). A list of the criteria is presented in Table 20.

Table 20 lists these EPA criteria for TCDD: 0.010 micrograms per liter (ug/l) (10,000 ppq) for the acute protection of freshwater aquatic life; 0.00001 ug/l (10 ppq) for the chronic protection of freshwater aquatic life; 0.000014 nanograms per liter (ng/l) (0.014 ppq) for the protection of human health from fish consumption; 0.000013 ng/l (0.013 ppq) for the protection of human health from fish consumption and water ingestion. The most stringent EPA TCDD criterion, then, is 0.013 ppq.

Petitioners request that the Commission amend subparagraph (2)(p)(B) of each of the sections of OAR chapter 340, division 41, listed above to read as follows (matter to be added is highlighted):

> Levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin shall not exceed 0.0023 nanograms per liter (2.3 parts per quadrillion). Levels of other toxic substances shall not exceed the most recent criteria values for organic and inorganic pollutants established by EPA and published in **Quality Criteria for Water** (1986). A list of the criteria is presented in Table 20.

Thus, following the requested amendment, subparagraph (2)(p)(B) of each of the amended sections of OAR chapter 340, division 41, would read:

> Levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin shall not exceed 0.0023 nanograms per liter (2.3 parts per quadrillion). Levels of other toxic substances shall not exceed the most recent criteria values for

organic and inorganic pollutants established by EPA and published in **Quality Criteria for Water** (1986). A list of the criteria is presented in Table 20.

V. LEGAL BACKGROUND

The Commission's function is "to establish the policies for the operation of the department [DEQ]." ORS 468.015. In particular, the Commission is to "establish standards of quality and purity for the waters of the state." ORS 468.735(1).

The federal Clean Water Act also requires the Commission, as the state agency responsible for water pollution control, to adopt water quality standards for the waters of the state. See 33 U.S.C. § 1313(c)(1). Water quality "standards" "consist of the designated uses of the . . . waters involved and the water quality criteria for such waters based upon such uses." 33 U.S.C. § 1313(c)(2)(A). For substances such as TCDD that are listed as toxic pollutants under the Clean Water Act, states must adopt "specific numerical criteria" for the pollutants. See 33 U.S.C. § 1313(c)(2)(B). All water quality criteria adopted by a state are subject to review by EPA for consistency with the Clean Water Act. See 33 U.S.C. § 1313(c)(3).

Section 304 of the Clean Water Act requires EPA to "develop and publish . . . criteria for water quality." 33 U.S.C. § 1314(a)(1). The most recent collection of these

criteria, including those for TCDD, are published in the EPA document <u>Quality Criteria for Water 1986</u>, EPA 440/5-86-001.

EPA's water quality criteria are intended only as guidance for other federal agencies and the states; the states are not required to adopt EPA's criteria as their own. The preamble to <u>Quality Criteria for Water 1986</u> emphasizes:

> These criteria are not rules and they do not have regulatory impact. Rather, these criteria present scientific data and guidance of the environmental effects of pollutants which can be useful to derive regulatory requirements based on considerations of water quality impacts.

So long as a state's water quality criteria are derived through "scientifically defensible methods," EPA will approve the criteria although the criteria may differ from EPA's guidance criteria. <u>See</u> 40 C.F.R. § 131.11(b)(1) (1990). Indeed, EPA recently approved Maryland's (1990) and Virginia's (1991) TCDD water quality criteria of 1.2 ppq, which are nearly 100 times greater than EPA's guidance criterion of 0.013 ppq.[3]

VI. REASONS FOR THE RULE AMENDMENT

A. <u>Basis for the Present TCDD Criterion of 0.013 ppq</u>

Oregon's present TCDD criterion of 0.013 ppq was adopted directly from EPA's guidance criterion for the protection of human health from the consumption of fish and the

---

[3] EPA's approval of Maryland's TCDD water quality criterion is attached as Appendix C; EPA's approval of Virginia's water quality criterion is attached as Appendix D.

ingestion of water. EPA's guidance criterion was based on studies of tumors in rats that had been fed high doses of TCDD. Appendix A, p. 2-11. EPA assumed that the incidence of tumors in rats fed high doses of TCDD would be linearly related to the incidence of tumors in humans exposed to low doses of TCDD and that there was no threshold dose below which TCDD would not pose some risk of cancer, i.e., any exposure to humans greater than zero posed a risk of cancer. See Appendix A, p. 2-12.

Using these assumptions, the incidence of tumors in rats fed high doses of TCDD, and a "risk level" of 1 in 1,000,000 (1×10^{-6}), EPA derived an acceptable daily intake (ADI) for TCDD of 0.006 picograms per kilogram of body weight per day (pg/kg/d). That is, EPA's water quality criterion for TCDD is based on the assumption that humans can with reasonable risk consume up to 0.006 pg/kg/d of TCDD. See Appendix A, p. iv.

To derive a guidance water quality criterion for TCDD from an ADI of 0.006 pg/kg/d, EPA used the following simple formula:

$$WQS = (ADI \times BW)/[(BCF \times FCR) + WCR]$$

where

WQS = water quality standard (criterion), expressed in picograms per liter (pg/L), or ppq

ADI = acceptable daily intake, expressed in pg/kg/d

BW = body weight, expressed in kilograms (kg)

BCF = bioconcentration factor

WCR = water consumption rate, expressed in liters per day

FCR = fish consumption rate, expressed in kilograms per day (kg/d).

Appendix A, p. iv.

The bioconcentration factor (BCF) is the concentration of a substance in fish tissue divided by its dissolved concentration in the water in which the fish lives. See Appendix A, p. 4-1. It is a measure of the degree to which a fish takes up a dissolved substance in the water and concentrates the substance in its tissues. Thus, if a dissolved substance is present in water at a concentration of one part per million and is present in the tissues of fish that live in the water at a concentration of 100 parts per million, the BCF is 100.

Employing the formula set forth above, it may be seen that the appropriate water quality criterion (the WQS) will increase as either the ADI or body weight increases and that it will decrease as either the BCF or fish or water consumption increases. In deriving its TCDD water quality criterion of 0.013 ppq, EPA assumed an ADI of 0.006 pg/kg/d, an average body weight of 70 kilograms, a BCF of 5000, average fish consumption of 0.0065 kilograms per day, and average water consumption of 2.0 liters per day. Appendix A, p. iv.

B. New Scientific Information and Region-Specific Exposure Data

New scientific information concerning TCDD and region-specific TCDD exposure information support the adoption of a substantially less stringent TCDD criterion for Oregon. This information and its use in the development of a TCDD criterion for Oregon are described in detail in Appendices A and B. The following is a summary.

1. Acceptable Daily Intake of TCDD

New scientific information concerning the mechanism by which TCDD causes toxic effects, epidemiologic studies of TCDD exposures, and the recent reevaluation of the animal studies on which EPA relied in developing its guidance TCDD criterion, demonstrate that EPA's ADI for TCDD is unwarrantedly stringent by several orders of magnitude. Whereas EPA assumed an ADI for TCDD of 0.006 pg/kg/d, this new scientific information demonstrates that an ADI for TCDD of 1 to 10 pg/kg/d would fully protect human health, even under conservative assumptions. See Appendix A, section 2; Appendix B, pp. 8-9.

EPA's guidance TCDD criterion assumed that any exposure to TCDD above zero produced a risk of cancer. Recent scientific research, however, shows that the toxic effects associated with exposure to TCDD are "receptor mediated." See Appendix A, pp. 2-9 to 2-10; Appendix B, pp. 5-8. This, in turn, indicates that there is a threshold dose of TCDD below which TCDD has no toxic effects. <u>See</u> <u>id.</u> The existence of such a threshold is also supported by animal research and by epidemiologic studies. The latter studies have not shown evidence of increased cancer risk from low-level environmental exposures to TCDD. <u>See</u> Appendix A, pp. 2-9.

In addition to the evidence for a TCDD toxicity threshold, a recent reevaluation of the animal study on which EPA relied in developing its ADI for TCDD shows that EPA's ADI is scientifically unsound. A 1978 study by Dr. R. J. Kociba and others showed that rats fed high doses of TCDD developed liver lesions. Appendix A, p. 2-11; Appendix B, pp. 3-5. At EPA's request, Dr. Robert Squire in 1980 evaluated these lesions and reported that a number of the lesions were cancerous tumors. <u>Id.</u> EPA used these results to classify TCDD as a "probable" human carcinogen and to develop its ADI for TCDD of 0.006 pg/kg/d. <u>Id.</u> Since that time, however, the methodology for evaluating rat liver lesions has changed considerably. Using this new methodology, which is the methodology accepted by EPA, Dr. Squire and an independent pathology working group (PWG) in 1990 reevaluated the results of the 1978 Kociba study. <u>See</u> Appendix A, pp. 2-11 to 2-12; Appendix B, pp. 3-5. Upon reevaluation, substantially fewer cancerous tumors were found. <u>Id.</u> Moreover, the tumors were associated with large TCDD doses that also induced extensive liver damage. <u>Id.</u>

Although the recent scientific information discussed above and in Appendices A and B suggests that EPA's use of a nonthreshold, linear model to estimate the risk of exposure to TCDD is not scientifically valid, Dr. R. E. Keenan and others have applied the results of the Kociba study, as reevaluated by the PWG in 1990, to the model used by EPA. See Appendix A, p. 2-12. Using this and other recent scientific information, Dr. Keenan calculated a cancer potency for TCDD that was 16 times lower than that calculated by EPA. At an appropriately conservative 10^{-5} risk level, Dr. Keenan's calculated cancer potency for TCDD equals an ADI of 1.0 pg/kg/d, i.e., an ADI approximately 167 times larger than EPA's ADI of 0.006 pg/kg/d. See id. Dr. Squire, as set forth in Appendix B, also believes that 1.0 pg/kg/d is an appropriate ADI for TCDD.

A model for calculating an ADI for TCDD that is more consistent with the latest scientific knowledge, however, is one that recognizes that TCDD acts through a threshold mechanism. See Appendix A, p. 2-13; Appendix B, pp. 5-8. The 1978 Kociba rat study reported no observable adverse effects in rats fed 1000 pg/kg/d of TCDD. Applying the widely accepted safety factor of 100 to this "no observable adverse effect level" (NOAEL) of 1000 pg/kg/d, one obtains an ADI of 10 pg/kg/d for TCDD. Id.

Many North American and European governments, including those in Canada, the Netherlands, Germany, and the United Kingdom, have used a threshold model and safety factors

to calculate an ADI for TCDD. <u>See</u> Appendix A, pp. 2-12 to 2-13. Most recently, this approach was used by a working group of the World Health Organization to recommend an ADI for TCDD of 10 pg/kg/d and by the Washington Department of Health to develop an ADI for TCDD of 20 pg/kg/d. Appendix A, p. 2-13.

In sum, the weight of the most recent scientific evidence supports an ADI for TCDD of between 1.0 and 10.0 pg/kg/d rather than EPA's now outdated ADI of 0.006 pg/kg/d. As set forth in Appendices A and B, an ADI of 1.0 pg/kg/d is fully protective of human health from all forms of TCDD-induced toxicity, including cancer, reproductive effects, and immunotoxicity.

2. <u>Regulatory Bioaccumulation Multiplier (RBM)</u>

EPA's TCDD criterion was calculated using a bioconcentration factor (BCF) of 5000. A BCF, however, takes into account only the uptake of dissolved compounds through fish gill surfaces. Other means of accumulating substances in fish tissues, such as ingestion of food and sediment, are not addressed. Appendix A, pp. 4-1 to 4-2.

Section 4.3 of Appendix A describes the development of a regulatory bioaccumulation multiplier (RBM). The RBM is the concentration of a substance in the edible portion of fish tissues divided by the total amount of the substance (dissolved and adsorbed to particulates) added to the water body per unit volume of water. Appendix A, p. 4-6. Thus, the RBM is the degree to which a substance will be concentrated in the edible

portion of fish tissues through all accumulation methods. Id. The advantage of the RBM is that increases in discharges of a substance to a water body can be directly related to increases in the concentration of that substance in edible fish tissues in that water body. See Appendix A, p. 4-7.

A wide variation in BCFs and bioaccumulation factors (BAFs) has been reported for TCDD. See id. When converted into RBMs, however, the reported BCFs and BAFs fall within a relatively narrow range of 600 to 6440 and average 3600. Id. Therefore, the multiplier of 5000 used by EPA as a BCF is scientifically sound as an RBM, albeit for different reasons. Appendix A, p. 4-8.

3. Fish Consumption

The principal route by which humans are exposed to TCDD discharged into water bodies is through the consumption of fish that live in those water bodies. Appendix A, p. 5-1. The study set forth in Appendix A chose the Columbia River as a representative river to characterize Oregon fish consumption patterns. In addition to characterizing the fish consumption patterns of the general population, it also characterizes the fish consumption patterns of two subpopulations likely to be greater consumers of fish: recreational anglers and Native Americans.

The mean consumption rate of Columbia River fish for the general population is 0.91 grams per day. Appendix A, p. 5-3. For recreational anglers, the median consumption

estimate is 5.8 grams per day, and for Native Americans, the mean consumption estimate is 16.4 grams per day. Appendix A, pp. 5-7 to 5-8. Native Americans, however, consume a larger proportion of anadromous fish than do recreational anglers. Appendix A, p. 5-8. Reported TCDD concentrations of anadromous fish, which spend little time within the river, are far below those of resident fish species. Id. If this difference in consumption patterns is taken into account, recreational anglers are the most exposed population. Id. For this reason, the most appropriate fish consumption rate to employ in setting a TCDD water quality criterion for Oregon is 5.8 grams per day. Appendix A, p. 5-9.

4. Consumption of Water

EPA's water quality criterion for TCDD is based on an assumed daily consumption of water of 2.0 liters per day. This consumption rate is derived from the daily ration of water required by U.S. Army field personnel. Appendix A, p. 6-1. Section 6 of Appendix A demonstrates that, although 2.0 liters per day of liquids may be a reasonable consumption rate, only approximately 60 percent of liquids consumed are water or water-based soups or beverages. Thus, a more realistic water consumption rate is 1.2 liters per day. Id.

C. <u>Calculation of an Oregon TCDD Water Quality Criterion</u>

Substituting only a regulatory bioaccumulation multiplier (RBM) for the bioconcentration (BCF) used by EPA, the formula for deriving an Oregon water quality criterion for TCDD is as follows:

$$WQS = (ADI \times BW)/[(RBM \times FCR) + WCR]$$

where

WQS = water quality standard (criterion), expressed in picograms per liter (pg/L), or ppq

ADI = acceptable daily intake, expressed in pg/kg/d

BW = body weight, expressed in kilograms (kg)

RBM = regulatory bioaccumulation multiplier

WCR = water consumption rate, expressed in liters per day

FCR = fish consumption rate, expressed in kilograms per day (kg/d).

Appendix A, p. 9-3.

As discussed above, a scientifically sound ADI for TCDD is 1.0 to 10.0 pg/kg/d, not the 0.006 pg/kg/d used by EPA. Appendix A uses the most conservative of the ADIs within this range, 1.0 pg/kg/d. <u>Id.</u> Appendix A retains EPA's assumption that average body weight is 70 kg, and uses an RBM of 5000, which is equal to EPA's BCF of 5000. <u>Id.</u> Using fish consumption data for the Columbia River and protecting recreational anglers, the most exposed population group, Appendix A uses a fish consumption rate of 0.0058 kg/d, rather than EPA's assumed fish consumption rate of 0.0065 kg/d. <u>Id.</u>

Finally, Appendix A uses a realistic water consumption rate of 1.2 liters per day rather than EPA's assumed water consumption rate of 2.0 liters per day. Id. Inserting these values into the formula above yields a TCDD water quality criterion of 2.3 picograms per liter or 2.3 ppq. Id.

D. A TCDD Water Quality Criterion of 2.3 ppq for the Protection of Human Health Also Protects Other Designated Beneficial Uses

Section 3 of Appendix A discusses the reported effects of TCDD on aquatic life. For long-term exposures to fish, the lowest TCDD concentration for which adverse effects have been reported is 38 ppq in a study of rainbow trout. Appendix A, p. 3-6. No adverse effects for long-term exposure have been reported at concentrations ranging from 1.1 ppq to approximately 3000 ppq. Id. Recent experimental stream studies have shown no adverse effects in cold-water fish species at TCDD concentrations of 3.5 ppq. Id. Moreover, evidence suggests that fish are more sensitive to TCDD than other aquatic organisms. Appendix A, p. 3-7. For these reasons, a TCDD water quality criterion of 2.3 ppq would protect designated beneficial uses other than those involving human health. See Appendix A, p. 9-3.

VII. EFFECTS OF ADOPTION OF THE PROPOSED AMENDMENTS

Because, as shown above and in more detail in Appendix A, a TCDD water quality criterion of 2.3 ppq would fully protect human health and designated beneficial uses of

Oregon waters, no adverse effects would follow from the adoption of this criterion. On the other hand, adoption of a less stringent criterion for TCDD may substantially reduce compliance costs for the pulp and paper industry, other industries, municipal sewage treatment plants, and other suspected sources of TCDD discharges. Adoption of a less stringent TCDD criterion would also help maintain the competitiveness of Oregon industries against industries in other states that have already adopted TCDD water quality criteria that are orders of magnitude less stringent than Oregon's existing criterion of 0.013 ppq.

VIII. CONCLUSION

For the foregoing reasons, the Commission should initiate rulemaking proceedings to adopt the amendments proposed by the Petitioners. The amendments would establish a water quality criterion for TCDD of 2.3 ppq in all waters of the state.

DATED: May 23, 1991.

John W. Gould
Lane Powell Spears Lubersky
800 Pacific Building
520 S.W. Yamhill Street
Portland, Oregon 97204
(503) 226-6151

Of Attorneys for Petitioner
James River II, Inc.

Richard Baxendale by MRC
Richard Baxendale
506 National Building
1008 Western Avenue
Seattle, Washington 98104
(206) 623-2848

Of Attorneys for Petitioner
Boise Cascade Corporation

BEFORE THE ENVIRONMENTAL QUALITY COMMISSION
OF THE STATE OF OREGON

In the matter of the petition of	)	
James River II, Inc., and Boise	)	
Cascade Corporation to amend	)	PETITION FOR RULE AMENDMENT
subparagraph (2)(p)(B) of Oregon	)	
Administrative Rules chapter	)	
340, division 41, sections 205,	)	(ORAL PRESENTATION
245, 285, 325, 365, 445, 485,	)	REQUESTED)
525, 565, 605, 645, 685, 725,	)	
765, 805, 845, 885, 925, and	)	
965.	)	

May 23, 1991

I. INTRODUCTION

James River II, Inc. (James River) and Boise Cascade Corporation (Boise Cascade) petition the Commission to amend subparagraph (2)(p)(B) of OAR chapter 340, division 41, sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965. Supporting the Petition are the Associated Oregon Industries, the Northwest Pulp & Paper Association[1], the City of St. Helens, the Association of Western Pulp and Paper Workers, Local 1, and the United Paper Workers International Union, Local 1097.

The sections of the Oregon Administrative Rules listed above establish water quality criteria for all of Oregon's water basins. Subparagraph (2)(p)(B) of each section is identical:

> Levels of toxic substances shall not exceed the most recent criteria values for organic and inorganic pollutants established by EPA [the U.S. Environmental Protection Agency] and published in **Quality Criteria for Water** (1986). A list of the criteria is presented in Table 20.

The most stringent of EPA's published criteria for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), as set forth in Table 20, is 0.000013 nanograms per liter, or 0.013 parts per quadrillion (ppq), for the protection of human health.

---

[1] Pope & Talbot, Inc., is a member of the Northwest Pulp & Paper Association but takes no position on the Petition.

A substantial body of new scientific evidence concerning the toxicity of TCDD has become available since EPA published its guideline TCDD criteria in 1984.[2] This new evidence overwhelmingly shows that TCDD is far less harmful than was originally assumed and that EPA's TCDD criterion of 0.013 ppq for the protection of human health is no longer scientifically defensible. The new evidence, together with evidence concerning TCDD that is specific to Oregon, is discussed in the "Supporting Document for the Establishment of an Ambient Water Quality Criterion for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin in the State of Oregon," attached as Appendix A, and in "An Assessment of Potential Carcinogenic Risk from 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)," attached as Appendix B. In accordance with the recommendations set forth in Appendix A, the Petitioners request that the Commission initiate rulemaking proceedings to amend subparagraph (2)(p)(B) of the sections listed above to provide that concentrations of TCDD shall not exceed 2.3 ppq in Oregon waters.

The Petitioners submit this Petition for Rule Amendment pursuant to ORS 183.390, OAR 340-11-046, and OAR 137-01-070. As provided in OAR 137-01-070(3)(b), the Petitioners

---

[2] EPA's Quality Criteria for Water 1986, EPA 440/5-86-001, was published in 1986, but EPA's criteria for TCDD were published in 1984, 49 Fed. Reg. 5831 (Feb. 15, 1984).

request an opportunity to make an oral presentation to the Commission on whether to grant the Petition.

II. PETITIONERS

Petitioner James River owns and operates a bleached kraft pulp and paper mill at Wauna, Oregon. The mill discharges process wastewater into the Columbia River pursuant to a National Pollutant Discharge Elimination System (NPDES) permit issued by the Oregon Department of Environmental Quality (DEQ). On November 14, 1990, DEQ issued a renewed NPDES permit for the mill which contained effluent limits for TCDD. James River subsequently requested a contested case hearing on the TCDD effluent limits and other conditions of the renewed permit. The contested case is now pending before the Commission. James River's address is:

James River II, Inc.
Wauna Mill
Route 2, Box 2185
Clatskanie, Oregon 97016

Boise Cascade owns and operates a bleached kraft pulp and paper mill at St. Helens, Oregon. The mill discharges process wastewater into a publicly owned treatment works operated by the City of St. Helens. The treatment works discharges effluent into the Columbia River pursuant to an NPDES permit issued by DEQ. On November 14, 1990, DEQ issued a renewed NPDES permit for the City which contained effluent limits for TCDD and which required the City to limit TCDD

discharges from the mill into its treatment works. The City subsequently requested a contested case hearing on the TCDD effluent limits and other conditions of its renewed permit. Boise Cascade is a party to that contested case. The contested case has been consolidated with the contested case concerning James River's renewed NPDES permit and is now pending before the Commission. Boise Cascade's address is:

Boise Cascade Corporation
1600 S.W. Fourth Avenue
Portland, Oregon 97201

All correspondence concerning this petition should be directed to

John W. Gould
Lane Powell Spears Lubersky
800 Pacific Building
520 S.W. Yamhill Street
Portland, Oregon 97204

and

Richard Baxendale
506 National Building
1008 Western Avenue
Seattle, Washington 98104

III. OTHER INTERESTED PARTIES

The Petitioners believe that the other parties to the contested cases described above may be interested in the petition. In addition to DEQ, those parties and their attorneys are:

City of St. Helens

Represented by: Peter M. Linden
City Attorney
City of St. Helens
P.O. Box 278
St. Helens, Oregon 97051

Northwest Coalition for Alternatives to Pesticides
Columbia River United

Represented by: John E. Bonine
Western Environmental Law Clinic
School of Law
University of Oregon
Eugene, Oregon 97403

Pope and Talbot, Inc.

Represented by: Jay T. Waldron
David F. Bartz, Jr.
Schwabe, Williamson & Wyatt
1600-1950 Pacwest Center
1211 S.W. Fifth Avenue
Portland, Oregon 97204

UA Local 290, Plumbers and Steamfitters
Mike Jerkiewicz

Represented by: Linda K. Williams
1744 N.E. Clackamas Street
Portland, Oregon 97232

IV. RULE TO BE AMENDED

The Petitioners request that the Commission amend subparagraph (2)(p)(B) in each of the following sections of Oregon Administrative Rules chapter 340, division 41: 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965. Subparagraph (2)(p)(B) of each of these sections is identical:

> Levels of toxic substances shall not exceed the most recent criteria values for organic and inorganic pollutants

established by EPA and published in **Quality Criteria for Water** (1986). A list of the criteria is presented in Table 20.

Table 20 lists these EPA criteria for TCDD: 0.010 micrograms per liter (ug/l) (10,000 ppq) for the acute protection of freshwater aquatic life; 0.00001 ug/l (10 ppq) for the chronic protection of freshwater aquatic life; 0.000014 nanograms per liter (ng/l) (0.014 ppq) for the protection of human health from fish consumption; 0.000013 ng/l (0.013 ppq) for the protection of human health from fish consumption and water ingestion. The most stringent EPA TCDD criterion, then, is 0.013 ppq.

Petitioners request that the Commission amend subparagraph (2)(p)(B) of each of the sections of OAR chapter 340, division 41, listed above to read as follows (matter to be added is highlighted):

> Levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin shall not exceed 0.0023 nanograms per liter (2.3 parts per quadrillion). Levels of other toxic substances shall not exceed the most recent criteria values for organic and inorganic pollutants established by EPA and published in **Quality Criteria for Water** (1986). A list of the criteria is presented in Table 20.

Thus, following the requested amendment, subparagraph (2)(p)(B) of each of the amended sections of OAR chapter 340, division 41, would read:

> Levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin shall not exceed 0.0023 nanograms per liter (2.3 parts per quadrillion). Levels of other toxic substances shall not exceed the most recent criteria values for

organic and inorganic pollutants established by EPA and published in **Quality Criteria for Water** (1986). A list of the criteria is presented in Table 20.

V. LEGAL BACKGROUND

The Commission's function is "to establish the policies for the operation of the department [DEQ]." ORS 468.015. In particular, the Commission is to "establish standards of quality and purity for the waters of the state." ORS 468.735(1).

The federal Clean Water Act also requires the Commission, as the state agency responsible for water pollution control, to adopt water quality standards for the waters of the state. See 33 U.S.C. § 1313(c)(1). Water quality "standards" "consist of the designated uses of the . . . waters involved and the water quality criteria for such waters based upon such uses." 33 U.S.C. § 1313(c)(2)(A). For substances such as TCDD that are listed as toxic pollutants under the Clean Water Act, states must adopt "specific numerical criteria" for the pollutants. See 33 U.S.C. § 1313(c)(2)(B). All water quality criteria adopted by a state are subject to review by EPA for consistency with the Clean Water Act. See 33 U.S.C. § 1313(c)(3).

Section 304 of the Clean Water Act requires EPA to "develop and publish . . . criteria for water quality." 33 U.S.C. § 1314(a)(1). The most recent collection of these

criteria, including those for TCDD, are published in the EPA document Quality Criteria for Water 1986, EPA 440/5-86-001.

EPA's water quality criteria are intended only as guidance for other federal agencies and the states; the states are not required to adopt EPA's criteria as their own. The preamble to Quality Criteria for Water 1986 emphasizes:

> These criteria are not rules and they do not have regulatory impact. Rather, these criteria present scientific data and guidance of the environmental effects of pollutants which can be useful to derive regulatory requirements based on considerations of water quality impacts.

So long as a state's water quality criteria are derived through "scientifically defensible methods," EPA will approve the criteria although the criteria may differ from EPA's guidance criteria. See 40 C.F.R. § 131.11(b)(1) (1990). Indeed, EPA recently approved Maryland's (1990) and Virginia's (1991) TCDD water quality criteria of 1.2 ppq, which are nearly 100 times greater than EPA's guidance criterion of 0.013 ppq.[3]

VI. REASONS FOR THE RULE AMENDMENT

A. Basis for the Present TCDD Criterion of 0.013 ppq

Oregon's present TCDD criterion of 0.013 ppq was adopted directly from EPA's guidance criterion for the protection of human health from the consumption of fish and the

[3] EPA's approval of Maryland's TCDD water quality criterion is attached as Appendix C; EPA's approval of Virginia's water quality criterion is attached as Appendix D.

ingestion of water. EPA's guidance criterion was based on studies of tumors in rats that had been fed high doses of TCDD. Appendix A, p. 2-11. EPA assumed that the incidence of tumors in rats fed high doses of TCDD would be linearly related to the incidence of tumors in humans exposed to low doses of TCDD and that there was no threshold dose below which TCDD would not pose some risk of cancer, i.e., any exposure to humans greater than zero posed a risk of cancer. See Appendix A, p. 2-12.

Using these assumptions, the incidence of tumors in rats fed high doses of TCDD, and a "risk level" of 1 in 1,000,000 (1×10^{-6}), EPA derived an acceptable daily intake (ADI) for TCDD of 0.006 picograms per kilogram of body weight per day (pg/kg/d). That is, EPA's water quality criterion for TCDD is based on the assumption that humans can with reasonable risk consume up to 0.006 pg/kg/d of TCDD. See Appendix A, p. iv.

To derive a guidance water quality criterion for TCDD from an ADI of 0.006 pg/kg/d, EPA used the following simple formula:

$$WQS = (ADI \times BW)/[(BCF \times FCR) + WCR]$$

where

WQS = water quality standard (criterion), expressed in picograms per liter (pg/L), or ppq

ADI = acceptable daily intake, expressed in pg/kg/d

BW = body weight, expressed in kilograms (kg)

BCF = bioconcentration factor

WCR = water consumption rate, expressed in liters per day

FCR = fish consumption rate, expressed in kilograms per day (kg/d).

Appendix A, p. iv.

The bioconcentration factor (BCF) is the concentration of a substance in fish tissue divided by its dissolved concentration in the water in which the fish lives. See Appendix A, p. 4-1. It is a measure of the degree to which a fish takes up a dissolved substance in the water and concentrates the substance in its tissues. Thus, if a dissolved substance is present in water at a concentration of one part per million and is present in the tissues of fish that live in the water at a concentration of 100 parts per million, the BCF is 100.

Employing the formula set forth above, it may be seen that the appropriate water quality criterion (the WQS) will increase as either the ADI or body weight increases and that it will decrease as either the BCF or fish or water consumption increases. In deriving its TCDD water quality criterion of 0.013 ppq, EPA assumed an ADI of 0.006 pg/kg/d, an average body weight of 70 kilograms, a BCF of 5000, average fish consumption of 0.0065 kilograms per day, and average water consumption of 2.0 liters per day. Appendix A, p. iv.

B. <u>New Scientific Information and Region-Specific Exposure Data</u>

New scientific information concerning TCDD and region-specific TCDD exposure information support the adoption of a substantially less stringent TCDD criterion for Oregon. This information and its use in the development of a TCDD criterion for Oregon are described in detail in Appendices A and B. The following is a summary.

1. <u>Acceptable Daily Intake of TCDD</u>

New scientific information concerning the mechanism by which TCDD causes toxic effects, epidemiologic studies of TCDD exposures, and the recent reevaluation of the animal studies on which EPA relied in developing its guidance TCDD criterion, demonstrate that EPA's ADI for TCDD is unwarrantedly stringent by several orders of magnitude. Whereas EPA assumed an ADI for TCDD of 0.006 pg/kg/d, this new scientific information demonstrates that an ADI for TCDD of 1 to 10 pg/kg/d would fully protect human health, even under conservative assumptions. <u>See</u> Appendix A, section 2; Appendix B, pp. 8-9.

EPA's guidance TCDD criterion assumed that any exposure to TCDD above zero produced a risk of cancer. Recent scientific research, however, shows that the toxic effects associated with exposure to TCDD are "receptor mediated." <u>See</u> Appendix A, pp. 2-9 to 2-10; Appendix B, pp. 5-8. This, in turn, indicates that there is a threshold dose of TCDD below which TCDD has no toxic effects. See id. The existence of such a threshold is also supported by animal research and by epidemiologic studies. The latter studies have not shown evidence of increased cancer risk from low-level environmental exposures to TCDD. See Appendix A, pp. 2-9.

In addition to the evidence for a TCDD toxicity threshold, a recent reevaluation of the animal study on which EPA relied in developing its ADI for TCDD shows that EPA's ADI is scientifically unsound. A 1978 study by Dr. R. J. Kociba and others showed that rats fed high doses of TCDD developed liver lesions. Appendix A, p. 2-11; Appendix B, pp. 3-5. At EPA's request, Dr. Robert Squire in 1980 evaluated these lesions and reported that a number of the lesions were cancerous tumors. Id. EPA used these results to classify TCDD as a "probable" human carcinogen and to develop its ADI for TCDD of 0.006 pg/kg/d. Id. Since that time, however, the methodology for evaluating rat liver lesions has changed considerably. Using this new methodology, which is the methodology accepted by EPA, Dr. Squire and an independent pathology working group (PWG) in 1990 reevaluated the results of the 1978 Kociba study. See Appendix A, pp. 2-11 to 2-12; Appendix B, pp. 3-5. Upon reevaluation, substantially fewer cancerous tumors were found. Id. Moreover, the tumors were associated with large TCDD doses that also induced extensive liver damage. Id.

Although the recent scientific information discussed above and in Appendices A and B suggests that EPA's use of a nonthreshold, linear model to estimate the risk of exposure to TCDD is not scientifically valid, Dr. R. E. Keenan and others have applied the results of the Kociba study, as reevaluated by the PWG in 1990, to the model used by EPA. <u>See</u> Appendix A, p. 2-12. Using this and other recent scientific information, Dr. Keenan calculated a cancer potency for TCDD that was 16 times lower than that calculated by EPA. At an appropriately conservative 10^{-5} risk level, Dr. Keenan's calculated cancer potency for TCDD equals an ADI of 1.0 pg/kg/d, <u>i.e.</u>, an ADI approximately 167 times larger than EPA's ADI of 0.006 pg/kg/d. <u>See</u> <u>id.</u> Dr. Squire, as set forth in Appendix B, also believes that 1.0 pg/kg/d is an appropriate ADI for TCDD.

A model for calculating an ADI for TCDD that is more consistent with the latest scientific knowledge, however, is one that recognizes that TCDD acts through a threshold mechanism. <u>See</u> Appendix A, p. 2-13; Appendix B, pp. 5-8. The 1978 Kociba rat study reported no observable adverse effects in rats fed 1000 pg/kg/d of TCDD. Applying the widely accepted safety factor of 100 to this "no observable adverse effect level" (NOAEL) of 1000 pg/kg/d, one obtains an ADI of 10 pg/kg/d for TCDD. <u>Id.</u>

Many North American and European governments, including those in Canada, the Netherlands, Germany, and the United Kingdom, have used a threshold model and safety factors

to calculate an ADI for TCDD. <u>See</u> Appendix A, pp. 2-12 to 2-13. Most recently, this approach was used by a working group of the World Health Organization to recommend an ADI for TCDD of 10 pg/kg/d and by the Washington Department of Health to develop an ADI for TCDD of 20 pg/kg/d. Appendix A, p. 2-13.

In sum, the weight of the most recent scientific evidence supports an ADI for TCDD of between 1.0 and 10.0 pg/kg/d rather than EPA's now outdated ADI of 0.006 pg/kg/d. As set forth in Appendices A and B, an ADI of 1.0 pg/kg/d is fully protective of human health from all forms of TCDD-induced toxicity, including cancer, reproductive effects, and immunotoxicity.

2. <u>Regulatory Bioaccumulation Multiplier (RBM)</u>

EPA's TCDD criterion was calculated using a bioconcentration factor (BCF) of 5000. A BCF, however, takes into account only the uptake of dissolved compounds through fish gill surfaces. Other means of accumulating substances in fish tissues, such as ingestion of food and sediment, are not addressed. Appendix A, pp. 4-1 to 4-2.

Section 4.3 of Appendix A describes the development of a regulatory bioaccumulation multiplier (RBM). The RBM is the concentration of a substance in the edible portion of fish tissues divided by the total amount of the substance (dissolved and adsorbed to particulates) added to the water body per unit volume of water. Appendix A, p. 4-6. Thus, the RBM is the degree to which a substance will be concentrated in the edible

portion of fish tissues through all accumulation methods. Id. The advantage of the RBM is that increases in discharges of a substance to a water body can be directly related to increases in the concentration of that substance in edible fish tissues in that water body. See Appendix A, p. 4-7.

A wide variation in BCFs and bioaccumulation factors (BAFs) has been reported for TCDD. See id. When converted into RBMs, however, the reported BCFs and BAFs fall within a relatively narrow range of 600 to 6440 and average 3600. Id. Therefore, the multiplier of 5000 used by EPA as a BCF is scientifically sound as an RBM, albeit for different reasons. Appendix A, p. 4-8.

3. Fish Consumption

The principal route by which humans are exposed to TCDD discharged into water bodies is through the consumption of fish that live in those water bodies. Appendix A, p. 5-1. The study set forth in Appendix A chose the Columbia River as a representative river to characterize Oregon fish consumption patterns. In addition to characterizing the fish consumption patterns of the general population, it also characterizes the fish consumption patterns of two subpopulations likely to be greater consumers of fish: recreational anglers and Native Americans.

The mean consumption rate of Columbia River fish for the general population is 0.91 grams per day. Appendix A, p. 5-3. For recreational anglers, the median consumption

estimate is 5.8 grams per day, and for Native Americans, the mean consumption estimate is 16.4 grams per day. Appendix A, pp. 5-7 to 5-8. Native Americans, however, consume a larger proportion of anadromous fish than do recreational anglers. Appendix A, p. 5-8. Reported TCDD concentrations of anadromous fish, which spend little time within the river, are far below those of resident fish species. Id. If this difference in consumption patterns is taken into account, recreational anglers are the most exposed population. Id. For this reason, the most appropriate fish consumption rate to employ in setting a TCDD water quality criterion for Oregon is 5.8 grams per day. Appendix A, p. 5-9.

4. Consumption of Water

EPA's water quality criterion for TCDD is based on an assumed daily consumption of water of 2.0 liters per day. This consumption rate is derived from the daily ration of water required by U.S. Army field personnel. Appendix A, p. 6-1. Section 6 of Appendix A demonstrates that, although 2.0 liters per day of liquids may be a reasonable consumption rate, only approximately 60 percent of liquids consumed are water or water-based soups or beverages. Thus, a more realistic water consumption rate is 1.2 liters per day. Id.

C. Calculation of an Oregon TCDD Water Quality Criterion

Substituting only a regulatory bioaccumulation multiplier (RBM) for the bioconcentration (BCF) used by EPA, the formula for deriving an Oregon water quality criterion for TCDD is as follows:

$$WQS = (ADI \times BW)/[(RBM \times FCR) + WCR]$$

where

WQS = water quality standard (criterion), expressed in picograms per liter (pg/L), or ppq

ADI = acceptable daily intake, expressed in pg/kg/d

BW = body weight, expressed in kilograms (kg)

RBM = regulatory bioaccumulation multiplier

WCR = water consumption rate, expressed in liters per day

FCR = fish consumption rate, expressed in kilograms per day (kg/d).

Appendix A, p. 9-3.

As discussed above, a scientifically sound ADI for TCDD is 1.0 to 10.0 pg/kg/d, not the 0.006 pg/kg/d used by EPA. Appendix A uses the most conservative of the ADIs within this range, 1.0 pg/kg/d. Id. Appendix A retains EPA's assumption that average body weight is 70 kg, and uses an RBM of 5000, which is equal to EPA's BCF of 5000. Id. Using fish consumption data for the Columbia River and protecting recreational anglers, the most exposed population group, Appendix A uses a fish consumption rate of 0.0058 kg/d, rather than EPA's assumed fish consumption rate of 0.0065 kg/d. Id.

Finally, Appendix A uses a realistic water consumption rate of 1.2 liters per day rather than EPA's assumed water consumption rate of 2.0 liters per day. Id. Inserting these values into the formula above yields a TCDD water quality criterion of 2.3 picograms per liter or 2.3 ppq. Id.

D. A TCDD Water Quality Criterion of 2.3 ppq for the Protection of Human Health Also Protects Other Designated Beneficial Uses

Section 3 of Appendix A discusses the reported effects of TCDD on aquatic life. For long-term exposures to fish, the lowest TCDD concentration for which adverse effects have been reported is 38 ppq in a study of rainbow trout. Appendix A, p. 3-6. No adverse effects for long-term exposure have been reported at concentrations ranging from 1.1 ppq to approximately 3000 ppq. Id. Recent experimental stream studies have shown no adverse effects in cold-water fish species at TCDD concentrations of 3.5 ppq. Id. Moreover, evidence suggests that fish are more sensitive to TCDD than other aquatic organisms. Appendix A, p. 3-7. For these reasons, a TCDD water quality criterion of 2.3 ppq would protect designated beneficial uses other than those involving human health. See Appendix A, p. 9-3.

VII. EFFECTS OF ADOPTION OF THE PROPOSED AMENDMENTS

Because, as shown above and in more detail in Appendix A, a TCDD water quality criterion of 2.3 ppq would fully protect human health and designated beneficial uses of

Oregon waters, no adverse effects would follow from the adoption of this criterion. On the other hand, adoption of a less stringent criterion for TCDD may substantially reduce compliance costs for the pulp and paper industry, other industries, municipal sewage treatment plants, and other suspected sources of TCDD discharges. Adoption of a less stringent TCDD criterion would also help maintain the competitiveness of Oregon industries against industries in other states that have already adopted TCDD water quality criteria that are orders of magnitude less stringent than Oregon's existing criterion of 0.013 ppq.

VIII. CONCLUSION

For the foregoing reasons, the Commission should initiate rulemaking proceedings to adopt the amendments proposed by the Petitioners. The amendments would establish a water quality criterion for TCDD of 2.3 ppq in all waters of the state.

DATED: May 23, 1991.

John W. Gould
Lane Powell Spears Lubersky
800 Pacific Building
520 S.W. Yamhill Street
Portland, Oregon 97204
(503) 226-6151

Of Attorneys for Petitioner
James River II, Inc.

Richard Baxendale by MRC
Richard Baxendale
506 National Building
1008 Western Avenue
Seattle, Washington 98104
(206) 623-2848

Of Attorneys for Petitioner
Boise Cascade Corporation

SUPPORTING DOCUMENT FOR THE ESTABLISHMENT OF AN AMBIENT WATER QUALITY CRITERION FOR 2,3,7,8-TETRACHLORODIBENZO-*P*-DIOXIN IN THE STATE OF OREGON

ChemRisk™
Stroudwater Crossing
1685 Congress Street
Portland, Maine 04102
(207) 774-0012

May 14, 1991

ChemRisk™ - A Division of McLaren/Hart
MAY 14, 1991

Supporting Document for the Establishment of an Ambient Water Quality Criterion for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin in the State of Oregon

Table of Contents

Supporting Document for the Establishment of an Ambient Water Quality Criterion for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin in the State of Oregon

Table of Contents (Continued)

Supporting Document for the Establishment of an Ambient Water Quality Criterion for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin in the State of Oregon

List of Figures

Supporting Document for the Establishment of an Ambient Water Quality Criterion for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin in the State of Oregon

List of Tables

Supporting Document for the Establishment of an Ambient Water Quality Criterion for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin in the State of Oregon

EXECUTIVE SUMMARY

Under the Clean Water Act (CWA), the federal government has mandated that, by 1992, all states establish ambient water quality standards for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) as one of the 126 "priority pollutants" listed under Section 307(a) of the CWA. There are two basic options available to the states. One option available to states is to adopt EPA Ambient Water Quality Criteria (AWQC) as enforceable water quality standards. A number of state agencies have taken this approach and have adopted the default values proposed in the EPA's 1984 document, *Ambient Water Quality Criteria for 2,3,7,8-Tetrachlorodibenzo-p-dioxin.*

A second option, as referenced by Section 304(a)(1) of the CWA, is the development of a water quality standard based on the latest scientific knowledge regarding effects on human health and the environment. A number of states, including New Hampshire, Virginia, New York, Tennessee, South Carolina, Georgia, Alabama, Arkansas, Texas, Florida, and Maryland have chosen to use this approach in developing state-specific standards. New Hampshire and New York have adopted water quality standards of 1 part per quadrillion (ppq). EPA Region III has recently approved the 1.2 ppq standards for TCDD adopted by Maryland and Virginia. These state-specific standards are substantially different from the 0.013 ppq criterion proposed in the 1984 EPA document.

This second option is preferable because it reflects, among other things, the states' use of site-specific or regional-specific exposure factors, appropriate risk levels, and more recent scientific data on TCDD. Although EPA is now reviewing its own criterion through a formal process, it has not withdrawn the 0.013 ppq criterion as a recommended standard for states.

Critical analysis of the following key factors can lead to a scientifically sound and health-protective water quality criterion for dioxin:

- selection of an appropriate acceptable daily intake (ADI) for TCDD;
- acceptable limits of exposure to TCDD for aquatic organisms;
- bioconcentration/bioaccumulation potential for fish;
- variations in site-specific or region-specific fish consumption patterns;
- selection of an appropriate rate of water consumption; and
- appropriate stream flow rates.

Using the Columbia River as a representative waterbody, this technical support document presents the most recent literature on each of the key factors outlined above and develops a basis for a scientifically-defensible and health-protective water quality criterion for TCDD in the State of Oregon.

Acceptable Limits of Human Exposure

The weight of evidence clearly supports consideration of the receptor-mediated mechanism for toxicity when evaluating the human health risks from exposure to TCDD. Even when different threshold approaches have been used (i.e., threshold models, pharmacokinetic modeling, or toxicological safety factors), consistent acceptable daily intakes (ADIs) have been estimated. A number of European and North American governments have used a safety factor approach to estimate ADIs ranging from 1 to 10 picogram TCDD per kilogram body weight per day (pg/kg-day) (Ontario, 1985; van der Heijden et al., 1982; NCASI, 1987; U.K., 1989; Tollefson, 1991). Most of these countries have based their estimates primarily on the 1,000 pg/kg-day No-Observed-Adverse-Effect-Level (NOAEL) reported in the Kociba et al. (1978) cancer bioassay study of rats.

An ADI of 13 pg/kg-day can be derived from the most sensitive chronic noncarcinogenic effects study (Bowman et al., 1989). A daily intake for TCDD of 10 pg/kg-day was recently recommended by a working group of the World Health Organization (WHO, 1990) based on the application of safety factors to data reflecting reproductive effects, immunotoxicity, and carcinogenicity in the various laboratory animal species. The ADI of 20 pg/kg-day recently proposed by the Washington Department of Health (WDH, 1990), and developed using a pharmacokinetic model, is consistent with the ADIs developed by these other groups.

This numerical consistency among these estimated ADIs is not surprising in view of the fact that a common receptor mechanism is believed to mediate all TCDD toxic responses. Based on the most current scientific evidence, an ADI of 1 to 10 pg/kg-day is protective of human health for all toxic responses. This is orders of magnitude greater than the EPA's recommended intake level of 0.006 pg/kg-day based on a linear, nonthreshold model and a risk level of 10^{-6} (EPA, 1984).

Effects of Dioxin on Aquatic Biota

Although the available data are still somewhat limited, it appears that some species of fish are sensitive to the toxic effects of TCDD. The age and physiological state of the fish, concentration of TCDD in the water, and duration of exposure have a significant impact on the toxic effects observed. For short-term exposures to different life stages of fish, the Lowest-Observed-Effect-Concentrations (LOEC; the lowest concentrations at which effects have been observed) range from 100 to 107,000 ppq whereas the No-Observed-Effect-Concentrations (NOEC; the concentrations at which no effects have been observed) range from 10 to 1,050 ppq. For long-term exposures to different life stages of fish, published LOECs range from 38 to approximately 3,000 ppq. Recent experimental stream studies conducted on pulp and paper effluent discharges indicate that the NOEC exceeds 5.8 ppq for warm water species and 3.5 ppq for cold water species. Other published NOECs range as high as 3,000 ppq. Based on this review of the available data regarding aquatic toxicity, the weight of evidence supports the finding that ambient water concentrations of 3.5 to 5.8 ppq are protective of aquatic organisms.

Bioconcentration/Bioaccumulation of TCDD in Fish

Bioaccumulation multipliers for dioxin reported in the literature vary considerably. This variance can be attributed to differences in the experimental methodologies used in laboratory and field studies conducted over the past ten years to derive the multipliers.

Using the nominal water concentration based upon the total amount of TCDD added to the system, a consistently derived "regulatory bioaccumulation multiplier" (RBM) can be defined. This approach is similar to the regulatory approach used in establishing effluent discharge limits. When this approach is applied to the bioaccumulation studies reported in the literature, the reported multipliers for dioxin fall within a rather narrow range below the value of 5,000. Based on this analysis, the value of 5,000 constitutes the most scientifically based multiplier for regulatory purposes.

Fish Consumption

Ingestion of fish is clearly the most likely route of human exposure to TCDD from ambient water (EPA, 1984). Fish consumption rates are known to vary among various human populations. In order to address this, discreet estimates of fish consumption rates were made for the general population of the Columbia River basin as well as the two most sensitive subgroups, recreational anglers and Native Americans.

A per capita consumption rate of 0.91 grams per day (g/day) was estimated for the general population consuming Columbia River fish. Separate estimates of consumption by recreational anglers were derived for the upper and lower reaches of the river. This division was based on the relative absence of anadromous species in the upper reaches of the Columbia River. Using a computer simulation to estimate the distribution of consumption rates among the fishing population, median rates of 0.54 and 5.8 g/day were derived for the upper and lower reaches of the river, respectively. For the tribal Native American population, a per capita fish consumption rate of 16.4 g/day was estimated based on the portion of the commercial Native American catch retained for tribal consumption.

Although Native Americans are the highest consumers of Columbia River fish, they primarily consume anadromous species such as salmon which generally do not accumulate significant levels of dioxin during their brief migratory run. Consequently, the Native Americans are likely to have lower exposure to dioxin from fish. The most highly exposed population of Columbia River fish consumers are the recreational anglers in the lower reaches of the river, particularly since a high percentage of their catch is sturgeon in which measurable levels of dioxin have been observed. Consequently, the recreational anglers' estimated consumption rate of 5.8 g/day is the most appropriate basis for deriving a water quality criterion for ambient waters the State of Oregon.

Consumption of Water

At the present time, the EPA uses a value of 2.0 liters per day (L/day) to represent the average consumption of water by an adult. This value is based on the daily ration of water required by United States Army field personnel. While this number may be appropriate for a population that has little access to other beverages, it is likely to overestimate actual water consumption by average adults. Published data indicates that approximately 40% of the total daily fluid intake by the average adult consists of non-water-based as well as water-based beverages that are bottled or canned. Thus, if a total fluid consumption rate of 2 L/day is reasonable, it can be assumed that 60 percent, or 1.2 L/day, would be from a local source.

Appropriate Flow Conditions

To demonstrate compliance with ambient water quality standard dischargers measure dioxin concentration in their discharge and apply a dilution factor to estimate the ambient water concentration. The appropriate stream flow rate should be an estimate of long-term average exposure. For fish bioaccumulation prediction and long-term chronic exposure estimates a long-term average flow estimator is appropriate. The harmonic mean estimates the long-term average flow and is a more conservative estimate than the arithmetic mean.

Recommendation for a Scientifically Supportable Water Quality Criterion

While states may adopt a water quality standard that is identical to the EPA AWQC, they have been given the option of considering local environmental conditions and human exposure patterns in order to develop site-specific or region-specific numerical limits that are based on the latest scientific knowledge regarding effects on health and the environment.

The EPA AWQC for dioxin for bodies of water from which fish and water are consumed were developed in 1984 and calculated using the following equation:

$$\text{WQS} = (\text{ADI} \times \text{BW}) / [(\text{BCF} \times \text{FCR}) + \text{WCR}]$$

Where:

WQS	=	Water quality standard (pg/L)
ADD	=	Allowable daily dose (pg/kg-day)
BW	=	Body weight (kg)
BCF	=	Bioconcentration factor (L water/kg fish)
WCR	=	Water consumption rate (L/day)
FCR	=	Fish consumption rate (kg/day)

When deriving their AWQC for the ingestion of fish and water, the EPA assumed that the maximum allowable dose for humans was 0.006 pg/kg-day, based on a non-threshold approach and a 10^{-6} risk level. It was assumed that individuals ingested 6.5 grams of fish per day and 2 liters of water per day from a single source. Using a BCF of 5,000 for fish and a human body weight of 70 kg, an AWQC of 0.013 pg/L (ppq) was derived.

Since that time, however, considerably more has been learned about the behavior of dioxin. Our scientific understanding of the behavior of TCDD in the environment, in fish, and in humans has evolved over time to the extent that the EPA (1984) criteria are seriously outdated. Careful consideration of each factor in the AWQC equation and an evaluation of the weight of scientific evidence supporting their selection, will result in a scientifically-based standard for dioxin that is protective of human health.

Based on a conservative and health-protective allowable dose of 1 pg/kg-day, a body weight of 70 kg, a water consumption rate of 1.2 L/day, a fish consumption rate for the typical Columbia River angler of 5.8 g/day, and substituting a RBM of 5,000 for the BCF, a water quality criterion of 2.3 ppq for the State of Oregon can be derived, based on human health considerations. As it has been shown that NOECs for freshwater fish and other aquatic organisms range from 3.5 to 5.8 ppq, this proposed water quality criterion will also be protective of those species as well as being fully protective of public health.

Supporting Document for the Establishment of an Ambient Water Quality Criterion for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin in the State of Oregon

1.0 INTRODUCTION

The purpose of this document is to provide technical support for a scientifically valid ambient water quality criterion for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the State of Oregon. The document considers the latest scientific information on TCDD along with relevant site- and region-specific information.

A critical analysis of the following key factors is used to develop a scientifically accurate and health-protective ambient water quality criterion for TCDD:

- acceptable daily intake (ADI) levels for TCDD (Chapter 2);
- bioaccumulation/bioconcentration potential for fish (Chapter 4);
- site-specific or region-specific fish consumption rates (Chapter 5); and
- daily rate of water consumption by humans (Chapter 6).

Other factors that indirectly affect the development of a scientifically accurate and health-protective ambient water quality criterion for TCDD include:

- acceptable limits of TCDD exposure to aquatic organisms (Chapter 3);
- flow conditions in riverine waterbodies (Chapter 7);
- the appropriateness of the 10^{-5} and 10^{-6} risk levels (Chapter 8).

These seven factors are outlined in the following paragraphs and are discussed in detail throughout the remainder of this document.

Chapter 2 presents the carcinogenic and noncarcinogenic human health effects associated with exposure to dioxin and discusses the acceptable limits of human exposure. This is followed by discussions of the mechanism by which TCDD exerts its toxic effects, and the existence of a threshold for these effects. Both threshold and non-threshold models for carcinogenic dose response are presented along with a discussion of reproductive, teratogenic, fetotoxic and immunotoxic noncarcinogenic dose response. Chapter 2 concludes with a recommended ADI that is based on a receptor-mediated threshold approach and is protective of human health.

A discussion of the effects of dioxin on fish and other aquatic organisms is included in Chapter 3. A thorough review of the scientific literature on acute and chronic exposures to TCDD in water are presented along with a recommended concentration that is protective of aquatic organisms.

The importance of establishing a scientifically accurate bioaccumulation factor (BAF) for TCDD in fish is presented in Chapter 4. Following a review of all significant bioconcentration factors and BAFs reported in the scientific literature, a "regulatory BAF" is developed that constitutes the most scientifically sound multiplier available for regulatory purposes.

Fish consumption rates are developed for a representative river (the Columbia River) in Chapter 5. In addition to considering the general population living in the vicinity of the river, sensitive subpopulations such as recreational anglers and Native Americans are addressed. Consumption rates for these populations are determined by using the Latin Hypercube statistical simulation model.

Chapter 6 discusses a water consumption rate that reasonably reflects the amount of water consumed daily from local sources.

Appropriate river flow conditions are discussed in Chapter 7. Although flow conditions do not directly apply to the development of an ambient water quality criterion, an understanding of the river's flow is important for back-calculating pollutant levels to sources once a criterion has been developed.

Chapter 8 presents an overall perspective on risk and describes how the 10^{-6} risk level, rather than the more reasonable 10^{-5} risk level, has not been used consistently at either the state or federal level for risk management decision making. Although this discussion may have more relevance to a non-threshold model than to the recommended threshold model, it is important to point out the inconsistencies in using an overly conservative risk level.

Chapter 9 briefly summarizes the preceding chapters and recommends a scientifically valid ambient water quality criterion for TCDD in the State of Oregon.

2.0 ACCEPTABLE LIMITS OF HUMAN EXPOSURE

A central tenet of the science of toxicology, first articulated by Paracelsus in the 1500's, states that the toxic and therapeutic properties of a given chemical are differentiated by the dose received. In the words of Paracelsus:

> "All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy."

It is this determination of an acceptable dose level, one at which there is reasonable surety that toxic effects will not occur, which is the focus of this chapter.

Acceptable doses of human exposure to agents in the environment, can be expressed in several ways, depending on the mechanism of action of the particular chemicals. An acceptable daily intake (ADI) is broadly defined as the threshold level of exposure to a chemical below which no adverse health effects would be expected to occur. More specifically, the toxic manifestations of a threshold-acting agent only occur when a specific level of exposure has resulted in the saturation of biological receptor sites. For example, compounds suspected of being carcinogens by promoting, rather than initiating carcinogenesis do not act directly upon the genetic material. Rather, mediation via a receptor or metabolic event is required before the promoter compound can cause a biologic response. Most of the phenobarbital type compounds such as DDT, PCBs, TCDD, and other chlorinated hydrocarbons are believed to be carcinogenic through a promoting mechanism on preexisting abnormal cells (Klaassen et al., 1986), thus a threshold is thought to exist for these types of chemicals.

In contrast, another type of exposure limit, the risk-specific dose (RsD), represents a dose of a substance which is associated with a specified cancer risk level (i.e., one in one hundred thousand) (EPA, 1988). Derivation and use of an RsD implies that any dose of the nonthreshold agent, regardless of quantity, would be associated with some level of risk. Direct acting genotoxic agents, such as 1,2,3,4-butadiene epoxide, dimethyl sulfate, and bis(chloromethyl)ether, are highly electrophilic compounds which directly interact with nucleophilic molecules such as DNA (Klaassen et al., (1986). For these types of compounds, mediation through an intermediary is not necessary for a toxic effect to occur, therefore, no threshold is not thought to exist. Determining a 'safe' level of exposure to these types of compounds involves the determination of an acceptable level of risk, and the RsD that would be associated with that risk.

Critical to the evaluation of the human risks associated with exposure to TCDD is the understanding of the mechanism by which TCDD elicits a toxic response. The following sections contain a detailed review of the noncarcinogenic and carcinogenic health effects of TCDD in humans and animals, the mechanisms of action of TCDD, threshold and nonthreshold models for carcinogenic response in humans, and dose-response models for noncarcinogenic extrapolations. ADIs are recommended in the final section (2.5), based on a consideration of the total weight of scientific evidence pertaining to TCDD's mechanism of action and toxicity in humans and animals.

2.1 Human Health Effects

Numerous epidemiologic studies have examined the potential association between TCDD exposure and a number of disease or mortality endpoints in humans (AMA, 1984; EPA, 1985; Fishbein, 1987; NCASI, 1987b; UAREP, 1988; Bond et al., 1989; Tollefson, 1991). Available data on human exposure is found primarily in studies involving industrial workers, herbicide sprayers, the exposed population in the Seveso, Italy accident, residents of Times Beach, Missouri, and U.S. Air Force personnel involved in the use of Agent Orange in Operation Ranch Hand. In these studies, the concentrations of TCDD to which people were exposed are generally considered to be much greater than would typically be encountered in the environment. In addition, the populations evaluated in many of these studies were exposed to multiple chemicals, thereby complicating the assessment of disease endpoints potentially attributable to TCDD exposure (Tollefson, 1991). Furthermore, the cohort sizes for many of the studies have been too small to allow statistical identification of small increases in cancer risk (Tollefson, 1991).

Epidemiological studies are generally observational rather than experimental and may, therefore, include a number of known or unknown biases. Though there are methodologies that can be used to minimize and control for many confounding factors inherent to epidemiological studies, there are usually several obstacles that cannot be adequately treated. These discrepancies must be considered when establishing a causal link between exposure and disease. For example, it is usually misleading to infer causality from a single epidemiological study because confounding factors or errors in characterizing exposure or disease within the study may lead to biases which affect the determination of relative risk (incidence rate of the exposed population divided by the incidence rate of the unexposed population). Therefore, epidemiologists look for consistency of findings among multiple studies before causal inference is made. The strength of the association is also considered in this characterization. In addition, the presence of a dose-response relationship adds credence to the studies since a positive correlation between the level of exposure and the occurrence of disease is generally expected to occur. Finally, biological plausibility is considered. The existence of supporting laboratory bioassay data substantiates similar findings in epidemiological studies.

2.1.1 Noncarcinogenic Health Effects

While epidemiologic studies have shown a definitive relationship between exposure to TCDD and chloracne, associations between exposure to high concentrations of chemicals containing TCDD and other non-cancerous effects have not been definitively established. Studies of the noncarcinogenic effects of TCDD in humans are briefly discussed below.

Chloracne is one long-term adverse health effect that can be definitively associated with human exposure to TCDD (Suskind, 1985; UAREP, 1988). This characteristic persistent dermatosis has been observed in cases of both acute and chronic exposure to relatively high concentrations of TCDD and can be induced following systemic uptake or dermal exposure (Kociba and Schwetz, 1982; Suskind, 1985; Kimbrough and Houk, 1987). The persistence of chloracne for several years following high-level occupational exposures is consistent with the relatively long (7 years) half-life of TCDD in humans. While chloracne is associated with exposure to a number of other chlorinated aromatic hydrocarbons (Kimbrough et al., 1984), Suskind (1985) has identified TCDD as the most potent chloracnegen.

Porphyria cutanea tarda (PCT) has been reported among workers accidentally exposed to complex chemical mixtures containing TCDD (UAREP, 1988). This condition is manifested by discoloration and increased fragility of the skin and hirsutism reportedly accompanies the altered urinary porphyrin excretion pattern in certain cases. Jirasek and coworkers (1973, 1974 as reported in UAREP, 1988) reported PCT in 11 of 78 workers from a plant in Czechoslovakia where the workers were engaged in the manufacture of phenoxy herbicides and hexachlorobenzene. Bleiberg et al. (1964) found PCT in 11 of 29 workers examined from a plant in New Jersey. Suskind (1983) observed PCT in workers manufacturing phenoxy herbicides at a plant in Nitro, West Virginia. In each of these populations, reexamination of workers at a later date indicated that the skin lesions associated with PCT had disappeared and only a few abnormalities in urinary porphyrin excretion patterns remained (Poland et al., 1971; Pazderova-Vejlupkova et al., 1981; Suskind and Hertzburg, 1984). Hobson (1984) concluded that the PCT seen in these populations was most likely attributable to exposure to hexachlorobenzene. Furthermore, PCT has not been a finding in studies of other human populations that were exposed to TCDD in the absence of hexachlorobenzene and trichlorophenol (UAREP, 1988).

In 1976 an industrial explosion at a 2,4,5-T plant in Seveso, Italy contaminated the surrounding area with several chemicals that contained concentrations of TCDD. Within days of the explosion, 187 cases of chloracne were reported (Crow, 1981). Kimbrough and Houk (1987), in their review of health effects of dioxins, noted that although liver effects, enlarged livers, and some abnormal results of certain liver function tests were reported, evaluation of the overall results of the health studies on the exposed population indicated no severe systemic health effects (Reggiani, 1978; 1980). Bruzzi (1983) compared rates of congenital anomalies (genital and neural tube defects) in the Seveso region with those in the unexposed Lombardi region. Incidence rates were found to be higher in the Seveso region than in the Lombardi area. When looking only at the Seveso region, however, there was little correlation between incidence rates and the extent of potential exposure within the region. In fact, fewer genital anomalies were observed in the high exposure area than in the unexposed sections of Seveso. Therefore, no positive conclusions could be drawn from the study. In a more recent report concerning birth defects, Mastroiacovo et al. (1988) did not demonstrate an increased risk of birth defects associated with exposure to TCDD (UAREP, 1988).

In the Times Beach, Missouri area, residents were potentially exposed to TCDD when wastes contaminated with TCDD were mixed with salvage oil and sprayed on various sites for dust control (Kimbrough and Houk, 1987). Several acute effects were reported in individuals exposed to contaminated soil in riding arenas (Kimbrough and Houk, 1987). A pilot study conducted on a small group of people from another contaminated area found no significant differences in test results between unexposed and possibly exposed groups (CDC, 1984). Hoffman et al. (1986) reported results of a study intended to assess immunologic response of mobile home park residents potentially exposed to areas in which TCDD-contaminated waste oil had been sprayed. These authors reported a significantly increased frequency of anergy and relative anergy compared to controls. Hoffman et al. (1986) interpreted these findings as evidence that TCDD exposure was associated with depressed cell-mediated immunity. However, because the results may have been biased due to shortcomings in experimental design and because researchers eliminated a significant portion of the data, reviewers of this study, (Dean and Kimbrough, 1986), have questioned its value for identifying an immunologic hazard. Results of a follow-up study (Evans et al., 1987) involving participants who were initially anergic or relatively anergic indicated that none of the participants were anergic, and only one exposed subject and one unexposed subject were relatively anergic in the repeat test. In view of the experimental design, and data interpretation problems and in light of the failure of Evans et al. (1987) to corroborate the initial results, an immunologic hazard has not been demonstrated by Hoffman et al. (1986).

2.1.2 Human Carcinogenicity

A number of studies have examined the association of increased cancer rates with exposure to dioxin and dioxin contaminated materials (Armstrong, 1983; Bond et al., 1983, 1989; Cook et al., 1986; Eriksson et al., 1984; Filipini et al., 1981; Fingerhut et al., 1991; Kimbrough, 1990; Lathrop et al., 1983, 1984; Lipson, 1983; Mastroiacovo et al., 1988; Minister of Veteran's Affairs, 1983; Moses et al., 1984; Nelson et al., 1979; Pocchiari et al., 1979; Reggiani, 1978, 1980; Smith et al., 1982; Suskind and Hertzberg, 1984; Zack and Gaffery, 1983). Certain studies have suggested a positive association between exposure to chemicals containing TCDD and soft tissue sarcoma and malignant lymphoma (Hardell and Sandstrom, 1979; Eriksson et al., 1981; Hardell et al., 1981). Fingerhut et al. (1991) have recently reported a possible relationship between high-level occupational exposures and soft tissue sarcoma and respiratory cancers. However, the positive associations identified in these studies are equivocal, and are not supported by the results of other epidemiologic studies (Smith et al., 1982, 1983; Pearce et al., 1986; Smith and Pearce, 1986; Wiklund and Holm, 1986).

Case-control studies of workers in Sweden exposed to phenoxy acid herbicides or chlorophenols reported a statistically significant increased risk of soft-tissue sarcomas and malignant lymphomas (Hardell and Sandstrom, 1979; Eriksson et al., 1981; Hardell et al., 1981). These Swedish studies have been interpreted as showing evidence for an association between soft-tissue sarcoma and exposure to TCDD (Fingerhut, 1991a). However, the major limitations of the studies concern the amount of exposure to TCDD. Exposure history was assessed retrospectively by questionnaire at a time when herbicide use was receiving widespread media attention (2,4,5-T was banned in Sweden in 1977) (Tollefson, 1991). This publicity could have influenced the soft-tissue sarcoma cases to overestimate their exposure or have contributed to recall bias (Tollefson, 1991).

The results of other epidemiologic studies involving herbicide exposure (Smith et al., 1982a; 1982b; 1983; Pearce et al., 1986; Smith and Pearce, 1986; Wiklund and Holm, 1986) have not supported the findings of the Hardell studies (Hardell and Sandstrom, 1979; Eriksson et al., 1981; Hardell et al., 1981. For example, a cohort study of Swedish agricultural and forestry workers, a cohort similar to the earlier Hardell studies, linked occupational data from the census with mortality data. Using this approach no increased relative risk of soft-tissue sarcoma was observed when the cohort was compared to Swedish men employed in other industries, even though the exposure of agricultural and forestry workers to phenoxy acids was estimated to be greater than that of other occupational groups (Wiklund and Holm, 1986).

Interestingly, the Wiklund and Holm (1986) census linkage study showed no increased risk for all agriculture and forestry workers, even at the upper 95% confidence limit of the relative risk estimate which was 1.0. These findings raise questions concerning the results of the Hardell case-control studies (Hardell and Sandstrom, 1979; Eriksson et al., 1981; Hardell et al., 1981), which have not been satisfactorily resolved (UAREP, 1988). Limitations associated with any case-control study, however, includes the absence of an objective means to qualify or validate human exposure levels, recall bias, observation bias, and misdiagnosis of tumors (UAREP, 1988). In addition, the high relative risks reported in the Hardell studies (Hardell and Sandstrom, 1979; Eriksson et al., 1981; Hardell et al., 1981) were associated with exposure to "TCDD-contaminated herbicides" and therefore included exposure to a myriad of chemicals that may produce adverse health effects (Tollefson, 1991). Furthermore, corroborative evidence has not been found from studies in other countries.

Case-control studies in New Zealand have found no evidence of a relationship between occupational exposure to phenoxy herbicides and soft-tissue sarcoma (Smith et al., 1982b, 1983; Smith and Pearce, 1986). Pearce et al. (1985); however, reported that agricultural workers were at an increased risk of developing non-Hodgkin's lymphoma. The subsequent interview phase of this study, however, did not suggest that exposure to phenoxy herbicides was the explanation for the increased risk estimate; no significant difference regarding potential exposures to phenoxy herbicides or chlorophenol was observed between cases and controls (Pearce et al., 1986). In addition, a study of professional 2,4,5-T herbicide sprayers in New Zealand also found no significant increase in the risk of miscarriages or birth defects (Smith et al., 1982a).

Hoar et al. (1986), in a National Cancer Institute case-control study of workers involved in the agricultural use of herbicides in Kansas, demonstrated an association between the use of phenoxyacetic acid herbicides, specifically 2,4-dichlorophenoxyacetic acid (2,4-D), and non-Hodgkin's lymphoma. An association was not found between exposure and either soft-tissue sarcoma or Hodgkin's disease. Hoar et al. (1986), however, reported that 2,4-D does not contain TCDD, nor would one expect it to be formed in the synthesis of this herbicide.

Axelson et al. (1980) reported statistically ($p<0.05$) increased mortality associated with stomach cancer (RR=7.7) in Swedish railroad workers exposed to phenoxy acids possibly contaminated with TCDD. Interpretation of these results are limited by inadequately controlled confounding factors (NCASI, 1987b) and exposure to a mixture of chemicals including amitrole which has been demonstrated to be carcinogenic in both mice and rats (IARC, 1987).

Numerous epidemiological studies have been conducted on Vietnam veterans exposed to Agent Orange and other defoliants used extensively in Vietnam. Agent Orange contains two phenoxyherbicides, 2,4,5-T and 2,4-D, and concentrations of TCDD, a known contaminant of 2,4,5-T. In a recently released report, the Center for Disease Control (CDC) (1990) examined the risks related to a number of cancers (non-Hodgkin's lymphoma, soft tissue and other sarcomas, Hodgkin's disease, and nasal, nasopharyngeal, and primary liver cancers) in veterans who had served in Vietnam during the period of time when Agent Orange was used. The focus of the study was to determine whether the incidence of these cancers was higher in Vietnam veterans than in men who did not serve in Vietnam. This study reported an increased risk of non-Hodgkin's lymphoma among Vietnam veterans relative to men who did not serve in Vietnam, but no increased risk for the other five cancers. However, the study concluded that there was no evidence to support the contention that an increased risk of contracting non-Hodgkin's lymphoma was related to Agent Orange. In fact, the pattern of risk among subgroups of Vietnam veterans appeared to be opposite of the pattern of Agent Orange use in Vietnam. Those personnel involved in areas with heavy Agent Orange use were at somewhat lower risk than those land-based personnel in areas of lower Agent Orange use, and Navy veterans who served on ocean-going ships tended to be at higher risk of non-Hodgkin's lymphoma than Vietnam veterans who served on land. (CDC, 1990).

Lathrop et al. (1987) reported that there is not sufficient plausible or consistent scientific evidence at this time to implicate a causal relationship between herbicide exposure and the adverse health effects observed in the Ranch Hand group. In a study conducted in New York State, no statistically significant positive association was found between soft-tissue sarcoma and history of Vietnam service, history of exposure to Agent Orange, TCDD, or 2,4,5-T, history of herbicide or pesticide exposure, or history of any military service (Greenwald et al., 1984). Kang et al. (1986) found no association between soft-tissue sarcoma and previous military service in Vietnam in a case-control study of Vietnam veterans diagnosed with soft-tissue sarcoma and treated at Veterans Administration hospitals.

Zack and Suskind (1980) conducted a mortality study of 121 white male chemical workers exposed to TCDD contaminated chemicals at a Monsanto chemical plant in Nitro, West Virginia. The primary exposure occurred when a trichlorophenol (TCP) reactor malfunctioned, releasing TCDD contaminated TCP into the environment. The workers in this study were assigned to contain and cleanup following the TCP release. Following a latency period of 29 years, no statistically significant increased mortality was found to be associated with any health effect. A total of nine malignant neoplasms were reported, five of which were respiratory cancers. According to Zack and Suskind (1980), four of the five respiratory cancer cases were smokers.

In a subsequent study, Zack and Gaffey (1983) evaluated the health effects associated with long-term exposures at the same plant, including exposures during the runaway reactor accident. The cohort was comprised of 884 white male workers of which 163 were deceased. The only statistically significant finding was increased mortality associated with bladder cancers. When the authors split the cohort into two groups, those exposed to 2,4,5-T and those not exposed to 2,4,5–T, they found that the unexposed group showed a statistically significant increased mortality associated with bladder cancers while the exposed group did not.

Suskind and Hertzberg (1984) noted that the Monsanto workers were exposed to many different chemicals including p-aminobiphenyl, a known bladder carcinogen in humans (IARC, 1987; DHHS, 1989). Bladder tumors and bladder cancers associated mortality were evaluated separately for workers with either no 2,4,5-T or p-aminobiphenyl exposure; only 2,4,5-T exposure; only p-amino biphenyl exposure; or with both 2,4,5-T and p-aminobiphenyl exposure. All bladder tumors and cancers occurred in either the p-aminobiphenyl only exposure group or the group exposed to both p-aminobiphenyl and 2,4,5-T (Suskind and Hertzberg, 1984). Consequently, the International Agency for Research on Cancer (IARC) has used the Zack and Gaffey (1983) study in support of p-aminobiphenyl as a Group 1 carcinogen (sufficient evidence for carcinogenicity in humans) based on increased mortality associated with bladder cancers (IARC, 1987).

Thiess et al. (1982) reported a statistically significant ($p<0.05$) increase in mortality associated with stomach cancer (3 cases) in a cohort of 76 workers potentially exposed to TCDD following a trichlorophenol reactor accident in 1953 at a BASF plant in Ludwigshafen, Federal Republic of Germany. However, the choice of comparison groups and the small number of stomach cancer deaths observed raise important questions (Kimbrough and Houk, 1987). Follow-up data for the workers in the Thiess et al. (1982) study indicated that no additional stomach cancer deaths had occurred, and although deaths due to stomach cancer were reported to be greater than expected, the differences were not statistically significant (Lehnert and Szadkowski, 1986). Moreover, the positive finding of the Thiess et al. (1982) study associating stomach cancer with TCDD exposure has not been duplicated in other epidemiologic studies (Tollefson, 1991).

Zober et al. (1990) recently reported results of a 34-year follow-up study of chemical workers previously studied by Thiess et al. (1982) and Lehnert and Szadkowski (1986). The Zober et al. (1990) study evaluated mortality of a cohort of 247 BASF employees who were divided into four different cohorts based on exposure information. These cohorts were compared to the national population. Cohort C1 (n=69) consisted of the most heavily exposed workers, i.e. those exposed in the TCP reactor accident. Cohort C2 (n=84) was identified as members of cohort C1 plus individuals who were primarily involved in cleanup and medical activities related to the reactor accident, whereas cohort C3 included all of cohorts C1 and C2 in addition to all other potentially exposed individuals through December 31, 1987. Finally, these investigators evaluated mortality for those employees who had been diagnosed with chloracne.

No statistically significant increased mortality associated with any malignant neoplasm was observed in the C1 and C3 cohorts. However, in the C2 cohort, Zober et al. (1990) reported a statistically significant increase in mortality associated with cancer of the larynx (1 case observed, 0.03 cased expected). Because the increased mortality associated with this cancer was due to a single case, the statistical significance of that increase may not be biologically compelling. Furthermore, the authors noted that the power of the study to detect levels of risks associated with specific tumors sites was weak. In the same cohort, however, a statistically significant increase in mortality associated with all malignant neoplasms and "other and unspecified" malignant neoplasms was also reported. According to Zober et al. (1990), the "other and unspecified" malignant neoplasms include a case of pleural mesothelioma in a worker with known asbestos exposure. These investigators further noted that workers were also exposed to other chemicals at the plant including aromatic amines. Finally, in the chloracne cohort with over 20 years of exposure, (presumably those with the greatest exposure to TCDD), a statistically significant increase in mortality associated with all malignant neoplasms was observed (SMR=201; 14 cases observed and 6.96 cases expected).

Except for the single larynx cancer case in the C2 cohort, there were no statistically significant increases associated with specific tumor sites. It appears that the statistical significance of the combined tumor mortalities is primarily due to cancer cases reported as "other and unspecified" malignant neoplasms. According to Zober et al. (1990), this classification included a biliary tract carcinoma, gastrointestinal tract carcinoma, and a pleural mesothelioma. If mortality associated with malignant cancers at individual tumor sites had been evaluated separately, it is likely that the SMRs would not be significantly elevated. Zober et al. (1990) concluded that a substantial excess of cancer should have been observed in this study, if in fact TCDD was a highly potent carcinogen. However, the authors also noted that no strong conclusions could be drawn from the results of this study. The possible misclassification of tumors, appropriateness of the reference group, initial definition of the cohort, and most importantly, inadequately controlled confounding factors, particularly that of other chemical exposures, suggest that there are a number of shortcomings associated with this mortality study which may also be common to other mortality studies of TCDD.

Most recently, Fingerhut et al. (1991a,b) reported the results of an epidemiologic study conducted by NIOSH involving male chemical workers at 12 chemical plants in the U.S., one of which was the Monsanto chemical plant discussed earlier in this review. A cohort consisting of 5,172 individuals who had been assigned to the production of substances that were evidently contaminated with TCDD was studied. Mortality associated with combined cancers was slightly but significantly increased for the overall cohort. When separated into low- and high-exposure subcohorts, however, the low-exposure group showed no increased mortality associated with any cancers (Fingerhut, 1991a,b). In the high-exposure subcohort of 1,520 workers who had exposure periods of at least one year and latency periods of 20 years or more, mortalities for soft tissue sarcomas and respiratory cancers were significantly increased.

A number of confounding factors, including smoking and exposure to other chemicals, have bearing upon the interpretation of the results of this study. The workers in this cohort were exposed to high concentrations of a number of chemicals, including 2,4,5-trichlorophenol, monochloroacetic acid, 1,2,4,5-tetrachlorobenzene, hexachlorophene, and phenoxy herbicides. According to Suskind and Hertzberg (1984), workers at the Nitro, West Virginia plant were also exposed to p-aminobiphenyl, diphenylguanidine, the benzothiazolesulfonamides, m-cresol derivatives, p-phenylenediamine derivatives, 4,4'-dithiodimorpholin, ethyl parathion, methyl parathion, o-dichlorobenzene, p-dichlorobenzene, p-nitrophenol, and toluene and mercaptobenzothiazole derivatives of tetramethylinramdisulfide and trimethylquinoline components. The impact on mortality associated with these additional and combined chemical exposures was not evaluated by Fingerhut et al. (1991a,b). Although TCDD was a contaminant of some of these chemicals, it was only present at approximately the part per million level, therefore, any conclusions suggesting that TCDD was the causative agent in this study would be speculative.

Other limitations associated with the Fingerhut et al. (1991a,b) study may affect its interpretation. First, mortality in this study was measured using Standard Mortality Ratios (SMRs), which are calculated by comparing the observed deaths in the cohorts with the expected number of deaths for the general population. For rare cancers, such as soft-tissue sarcoma, it is necessary to compare cohorts with a sufficiently large population in order to generate a statistically meaningful number of expected deaths. This approach assumes that the expected number of deaths in the general population for a given disease endpoint is comparable to the expected number of deaths in the study population. However, national mortality rates do not always agree with local rates, and when local or county mortality rates are higher than national rates, comparison to national mortality rates may result in artificially elevated SMRs (Mausner and Kramer, 1985). In addition, though the Fingerhut et al. (1991a,b) cohort consisted only of male chemical manufacturing workers, comparisons were made to national mortality rates. A more appropriate reference group would have been male chemical workers not involved with production of TCDD contaminated chemicals.

Furthermore, Fingerhut et al. (1991a,b) noted that a lack of diagnostic consistency among clinicians and pathologists resulted in the misclassification of tumor types and cause of death for cases both in the cohort and in the comparison group. The authors concluded that "the interpretation of the increased mortality from soft-tissue sarcoma in our study is limited by the small number of cases and the fact that the cause of death was sometimes misclassified on the death certificates of the workers and in the U.S. population." Finally, an increased incidence in the types of tumors that one might expect to see based on studies of highly exposed laboratory animals, namely hepatocarcinomas or adenomas, were not observed in the NIOSH study.

Fingerhut et al. (1991a,b) also measured serum lipid levels in a sample of 253 workers from two of the twelve plants studied. In the most highly exposed individuals, post-latency serum lipid TCDD levels were found to be as much as 500 times higher than normal background levels of approximately 7 ppt (Patterson et al., 1987). By extrapolating measured serum levels back to the date of last exposure, Fingerhut et al. (1991b) estimated that pre-latency serum levels were as much as 4,500 times background levels, indicating that exposures were considerably higher than those incurred today by the general population from environmental sources.

Because Fingerhut et al. (1991a,b) demonstrated a significant trend in increasing TCDD serum levels with increasing chemical exposure, it is very likely that the same type of trend for the other chemical exposures would have been observed had these data been gathered. No causative relationship was established for human carcinogenicity and TCDD exposure from this analysis. In fact, even though the authors observed very high serum lipid TCDD levels in some of the exposed population, they (Fingerhut et al., 1991a) concluded that:

> "This study of mortality among workers with occupational exposure to TCDD does not confirm the high relative risks reported for many cancers in previous studies."

Although certain studies have suggested a positive association between exposure to chemicals containing TCDD as a contaminant and certain types of cancers (Hardell and Sandstrom, 1979; Eriksson et al., 1981; Hardell et al., 1981; Fingerhut et al., 1991a,b), other epidemiologic studies have not confirmed these positive associations (Smith et al., 1982, 1983; Pearce et al., 1986; Smith and Pearce, 1986; Wiklund and Holm, 1986). In recent reviews of the major human studies, Kimbrough (1991) and Tollefson (1991) have concluded that the evidence for an association of TCDD with human cancer is equivocal. The majority of the available epidemiologic studies on the association of cancer to TCDD exposure provide little evidence that dioxin is a potent carcinogen in humans (Tollefson, 1991). While the converse cannot be ruled out on the bases of currently available data (Tollefson, 1991), it is unlikely that TCDD is a human carcinogen at low doses (Bond et al., 1989). The results of the very recent Fingerhut et al. (1991a,b) studies are consistent with this conclusion.

2.2 Mechanism of Action

The mechanism by which TCDD elicits a toxic response in humans and laboratory animals is critical to understanding the significance of low level environmental exposures. Equivocal epidemiologic data suggesting increased health risks from relatively high level occupational and catastrophic exposures and no evidence of increased cancer risk from low level environmental exposures, suggests that there exists a threshold level of exposure at which no toxic effects occur (Fingerhut et al., 1991a,b; Kimbrough, 1990). In combination with human and animal data, information elucidated from mechanistic studies can be used to quantitatively evaluate whether there is a biological threshold which must be exceeded before a toxic response is observed.

The underlying biological characteristics describing TCDD's threshold have been widely studied (Greig and Dematties, 1973; Poland et al., 1976; Nebert and Jenson, 1979; Poland and Knutson, 1982; Safe, 1986; Shu et al., 1987; Goldstein, 1989; Silbergeld and Gasiewicz, 1989; Greenlee, 1990; Leung et al., 1990; Nessel et al., 1990; Poland et al., 1990). In general, a biologic threshold for hepatotoxic effects was evident from studies of mice in which toxic effects to the liver were only observed when liver to adipose TCDD ratios exceeded 1.0 (Allen et al., 1975; Olson et al., 1980; Gasiewicz et al, 1983; Leung et al., 1990). Control animals in these studies had liver to adipose TCDD ratios of less than one, similar to the ratios observed in environmentally exposed human populations (Ryan et al., 1985; Faccetti et al., 1990; Leung et al., 1990c). These studies suggest that not only have doses administered to experimental animals exceeded the doses that are biologically relevant to human environmental exposures, but that a definitive level of exposure can be correlated with a physiologic response, a level that must be exceeded to result in a biologic response.

At the sub-cellular level, the receptor-mediated mechanism proposed by Poland et al. (1990), Greenlee et al. (1990), and Nessel et al. (1990) is viewed as the most scientifically valid hypothesis for explaining TCDD's mechanism of action (WDH, 1991; Roberts, 1991; Holloway, 1990). Poland and co-workers demonstrated that TCDD reversibly binds to a soluble cytosolic receptor protein (Ah receptor) to initiate a coordinated gene expression similar to the action of steroid hormones (Poland et al., 1976; Poland et al., 1984). Results of recent research indicate that the cytosolic receptor-TCDD complex (Ah/TCDD) translocates into the nucleus of the cell and binds to XRE, a xenobiotic response element (Gallo, personal communication, 1991), as well as induces arylhydrocarbon (AHH) activity (Greig and Dematties, 1973; Nebert and Jensen, 1979). The binding of the TCDD/Ah receptor with XRE is reversible and results in the induction of the cytochrome P450 enzymes, arylhydrocarbon hydralase P4501A1 and P4501A2 binding proteins, as well as synthesis of other biologically active proteins and hepatic microsomal binding proteins (Gallo, personal communication, 1991).

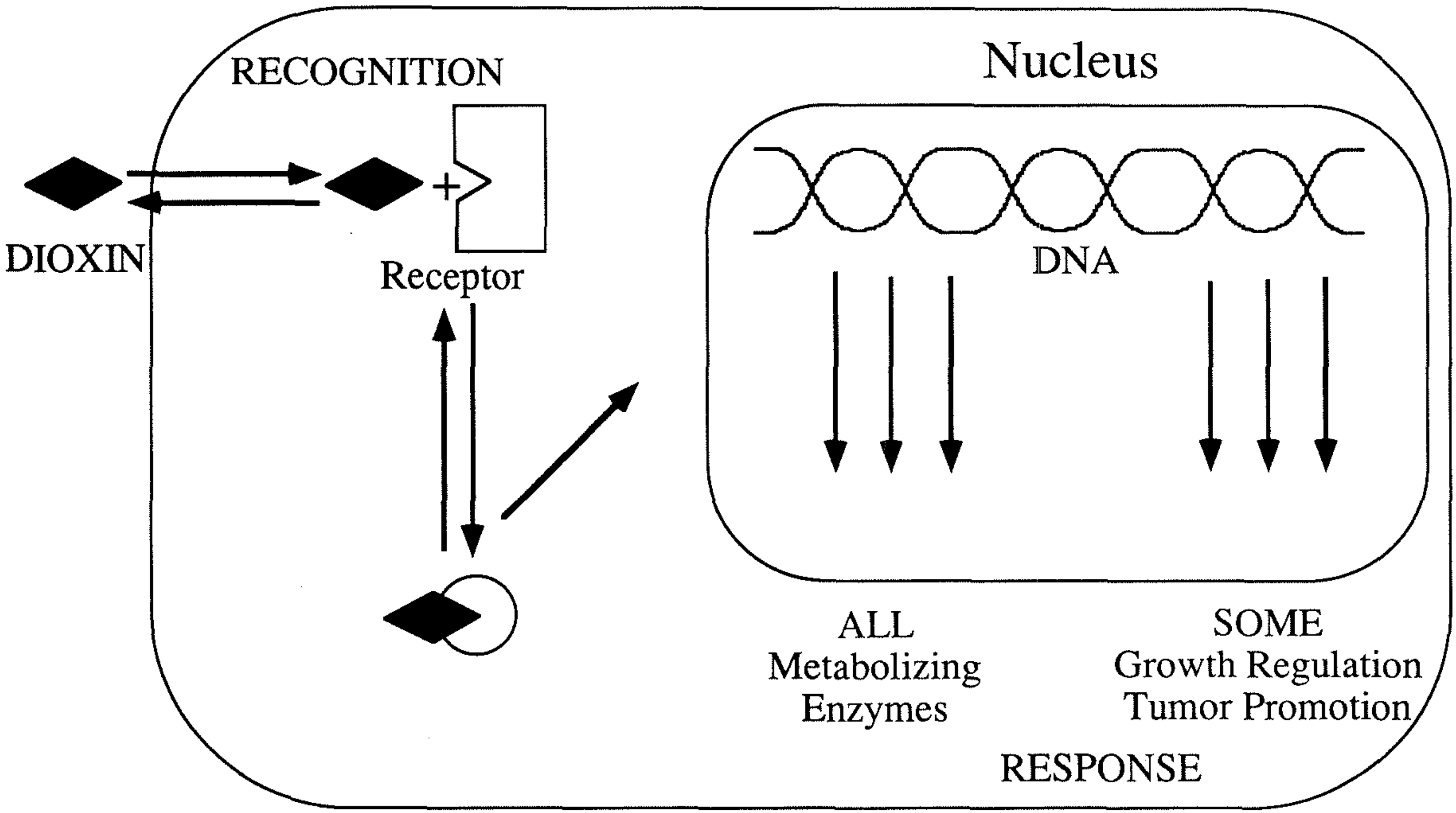
Activation of the Ah receptor and induction of AHH and the cytochrome P450 system are clearly biological markers of xenobiotic exposure, but not necessarily markers of TCDD exposure and toxicity. In fact, P450 induction is associated with both the positive and negative regulation of many naturally occurring enzyme systems in the body. Results of a recent bioassay conducted by Nessel et al. (1900) support previous in vitro mechanistic studies which had suggested that doses below a certain threshold should not activate the Ah receptor or induce enzymatic activity. Nessel et al. (1990) intratrachaelly instilled varying concentrations of TCDD into rats in a study designed to test the hypothesis that an enzymatic threshold for TCDD action could be demonstrated. This hypothesis was based on the premise that an exposure level could be defined that did not produce a positive Ah receptor response or induction of the cytochrome P450 system. These investigators observed that at TCDD dosages below 0.55 μg/kg no enzymatic reaction was elicited, whereas dosages above 0.55 μg/kg induced both AAH and cytochrome P450.

Consistent with the recent work of Poland et al. (1990), Greenlee et al. (1990), and Nessel et al. (1990), many researchers in the scientific community believe that all observed toxic effects associated with exposure to dioxin, including immunotoxicity, reproductive effects, and cancer, appear to be mediated through the Ah receptor (Birnbaum, 1990; Gallo, 1990; Scheuplein, 1990; van der Heijden, 1990). According to Gallo (1990), for dioxin to have an effect, it must reach a specific site, bind to a receptor, move into the nucleus, and bind to the genetic material (Figure 2-1). Gallo (1990) concluded that several thousand receptors must be occupied before any biological or toxic effect is seen. At doses which are too low to cause induction of cytochrome P450, no effects can occur (Birnbaum, 1990; Gallo, 1990; Scheuplein, 1990; van der Heijden 1990). Therefore, a "safe" dose for dioxin can be established (Birnbaum, 1990; Gallo, 1990; Scheuplein, 1990; van der Heijden, 1990).

2.3 Carcinogenic Dose Response

The epidemiologic evidence to date indicates that dioxin is less toxic to humans than once believed, and that the low levels of TCDD presently in the environment are not harmful to humans (Roberts, 1991; Scheuplein, 1990; van der Heijden, 1990; Gallo, 1990; Birnbaum, 1990; Kimbrough, 1990). Even at the much higher levels of TCDD exposure seen in certain chemical workers and other highly exposed populations (Fingerhut et al., 1991a,b; Kimbrough, 1990), data are limited and often equivocal (Tollefson, 1991). Without adequate dose-response data from epidemiologic studies, studies of laboratory animals have been used in an attempt to characterize the relationship between chronic exposure to TCDD and chronic health effects. In particular, carcinogenic effects and reproductive effects, the most sensitive endpoints observed in laboratory animals, are the basis for developing ADIs and RsDs for TCDD.

Figure 2-1. Mechanism of Dioxin Action on Target Cells



In the absence of adequate dose-response data from epidemiologic studies, extrapolations from animal toxicity bioassays have been made in an attempt to characterize the relationship between TCDD uptake and possible carcinogenic response in humans. The two-year chronic rat study conducted by Kociba et al. (1978) is typically cited as the primary evidence supporting the carcinogenicity of TCDD in laboratory animals. Based on the Kociba et al. (1978) bioassay and on the National Toxicology Program's (NTP) 1982 bioassay, the EPA (1985) classified dioxin as a probable (B2) human carcinogen because, in the opinion of EPA, the evidence in support of TCDD as a carcinogen in animals was sufficient while the evidence supporting TCDD's carcinogenicity in humans was inadequate. Consequently, the Kociba et al. (1978) rat bioassay has been used by the U.S. Environmental Protection Agency, the Centers for Disease Control, the U.S. Food and Drug Administration, and many government agencies in North America and Europe for estimating the human cancer risk to TCDD.

In the Kociba et al. (1978) study, 50 Sprague-Dawley (Spartan substrain) rats of each sex were maintained for up to 24 months on diets which provided 1,000, 10,000 or 100,000 pg/kg-day of TCDD with an additional 86 animals of each sex being maintained as study controls. At termination of the experiment, an extensive gross and histopathological examination was conducted on each animal. This examination revealed a dose-related toxic response to the liver characterized by severe hepatic toxicity and the presence of hepatocellular lesions (Kociba et al., 1978).

Because the incidence of hepatocellular lesions was the most sensitive adverse effect in the Kociba et al. (1978) bioassay, an accurate histopathological classification of these lesions is critical. In 1990, at the request of members of the Maine Scientific Advisory Panel (SAP), the histopathology slides of the liver lesions from the Kociba et al. (1978) study were reevaluated by an independent Pathology Working Group (PWG) using the current and widely accepted NTP classification system for proliferative lesions in the rat liver (Maronpot et al., 1986; McConnell et al., 1988). This protocol or criterion is the one now accepted by U.S. federal agencies, including the EPA. It is considerably different from the classification scheme of Squire and Leavitt (1975) used by Kociba and coworkers in 1978 and Squire in 1980 when they classified certain lesions as pre-malignant "neoplastic nodules" or "hyperplastic nodules". The current NTP guidelines distinguish between hyperplasia, a nonneoplastic response to degenerative changes in the liver, and an adenoma, a benign condition involving clear differentiation of cells from the surrounding tissue (Maronpot et al., 1986).

The independent panel was organized under the auspices of PATHCO, Inc. and included pathologists from the National Toxicology Program, Mallory Institute of Pathology, the Chemical Industry Institute of Toxicology (CIIT), as well as, the participation of scientists from the EPA, FDA, and the National Cancer Institute (NCI) (PWG, 1990a). The reevaluation of the liver pathology slides from the Kociba et al. (1978) study was conducted using the consensus diagnosis format endorsed by the NTP. A consensus was reached when 4 out of the 7 pathologists agreed on the classification of a lesion. Unlike previous histopathology reviews of the slides, the slides were read by PWG pathologists without their prior knowledge of the dose group from which the animals were drawn (PWG, 1990a).

The PWG (1990a) concluded that there were substantially fewer cancerous tumors (about 2/3 fewer) observed in the study than previously reported. The lesions previously referred to as "hyperplastic nodules" or "neoplastic nodules" were predominantly benign, hepatocellular adenomas and were usually associated with lesions of hepatic toxicity. While the original results indicated 11 hepatocellular carcinomas in the high dose group, the PWG (1990a) diagnosed only four malignant tumors. Furthermore, there was a distinct correlation between the presence of overt hepatotoxicity and the development of hepatic lesions (PWG, 1990a, 1990b), suggesting that the maximum tolerated dose had been exceeded in animals exposed at the higher doses (PWG, 1990b).

2.3.1 Nonthreshold Models

In the United States federal agencies have used nonthreshold dose-response models to extrapolate human dose response relationships from the Kociba et al. (1978) rat bioassay data. Differing cancer potency estimates for TCDD have been derived by the EPA (1985), the Centers for Disease Control (CDC) (Kimbrough et al., 1984), and the Food and Drug Administration (FDA) (1983) using these models. The use of these models was based on the assumption that there is no threshold for carcinogenesis. For example, the linearized multistage (LMS) model used by the EPA (1985) to estimate TCDD's carcinogenic potency forces the dose response curve through zero, i.e., it assumes that any dose results in a carcinogenic response and a certain level of risk.

Recent scientific information indicates that the use of linear dose-response models to estimate human risks from exposure to TCDD was not valid. TCDD is a considerably less potent carcinogen than previously thought by the EPA and by many well-respected scientists and, as described in Section 2.2.3, the weight of evidence to date clearly supports a receptor mediated response for all toxic responses to TCDD. Based on the acceptance of an exposure level of dioxin below which no effects will occur, the linear models traditionally used for dioxin should no longer be used to evaluate dioxin risk (van der Heijden, 1990).

If, however, one were to use the LMS model, then only the most recent and scientifically defensible tumor incidence data reported by PWG (1990a) should be modelled. Using the LMS model, ChemRisk (Keenan et al., 1990a; 1991a,b) calculated a cancer potency factor for TCDD of 9,700 (mg/kg-day)$^{-1}$ by (1) adjusting the PWG (1990b) tumor incidence data to account for early mortality in the Kociba et al. (1978) bioassay; (2) considering the combined incidence of hepatocellular carcinomas and adenomas; and (3) extrapolating from rats to humans using a body weight correction factor in accordance with the policies and scientific judgment of the U.S. FDA (1983) and the CDC (Kimbrough et al., 1984). This cancer potency factor is approximately 16-fold lower than the EPA's cancer potency factor of 156,000 (mg/kg-day)$^{-1}$ (EPA, 1985), and equates to a risk-specific dose, at a 10^{-5} risk level, of 1.0 pg/kg-day.

The Florida Department of Health and Rehabilitative Services (FDHRS, 1991) has recently proposed a cancer potency factor for TCDD of 809 (mg/kg-day)$^{-1}$, based on a log-normal model which considers a biological threshold in the calculation of the CPF. The log-normal model that (FDHRS, 1991) used does not force the dose extrapolation through zero, rather, it interprets the linear slope as it passes through the threshold level. At a 10^{-5} level of risk, this cancer potency factor correlates to a RsD of 12.4 pg/kg-day.

2.3.2 Threshold Models

A number of countries including Canada, the Netherlands, West Germany, and the United Kingdom have recognized that TCDD acts via a threshold mechanism. These countries have historically used a safety factor approach to estimate ADIs for TCDD (Ontario, 1985; van der

Heijden et al., 1982; NCASI, 1987; U.K., 1989; Tollefson, 1991). Nearly all ADIs for TCDD estimated by North American and Western European countries are based on the 1,000 pg/kg-day NOAEL reported in the Kociba study (Kociba et al., 1978). Following a review of the available data on exposure and uptake of TCDD, an ADI for TCDD was recently recommended by a working group of the World Health Organization (WHO, 1990). It was agreed that for general toxicological effects including reproductive effects, immunotoxicity, and carcinogenicity in the various laboratory animal species, a tolerable daily intake (TDI) of 10 pg/kg-day could be determined using the safety factor approach.

Recently, the Washington Department of Health (WDH) developed an ADI for 2,3,7,8-TCDD of 20 pg/kg-day. This ADI was derived using the results of pharmacokinetic modelling for TCDD (Leung et al., 1990), WDH (1991) estimated the TCDD dose that correlated with five percent occupancy of the cytosolic (Ah) receptor, a level of occupancy considered by the WDH to be a valid and conservative approach which would be supported by most scientists. Based on the model predictions of Leung et al. (1990), this level of occupancy falls between the Kociba et al. (1978) LOAEL of 10,000 pg/kg-day and the NOAEL of 1,000 pg/kg-day. Assuming a linear relationship for receptor occupancy between these two dose levels, WDH (1991) estimated a dose 2,000 pg/kg-day. Thus, a NOAEL of 2,000 pg/kg-day was derived for 5% receptor occupancy, a level at which no biologic response would be expected. WDH (1991) applied as 100-fold safety factor to this NOAEL resulting in an ADI of 20 pg/kg-day.

The classical safety factor approach addresses the problem associated with species to species extrapolations (laboratory animals to man) and the variability among humans. Most often a safety factor of ten is used to account for differences between species and another factor of ten is used to account for individual variability (Klaassen et al., 1986). In the case where a no observable adverse effect level (NOAEL) has been determined in a chronic bioassay, the ADI would be estimated by dividing the NOAEL by a safety factor of 100. The resulting ADI represents a daily dose of TCDD below which no adverse health effects would occur.

2.3.3 Summary: Carcinogenic Dose Response

Threshold models are the most appropriate method for estimating the dose-response relationship for TCDD in humans. The current understanding of the mechanism of action for TCDD, as discussed in Section 2.1, clearly indicates that a threshold exists for all toxic responses to TCDD. The requirement of Ah receptor mediation before the most sensitive marker of exposure is observed, induction of cytochrome P450, provides strong support for the growing scientific opinion that there is a dose at which no toxic effects occur. Consistent with other national and local governments who have developed acceptable daily intakes ranging to 20, or even 80 pg/kg-day, an ADI for carcinogenic effects of 10 pg/kg-day, based on the application of a safety factor of 100 to the NOAEL of 1,000 pg/kg-day observed in the 1978 Kociba et al. rat bioassay, is certainly fully protective of human health.

2.4 Noncarcinogenic Dose Response

Associations between exposure to TCDD and non-cancerous effects in humans have not been established. However, the noncarcinogenic toxicity of TCDD in animals has been studied in a number of acute, subchronic, and chronic studies (Kimbrough et al., 1984). These studies can be used to establish noncarcinogenic dose-response relationships in animals, and such information can be extrapolated to arrive at health-protective ADIs for humans.

TCDD has been shown to be extremely toxic to certain rodent species. The acute LD_{50} (the dose which is lethal to 50% of the animals tested) for guinea pigs is reported to be 0.6 µg/kg body weight. The sensitivity to TCDD toxicity is extremely variable among laboratory animal species. Kociba and Cabey (1985) found the LD_{50} for hamsters to be as high as 5,051 µg/kg; i.e., the hamster is over 8,400 times less sensitive to TCDD than is the guinea pig. Clinical signs of acute toxicity in laboratory animals are severe weight loss, hepatotoxicity, chloracne, thymic atrophy, and death.

Chronic high-level TCDD exposure has been shown to result in severe hepatotoxic effects in rats and mice (Kociba, 1984). Although numerous tumor types were observed, the liver was identified as the primary and most important target tissue for overt toxicity (Kociba et al., 1978). Furthermore, carcinogenicity observed in the liver was evident only at doses that elicited a severe noncarcinogenic toxic response in the study animals (Squire, 1990a). This was evidenced by the Kociba et al. (1978) observations of severe liver toxicity, diminished weight gain, and increased mortality.

2.4.1 Reproductive / Teratogenic / Fetotoxic Effects

Reproductive, immunotoxic, fetotoxic, and teratogenic effects in animals are considered to be the critical endpoints for assessing the chronic noncarcinogenic risk from exposure to TCDD, since human studies are limited and therefore insufficient for establishing a reference dose (RfD). Chronic exposure to TCDD has been shown to induce adverse reproductive, immunotoxic, fetotoxic, and teratogenic effects in several species of laboratory animals (EPA, 1985).

Exposure to TCDD has induced teratogenic effects, predominantly cleft palate and kidney anomalies, in several strains of mice (Smith et al., 1976). The no-observed-adverse-effect-level (NOAEL) for a teratogenic response in the mouse is 0.1 µg/kg-day (100,000 pg/kg-day) (Smith et al., 1976). Teratogenic effects have also been reported for several strains of rats (EPA, 1985). Review of the scientific literature clearly indicates that the rat is more susceptible to these types of noncarcinogenic effects than is the mouse. Because of the number of different studies conducted on laboratory animals, only those studies which demonstrate the lowest levels at which effects were observed are discussed below.

Murray et al. (1979) conducted a three-generation study of Sprague-Dawley rats fed a diet containing TCDD at dose levels of 0, 0.001, 0.01, and 0.1 µg/kg-day. At the highest dose group (0.1 µg/kg-day), fertility and neonatal survival were significantly reduced in the f_0 litters, and neonatal survival was reduced in the f_1 generation. At 0.01 µg/kg-day, fertility was significantly reduced in f_1 and f_2 generations but not in the f_0 generation, and statistically significant decreases in litter size, fetal and neonatal survival, and growth were observed. No effects on fertility, litter size, or postnatal body weight were observed in the 0.001 µg/kg-day dose group, nor was any consistent effect on neonatal survival observed. A significant decrease in postnatal survival was observed in an f_1 litter of the 0.001 µg/kg-day dose group but not in subsequent generations. Murray et al. (1979) concluded that the reproductive capacity of rats ingesting 0.001 µg/kg-day

(1,000 pg/kg-day) TCDD through three generations was not affected; consequently, 1,000 pg/kg-day represents a NOAEL for reproductive effects in rodents.

Nisbet and Paxton (1982) have argued that a more appropriate statistical analysis of the Murray et al. (1979) data indicates that there were decrements in reproductive performance at the 1,000 pg/kg-day dose level. They therefore maintain that the 1,000 pg/kg-day dose level was actually a LOAEL and not a true NOAEL. Scientists from the U.S. Centers for Disease Control (CDC) and the U.S. Department of Agriculture (USDA) have reviewed the Nisbet and Paxton (1982) reanalysis and have not agreed with their findings (Kimbrough et al., 1984). Furthermore, the FIFRA Scientific Advisory Panel concluded that although the data suggested an embryotoxic effect at 1,000 pg/kg-day, they concluded that 1,000 pg/kg-day represented a NOAEL (EPA, 1985).

A series of studies conducted on rhesus monkeys have evaluated the effects of chronic exposure to TCDD on body burden levels, reproductive success, maternal-to-infant transfer, and behavioral patterns (Schantz et al., 1986; Bowman et al., 1989a; 1989b). In these studies, adult female rhesus monkeys were chronically exposed (prior to and during gestation over 3.5 to 4 years) to 0, 5, or 25 ppt of TCDD in the diet. Reproductive toxicity was determined according to an Index of Overall Reproductive Success (IORS) which scored several reproductive events including numbers of conceptions, abortions, stillbirths, live births, and survival to weaning. The authors reported consistent evidence of reproductive impairments in monkeys fed 25 ppt TCDD in the diet, whereas there was no indication of reproductive deficit in the 5 ppt group (Bowman et al., 1989a). The daily dose of TCDD that each group of monkeys received can be estimated by considering the average adult monkeys' body weight (7.5 kg), the average daily consumption rate of food (190 g), and the concentration of TCDD in the food. Using the average body weight and food consumption rate one can estimate that the 5 ppt dose group received a daily TCDD dose of 130 pg/kg-day. This dose represents a NOAEL for reproductive toxicity in female rhesus monkeys.

Other chronic studies on monkeys have reported decreases in reproductive capacity following exposure to 50 and 500 ppt TCDD in the diet (1,300 and 13,000 pg/kg-day) for at least 7 months prior to breeding (Barsotti et al., 1979; Allen et al., 1979; Schantz et al, 1979). These studies substantiate the finding that 130 pg/kg-day is the most sensitive NOAEL reported for reproductive toxicity in primates. It should be noted that this NOAEL is lower than the NOAEL of 1,000 pg/kg-day reported by Murray et al. (1979) for reproductive success in rats.

In a subchronic fetotoxicity study, McNulty (1984) administered 2,3,7,8-TCDD to rhesus monkeys at cumulative doses of 0.2, 1.0, and 5.0 μg/kg between days 20 to 40 of gestation. The doses in this study were not chosen to establish a statistically rigorous dose-response relationship, but rather to find a dose that was reliably fetotoxic or teratogenic. Monkeys treated with 1.0 or 5.0 μg/kg showed signs of maternal toxicity and fetotoxicity; two of two monkeys in the high dose group aborted, while abortions occurred in 13 of the 16 pregnant monkeys in the 1.0 μg/kg dose group. None of the four mothers given 0.2 μg/kg in divided doses showed signs of toxicity and the three surviving offspring in the 0.2 μg/kg dose group showed no gross, radiologic, or histological abnormalities. However, there was one spontaneous abortion in this dose group. The abortion rate in the low dose group was similar to that in the controls (3/12), yet the authors concluded that the number of animals in the 0.2 μg/kg was far too small for statistical evaluation or to warrant a conclusion of no observable effect (McNulty, 1984).

Review of the scientific literature clearly indicates that primates are the most sensitive species to adverse reproductive effects, teratogenicity, and fetotoxicity following exposure to TCDD. Cleft palates and other anomalies of the soft palate have been reported in rhesus macaques administered either 1.0 μg/kg or 0.2 μg/kg TCDD in corn oil by gavage. The total dose was administered in nine doses from days 20 to 40 following insemination (Zingeser, 1979). Maternal toxicity, effects or fertility, and fetotoxicity (reduced conception, fetal resorption, abortion) were reported in monkeys exposed to 500 ppt TCDD (approximately 10 μg/kg-day) in the diet for 6 months prior to and during pregnancy (Barsotti et al., 1979). As previously described, Bowman et al. (1989) reported reduced reproductive capacity in monkeys exposed to 25 ppt TCDD (0.63 μg/kg-day) in the diet. This effect level is lower than the level of 10 μg/kg-day reported by Murray et al. (1979) to affect fertility in rats.

2.4.2 Immunotoxicity

The effects of TCDD on the immune response of animals vary widely and are highly dependent on species and age (U.K., 1989). The guinea pig has been identified as a species which is highly susceptible to TCDD's immunotoxicity (U.K., 1989). A LOAEL of 0.04 μg/kg-week was identified for immunotoxic effects in adult guinea pigs fed a diet containing TCDD weekly for 8 weeks. For adult animals, a "minimal effect level" of 0.04 μg/kg-week (40 ng/kg-week or 6,000 pg/kg-day) was determined (U.K., 1989).

2.4.3 Summary: Noncarcinogenic Dose Response

Studies of noncarcinogenic effects among various laboratory animals exposed to TCDD clearly indicate that primates are one of the most sensitive species. In fact, the scientific evidence to date suggest that nonhuman primates are more sensitive to the effects of TCDD than are humans (Kimbrough, 1990). Furthermore, humans appear to be less sensitive to the toxic effect of TCDD than most animals (Kimbrough, 1991). Animals and humans demonstrate different sensitivity to toxicological responses to dioxin due in part to toxicokinetics and Ah-receptor differences. As a result of toxicokinetic differences, the highest levels of dioxin in humans are found in fatty tissues, however, the reverse is true for animals. Most animals accumulate high concentrations of dioxin in vital organs (Kimbrough, 1991). In addition, human cells have fewer cytostolic Ah-receptors and a lower binding affinity to TCDD than animal cells (Kimbrough, 1990). As a result, animals would be expected to demonstrate a greater sensitivity to dioxin than humans.

When deriving acceptable daily intakes for humans based on chronic animal studies, a safety or uncertainty factor of 100 is typically applied to laboratory-derived NOAELs. This safety factor includes a factor of 10 for species differences (usually between rodents and humans) and a factor of 10 for variations in sensitivity within the human population. It is important to note that sub-human primates, in comparison to more resistent species, are very susceptible to the adverse effects of TCDD (Kimbrough, 1990). Therefore, the classical use of a 10-fold safety factor for species to species extrapolation may not be warranted in this particular case and a single safety factor of 10 to account for individual variability within the human population should provide an adequate margin of safety. Based on a NOAEL of 130 pg/kg-day for reproductive effects in rhesus monkeys (Bowman et al., 1989a), an ADI of 13 pg/kg-day can be determined by application of a 10-fold safety factor.

2.5 Recommended Acceptable Daily Intake

The weight of evidence clearly supports consideration of the receptor mediated mechanism for toxicity when evaluating the human health risks from exposure to TCDD. Incorporation of this concept has resulted, even when different threshold approaches (i.e., mathematical threshold models, pharmacokinetic modelling, or the classical safety factor approach) have been used, in consistent ADI estimates. A number of European and North American governments have considered TCDD's receptor mediated mechanism of action when establishing allowable daily intakes. These countries have historically used a safety factor approach to estimate ADIs for TCDD of between 1 and 10 pg/kg-day (Ontario, 1985; van der Heijden et al., 1982; NCASI, 1987; U.K., 1989; Tollefson, 1991). They have based their estimates primarily on the 1,000 pg/kg-day NOAEL reported in the Kociba et al. (1978) study and the application of safety factors of between 100 and 1,000. A TDI for TCDD of 10 pg/kg-day was recently recommended by a working group of the World Health Organization (WHO, 1990) based on the application of safety factors to data reflecting reproductive effects, immunotoxicity, and carcinogenicity in the various laboratory animal species. The ADI of 20 to 80 pg/kg-day proposed by the Washington Department of Health (WDH, 1990), and developed using a pharmacokinetic model, is also consistent with the ADIs developed by these other groups.

In addition, ADIs estimated from the Kociba et al. (1978) and Bowman et al. (1989) NOAELs are very similar. Whereas the Bowman et al. (1989) study supports an ADI of 13 pg/kg-day for chronic noncarcinogenic effects, the Kociba et al. (1978) study supports an ADI of 10 pg/kg-day for carcinogenic effects. This consistency is not surprising in view of the mechanism by which the Ah receptor is believed to mediate all toxic responses (Birnbaum, 1990; Poland et al., 1990; Greenlee et al., 1990; Nessal et al., 1990). When one correctly accounts for physiologic differences among species, regardless of the toxic endpoint, extrapolation from laboratory animals to humans at the cellular level should arrive at similar results.

As has been discussed in many of the above sections, the scientific weight of evidence indicates that the linear model should not be used to assess the risks of dioxin (van der Heijden, 1990; Kimbrough, 1991; Squire, 1991). Clearly, the more appropriate method for extrapolating to humans is the safety factor approach which recognizes the existence of a biological threshold. Based on the most current scientific evidence, an ADI in the range of 1 to 10 pg/kg-day is protective of human health for all toxic responses.

3.0 EFFECTS OF DIOXIN ON AQUATIC BIOTA

In deriving the 1984 Ambient Water Quality Criteria (AWQC) guidelines, the EPA concluded that the available data pertaining to the aquatic toxicity of TCDD were insufficient to support the development of national criteria based on aquatic health (EPA, 1984). While the available data are still somewhat limited, they do provide a basis for understanding the potential impacts of ambient water levels of dioxin on aquatic organisms. This section summarizes the available scientific literature regarding the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) to fish and other aquatic organisms.

The available data indicate that fish are sensitive to the toxic effects of 2,3,7,8-TCDD. This sensitivity, however, varies considerably among species. Additionally, age, concentration, physiological state and duration of exposure also have a significant impact (Cooper, 1989). It appears that smaller fish are more sensitive to TCDD than larger fish (Norris and Miller, 1973). Studies indicate that the manifestation of toxic effects are almost always delayed and occur after exposure has ended (Norris and Miller, 1973; Helder, 1980, 1981; Adams et al., 1986; Cooper, 1989).

The most commonly observed signs of TCDD toxicity in fish include edema, cutaneous hemorrhages, fin necrosis, decreased food intake, reduced growth rate, and delayed mortality (Miller et al., 1973; Norris and Miller, 1974; Hawkes and Norris, 1977; Yockim et al., 1978; Helder 1980, 1981; Branson et al., 1985; Kleeman et al., 1988; Mehrle et al., 1988; Spitsbergen et al., 1988a, 1988b; Wisk and Cooper, 1990). Immune responses appear to be unaltered except at very high, almost lethal concentrations (Spitzbergen et al., 1987). The histopathology of adult fish exposed to TCDD includes epithelial, lymphomyeloid, and cardiac lesions (Cook et al., 1991). No studies have been undertaken to determine if TCDD produces a carcinogenic response in fish (Cooper, 1989). Although an Ah receptor has now been identified in fish (personal communication Dr. K. Cooper, Rutgers University, 1990), additional research needs to be undertaken to define the mechanism of dioxin's toxicity.

Results of studies of acute and chronic exposure of fish and other aquatic organisms to TCDD in water are summarized in Table 3-1, Figure 3-1, Table 3-2 and Figure 3-2, respectively. Table 3-1 reports nominal concentrations (total amount of TCDD added to the exposure system divided by total volume of water in the system) as well as measured concentrations. Lowest-Observed-Effect-Concentrations (LOECs) and No-Observed-Effect-Concentrations (NOECs) were determined from these studies and are included in the summary tables. Table 3-3 summarizes the studies in which exposure was through routes other than the ambient water or in which LOECs and NOECs are expressed on a body burden basis. The toxicity studies are discussed in the following sections.

3.1 Effects of Acute Exposure to TCDD in Water

Concentrations of 7,100 ppq TCDD and greater caused significant mortality to fathead minnows exposed for 1 to 4 days in a static renewal system (Table 3-1) (Adams et al., 1986). Concentrations of 120 and 720 ppq TCDD did not result in increased mortality during the 60-day observation period.

Table 3-1. Effects of Acute Exposure of Fish and Other Aquatic Organisms to TCDD in Ambient Water

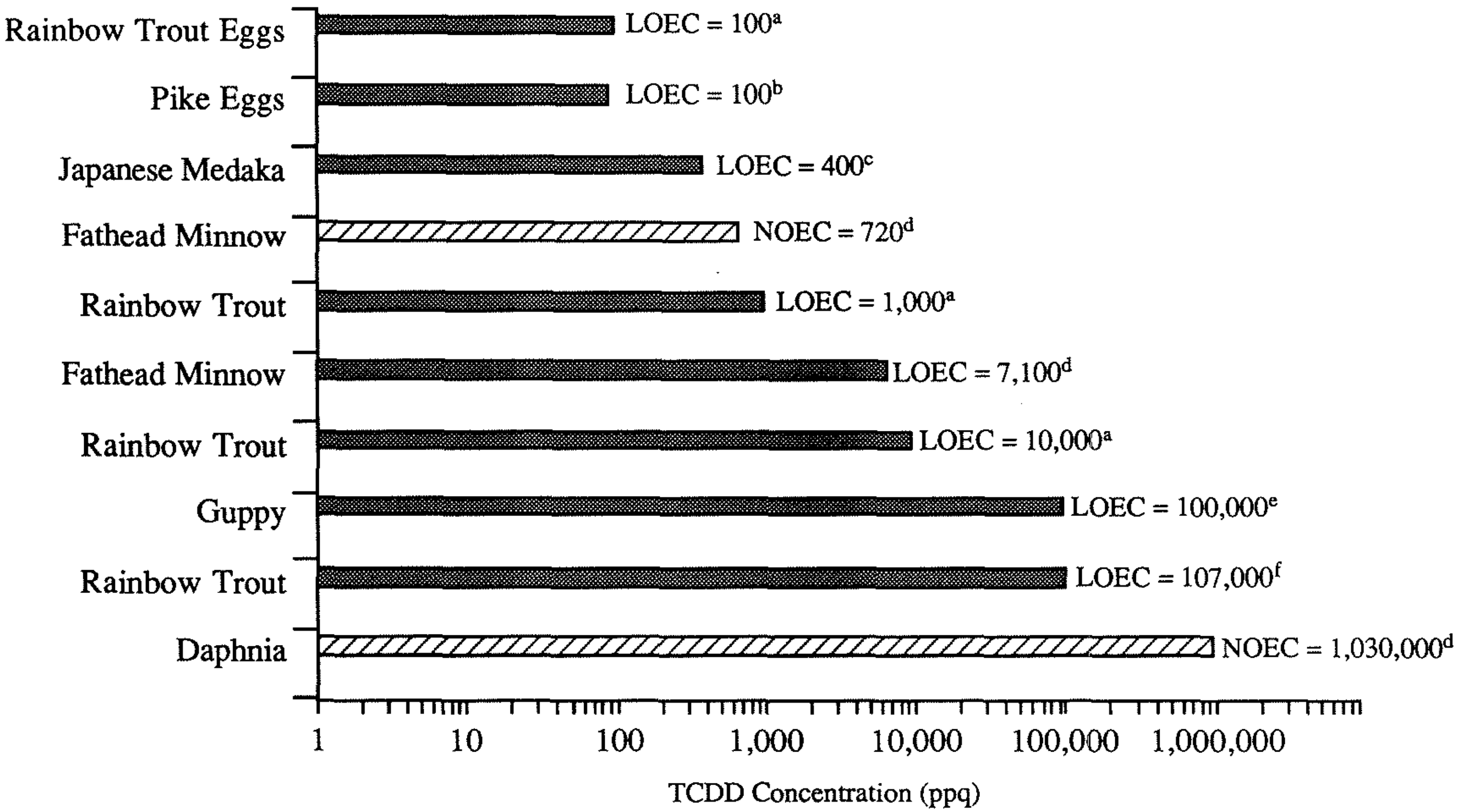
Species	Life Stage Exposed	Exposure Duration (hours)	Test Duration (days)	Carrier Solvent	TCDD Concentration in Water (ppq)	No-Observed-Effect-Concentration (ppq)	Lowest-Observed-Effect-Concentration[a] (ppq)	Effects[a]	Reference
Fathead minnow *Pimephales promelas*	juvenile (1 - 2 g)	24 - 96	150	acetone	0; 120; 720 7,100; 82,000	720	7,100	Mortality[b]	Adams et al., 1986
Guppy *Poecilia reticulatas*	9 - 40 mm	120	37	chloroform, acetone	0; 100,000; 1,000,000; 10,000,000	ND	100,000	Reduced survival[c], reduced food consumption[b], fin necrosis[b]	Miller et al., 1973; Norris and Miller,1974
Japanese medaka *Oryzias latipes*	embryo	3 (exposed on day of fertilization)	3	acetone	0; 400; 1,700; 5,900; 13,200; 31,700; 50,800	ND	400	Decrease in hatching incidence (EC50 14,000 ppq)[d], lesions (EC50 3,500 - 14,000 ppq)[d], mortality (3-day LC50 9,000 ppq)[d]	Wisk and Cooper, 1990
Japanese medaka *Oryzias latipes*	embryo	11 (exposed on day of fertilization)	11	acetone	0; 500; 2,400; 7,000;12,000; 33,500; 57,900	NR	NR	Lesions (EC50 2,200 ppq)[d]	Wisk and Cooper, 1990
Pike *Esox lucius*	eggs	96	≥23	DMSO, acetone	0; 100; 1,000; 10,000	ND	100	Retarded embryonic development[b], decreased growth of fry[c], increased fry mortality[b], edema[b], pathological changes in liver[b]	Helder, 1980
Rainbow trout *Salmo gairdneri*	eggs	96	168	DMSO, acetone	0; 100; 1,000; 10,000; 100,000	ND	100	Growth retardation[c], edemas[b], mortality[c], teratologic defects[b]	Helder, 1981

Table 3-1. Effects of Acute Exposure of Fish and Other Aquatic Organisms to TCDD in Ambient Water (Continued)

Species	Life Stage Exposed	Exposure Duration (hours)	Test Duration (days)	Carrier Solvent	TCDD Concentration in Water (ppq)	No-Observed-Effect-Concentration (ppq)	Lowest-Observed-Effect-Concentration [a] (ppq)	Effects [a]	Reference
Rainbow trout *Salmo gairdneri*	yolk sac fry	96	168	DMSO, acetone	0; 1,000	ND	1,000	Growth retardation[c], edemas[b], mortality[c], teratologic defects[b]	Helder, 1981
Rainbow trout *Salmo gairdneri*	juvenile (0.85 g)	(16 hr/day, 4 days)	70	DMSO, acetone	0; 10,000; 100,000	ND	10,000	Growth retardation[c], mortality [b], edemas[b]	Helder, 1981
Rainbow trout *Salmo gairdneri*	35 g	6	139	acetone	0; 107,000	ND	107,000	Increased relative liver weight[c], decreased body weight gain[b], fin rot[b], mortality [b]	Branson et al., 1985
Waterflea *Daphia magna*	young, adults	48	9	acetone	0; 200 - 1,030,000	1,030,000	ND	No effects reported at any concentration[b]	Adams, et al., 1986

a. Lowest-Observed-Effect-Concentration (LOEC) given in table relates to the most sensitive effect reported by the authors. The effects listed occurred either at the LOEC or at higher TCDD concentrations used in the study.
b. Statistical analysis was not reported.
c. Statistically significant.
d. LC50 or EC50 was statistically derived; however statistical analysis was not reported for comparison of treatment groups to controls.
ND = Not determined
NR = Not reported

Figure 3-1. Summary of Effect Levels from Acute Exposure Studies of Aquatic Organisms to TCDD in Water



References
- a. Helder, 1981
- b. Helder, 1980
- c. Wisk and Cooper, 1990
- d. Adams et al., 1986
- e. Miller et al., 1973; Norris and Miller, 1974
- f. Bronson et al., 1985

LOEC
NOEC

Table 3-2. Effects of Chronic Exposure of Fish and Other Aquatic Organisms to TCDD in Ambient Water

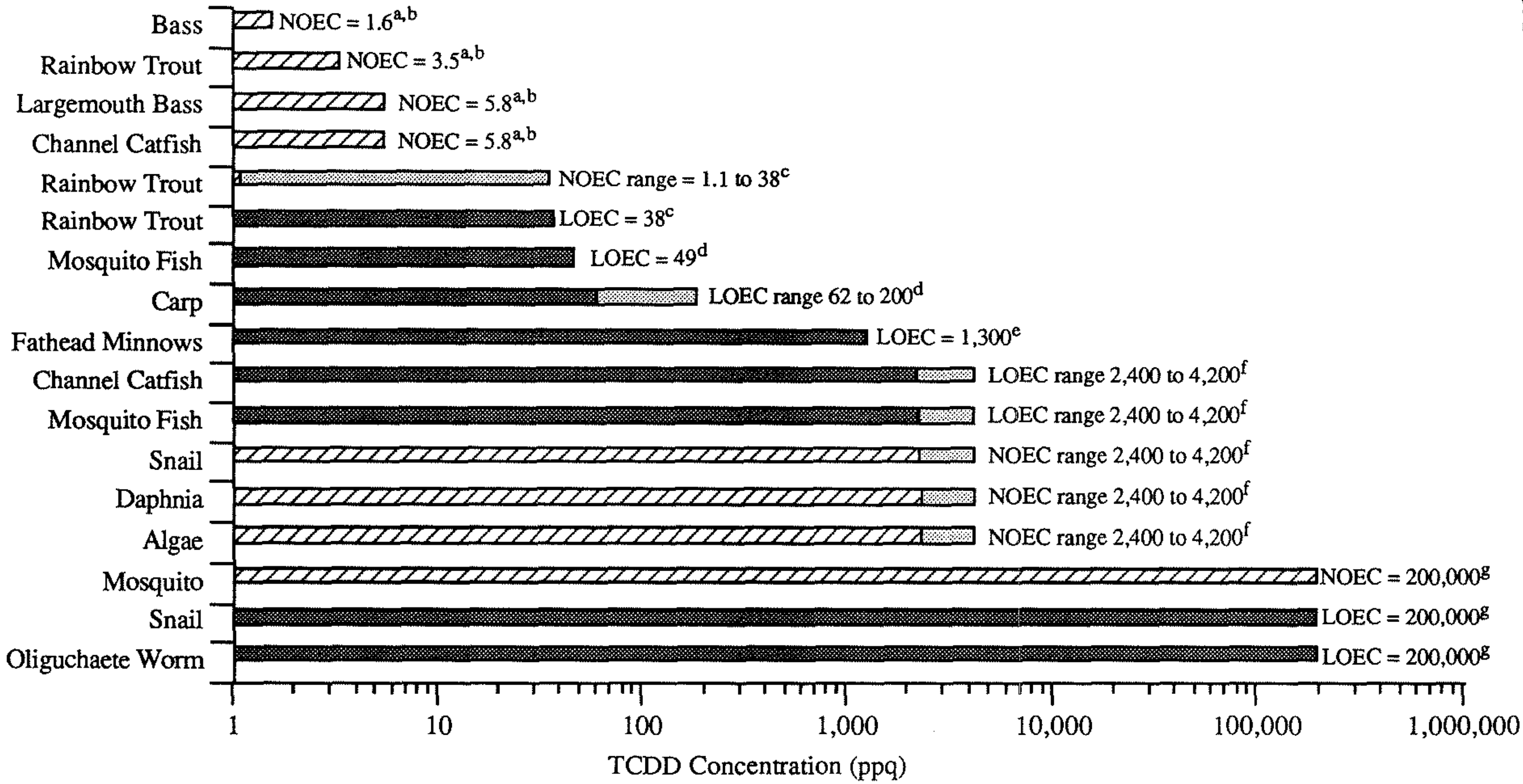
Species	Life Stage Exposed	Exposure Duration (days)	Test Duration (days)	Carrier Solvent	Nominal (Measured) TCDD Concentration in Water (ppq)	No-Observed-Effect-Concentration (ppq)	Lowest-Observed-Effect-Concentration[a] (ppq)	Effects[a]	Reference
Carp *Cyprinus carpio*	1-yr old (15 g)	71	132	dimethyl-formamide	0; 200 (62)	ND	62 - 200	Mortality[b], signs of overt toxicity[b], extensive pathology[b]	Cook et al., 1991
Channel catfish *Ictalurus punctatus*	fingerling	20	20	benzene	(2,400 - 4,200)	ND	2,400 - 4,200	Mortality[b], erratic swimming[b], fin necrosis[b], anal and lower jaw hemorrhaging[b]	Yockim et al., 1978
Fathead minnow *Pimephales promelas*	juvenile (0.5 - 1.0 g)	28	48	acetone	(0; 1,700; 6,700; 63,000)	ND	1,700	Mortality[b]	Adams et al., 1986
Fathead minnow *Pimephales promelas*	1 g	71	132	dimethyl-formamide	0; 200 (49 or 67)	ND	49 - 200	"Variety of toxic signs"[b]	Cook et al., 1991
Mosquito fish *Gambusia affinis*	NR	15	15	benzene	(2,400 - 4,200)	ND	2,400 - 4,200	Mortality[b], nasal hemorrhaging[b], listless swimming[b]	Yockim et al., 1978
Rainbow trout *Salmo gairdneri*	fry (0.38 g)	28	56	acetone	0 (1.1); 115 (38); 231 (79); 463 (176); 925 (382); 1,850 (789)	Between 1.1 and 38, according to authors	38	Reduced growth and survival[c], altered behavioral responses[b]	Mehrle et al., 1988
Algae *Oedogonium cardiacum*	NR	32	32	benzene	(2,400 - 4,200)	2,400 - 4,200	ND	No apparent adverse effects[b]	Yockim et al., 1978
Mosquito *Aedes aegypti*	larvae	17	30	acetone	0; 200,000	200,000	ND	No effects on pupation[b]	Miller et al., 1973

Table 3-2. Effects of Chronic Exposure of Fish and Other Aquatic Organisms to TCDD in Ambient Water (Continued)

Species	Life Stage Exposed	Exposure Duration (days)	Test Duration (days)	Carrier Solvent	Nominal (Measured) TCDD Concentration in Water (ppq)	No-Observed-Effect-Concentration (ppq)	Lowest-Observed-Effect-Concentration [a] (ppq)	Effects [a]	Reference
Oligochaete worm *Paranais sp.*	adult	55	55	acetone	0; 200,000	ND	200,000	Reduced number of worms[c]	Miller et al., 1973
Snail *Helosoma sp.*	NR	32	32	benzene	(2,400 - 4,000)	2,400 - 4,200	ND	No apparent adverse effects[b]	Yockim et al., 1978
Snail *Physa sp.*	adult	36	48	acetone	0; 200,000	ND	200,000	Reduced snail hatch[d]	Miller et al., 1973
Water flea *Daphnia magna*	NR	32	32	benzene	(2,400 - 4,200)	2,400 - 4,200	ND	No apparent adverse effects[b]	Yockim et al., 1978

a. Lowest-Observed-Effect-Concentration (LOEC) given in table relates to the most sensitive effect reported by the authors. The effects listed occurred either at the LOEC or at higher TCDD concentrations used in the study.
b. Statistical analysis was not reported.
c. Statistically significant.
d. Effect was reported, but was not statistically significant.
ND = Not determined
NR = Not reported

Figure 3-2. Summary of Effect Levels from Chronic Exposure Studies of Aquatic Organisms to TCDD in Water



a. Highest concentrations tested, actual NOEC may be higher.

References

b. NCASI, 1991
c. Mehrle et al., 1988
d. Cook et al., 1991
e. Adams et al., 1986
f. Yockim et al., 1978
g. Miller et al., 1973

LOEC
NOEC

Table 3-3. Effects of Exposure of Fish and Other Aquatic Organisms to TCDD via Several Exposure Routes

Species	Life Stage Exposed	Exposure Duration	Test Duration	Exposure Route	Dose Regimen	No-Observed-Effect-Concentration or Level	Lowest-Observed-Effect-Concentration or Level[a]	LD50	Effects[a]	Reference
Bluegill *Lepomis macrochirus*	30 g	single dose	80 days	ip injection	0; 1; 5; 25; 125 µg/kg	1 µg/kg	5 µg/kg	16 µg/kg	Mortality[b], decreased body weight gain[c], fin necrosis[d], cutaneous hemorrhage[d]	Kleeman et al., 1988
Bullhead *Ictalurus melas*	6 g	single dose	80 days	ip injection	0; 1; 5; 25; 125 µg/kg	1 µg/kg	5 µg/kg	5 µg/kg	Mortality[b], decreased body weight gain[e], fin necrosis[d]	Kleeman et al., 1988
Carp *Cyprinus carpio*	20 g	single dose	80 days	ip injection	0; 1; 5; 25; 125 µg/kg	1 µg/kg[f]	5 µg/kg[f]	3 µg/kg	Mortality[b], decreased body weight gain[e], fin necrosis[d], cutaneous hemorrhage[d], cutaneous hyper-pigmentation[d]	Kleeman et al., 1988
Coho Salomn *Oncorhynchus kisutch*	young	24, 48, 96 hrs	114 days	water	0; 0.054;0.54; 5.4; 54.0 ng/g wet wt. fish	0.54-5.4 ng/g wet wt. fish	0.054 ng/g wet wt. fish	ND	Feeding rate, survival[c] and reduced growth[c]	Miller et al., 1979
Guppy *Poecilia reticulatus*	8-12 mm	24 hrs	69 days	water	0; 0.08; 0.8; 8.0; 80.0 ng/g wet wt. fish	0.08 ng/g wet wt. fish	0.8 ng/g wet wt. fish	ND	Incidence of fin necrosis[c]	Miller et al., 1979

Table 3-3. Effects of Exposure of Fish and Other Aquatic Organisms to TCDD via Several Exposure Routes (Continued)

Species	Life Stage Exposed	Exposure Duration	Test Duration	Exposure Route	Dose Regimen	No-Observed-Effect-Concentration or Level	Lowest-Observed-Effect-Concentration or Level [a]	LD50	Effects[a]	Reference
Lake trout *Salvelinus namaycush*	eggs	48 hrs	NR	water	0; 34; 55; 121; 226; 302 pg/g egg weight	34 pg/g	55 pg/g	65 pg/kg	Sac fry mortality[d], hatchability[d], edema[d], hemorrhages[d]	Cook et al., 1991
Largemouth bass *Micropterus salmoides*	7 g	single dose	80 days	ip injection	0, 1, 5, 25, 125 μg/kg	5 μg/kg	25 μg/kg	11 μg/kg	Mortality[b], decreased body weight gain[e], fin necrosis[d], cutaneous hyperpigmentation[d]	Kleeman et al., 1988
Rainbow trout *Salmo gairdneri*	fingerling (3 - 7 g)	13 weeks	26 weeks	feeding	0; 494 pg/g diet	494 pg/g diet	ND	ND	No signs of TCDD toxicity, reduced growth rate, or increase in relative lethality[d]	Kleeman et al., 1986a
Rainbow trout *Salmo gairdneri*	35 g	single dose	80 days	ip injection	0; 1; 5; 25; 125 μg/kg	1 μg/kg	5 μg/kg	10 μg/kg	Mortality[b], decreased body weight gain[c], fin necrosis[d]	Kleeman et al., 1988
Rainbow trout *Salmo gairdneri*	juvenile (7.8 cm)	105 days	105 days	feeding	0; 2.3; 2,300; 2,300,000 pg/g diet (avg. intake of 0, 3.2×10^{-8}, 3.6×10^{-5}, 2.1×10^{-2} μg/g fish)	2,300 pg/g diet	2,300,000 pg/g diet	ND	Reduced food consumption[d], reduced body weight[c], fin erosion[d], reduced survival[d], liver pathology[d]	Hawkes and Norris, 1977

Table 3-3. Effects of Exposure of Fish and Other Aquatic Organisms to TCDD via Several Exposure Routes (Continued)

Species	Life Stage Exposed	Exposure Duration	Test Duration	Exposure Route	Dose Regimen	No-Observed-Effect-Concentration or Level	Lowest-Observed-Effect-Concentration or Level [a]	LD50	Effects[a]	Reference
Rainbow trout *Salmo gairdneri*	juvenile (6 - 10g, 25 - 45 g, 100 - 250 g)	single dose	up to 80 days	ip injection	0; 0.1; 1; 5; 25; 125 µg/kg	ND	1 µg/kg	10 µg/kg	Leukopenia and thrombocytopenia[c], mortality[b], reduced body weight gain[c], fin necrosis[d], lymphomyeloid lesions[d], epithelial lesions[d]	Spitsbergen et al., 1988a
Rainbow trout *Salmo gairdneri*	1.6 g	once a week	4 weeks	feeding	0; 0.0063; 6.3; 6,300 ng	6.3 ng	6,300 ng	ND	Mortality and growth[c]	Miller et al., 1973
Yellow perch *Perca flavescens*	fingerling (3 - 6 g)	13 weeks	26 weeks	feeding	0; 494 pg/g diet	494 pg/g diet	ND	ND	No effects on growth rate or lethality, or signs of TCDD toxicity[d]	Kleeman et al., 1986b
Yellow perch *Perca flavescens*	40 g	single dose	80 days	ip injection	0; 1; 5; 25; 125 µg/kg	1 µg/kg	5 µg/kg	3 µg/kg	Mortality[b], decreased body weight gain[c], fin necrosis[d], cutaneous hemorrhage[d]	Kleeman et al., 1988

Table 3-3. Effects of Exposure of Fish and Other Aquatic Organisms to TCDD via Several Exposure Routes (Continued)

Species	Life Stage Exposed	Exposure Duration	Test Duration	Exposure Route	Dose Regimen	No-Observed-Effect-Concentration or Level	Lowest-Observed-Effect-Concentration or Level [a]	LD50	Effects [a]	Reference
Yellow perch *Perca flavescens*	juvenile (20 g, 40 g)	single dose	80 days	ip injection	0; 1; 5; 25; 125 µg/kg	ND	1 µg/kg	3 µg/kg	Mortality[b], reduced body weight gain[c], fin necrosis[d], hemorrages[d], ascites[d], lymphomyeloid lesions[d], cardiac lesions[d], epithelial lesions including hepatocyte, lipidosis[d]	Spitsbergen et al., 1988b
Frog *Rana catesbiana*	tadpoles	single dose	50 days	ip injection	0; 25; 50; 100; 200; 1,000 µg/kg	1,000 µg/kg	ND	ND	No effects on survival[d], metamorphosis[d], or histology[d]	Beatty et al., 1976
Frog *Rana catesbiana*	adult (150 - 250 g)	single dose	35 days	ip injection	0; 50; 100; 250; 500 µg/kg	250 µg/kg	500 µg/kg	ND	Temporary reduced food consumption[d], no effects on survival or histology[d]	Beatty et al., 1976

a. Lowest-Observed-Effect-Concentration (LOEC) given in table relates to the most sensitive effect reported by the authors. The effects listed occurred either at the LOEC or at higher doses.
b. LD50s were statistically derived; statistical analysis was not reported for comparison of treatment groups to controls.
c. Statistically significant.
d. Statistical analysis was not reported.
e. Effect was reported by authors but was not statistically significant.
f. Although cutaneous hyperpigmentation was observed at 1 µg/kg, it is not clear whether this effect was significant.

ND = Not determined
NR = Not reported

In an additional experiment, Adams et al. (1986) exposed fathead minnows to TCDD concentrations of 1,700 ppq to 630,000 ppq for 28 days. The authors report a LC_{50} of 1,700 ppq, however no statistical analysis was performed.

Guppies exposed to 100,000 ppq TCDD or greater for 120 hours exhibited increased mortality (Table 3-1) (Miller et al., 1973; Norris and Miller, 1974). All treated fish died within 37 days following the start of the exposure period compared to no deaths in the control group. Survival time was reported to be significantly and positively correlated with body length, suggesting that smaller fish are considerably more sensitive to TCDD than larger fish. The authors reported a declining interest in swimming and feeding approximately 1 week after initial exposure. Fish that survived greater than 10 days exhibited fin necrosis.

Miller et al. (1973) fed young rainbow trout a diet containing 0, 0.0063 ng, 6.3 ng, and 6,300 ng TCDD per week for four weeks. Mortality and growth parameters were measured. There was no significant mortality in any of the exposure groups. Significant differences in growth were only observed in the high dose group (6,300 ng TCDD per week).

Wisk and Cooper (1990) exposed embryos of the Japanese medaka to TCDD in a static renewal system (Table 3-1). A concentration-related increased incidence of embryos with lesions was observed at water concentrations of 400 ppq (the lowest concentration tested) and greater. The EC50s for embryos with lesions and embryos with severe lesions were reported to be 3,500 and 14,000 ppq, respectively. The authors reported a concentration-dependent decrease in hatching incidence and a concentration-dependent increase in embryos that were dead by 3-day posthatch. The EC50 to prevent hatching was 14,000 ppq TCDD, and the LC50 for survival to 3-day posthatch was 9,000 ppq TCDD. In a separate experiment, the EC50 for embryos with lesions was reported to be 2,200 ppq TCDD. Based on a calculated ED50 for lesions of 0.24 pg TCDD/mg of dechorionated embryo (0.24 ppb), the authors noted that the Japanese medaka embryo is one of the most sensitive animals to TCDD. From experiments in which embryos were exposed to TCDD beginning on different days of embryonic development, Wisk and Cooper (1990) observed that the sensitive period for toxicity was during liver formation on days 4 and 5 of development.

Pike eggs exposed to TCDD at concentrations of 100 ppq and greater for 96 hours were reported to exhibit retarded egg development (Table 3-1) (Helder, 1980). Growth of fry was significantly reduced for several weeks following exposure to TCDD at all the concentrations tested. While egg mortality was not influenced by TCDD treatment, dose-related mortality of yolk sac and swimming fry was reported. Generalized edemas and pathological changes in the liver were also observed.

Helder (1981) found that exposure of rainbow trout eggs to 100 ppq TCDD (the lowest water concentration tested) for 96 hours resulted in significant growth retardation after 72 days (Table 3–1). Where eggs were exposed to 1,000 or 10,000 ppq TCDD, yolk sac fry developed edemas, and mortality was significantly greater than controls. In the 1,000 and 10,000 ppq TCDD treatment groups, teratologic defects were observed 12 weeks after fertilization. Yolk sac fry exposed to 1,000 ppq TCDD after hatching showed similar effects to those of fry exposed to TCDD at the egg stage (Helder, 1981). Juvenile rainbow trout exposed to 10,000 or 100,000 ppq TCDD for 96 hours exhibited growth retardation and showed slight edematous changes (Helder, 1981).

Branson et al. (1985) reported that rainbow trout exposed to 107,000 ppq TCDD for 6 hours exhibited an increase in relative liver weights by day 42 and a decrease in body weight gain (Table 3-1).

Cook et al. (1991) exposed fertilized eggs from Lake Superior lake trout to TCDD in water for 48 hours (Table 3-3). Rather than report the water concentrations used, the authors reported the concentrations of TCDD accumulated in the eggs by the end of the exposure period; these ranged from 34 to 302 pg/g for the treatment groups. After the 48-hour exposure, the eggs were removed to TCDD-free water. The authors reported that embryo development and mortality was not affected by TCDD until about one week before the onset of hatching at which time embryos containing the highest TCDD concentration exhibited toxicity. Hatchability of eggs was reported to be decreased at whole egg TCDD concentrations greater or equal to 226 pg/g. Cook et al. found that the sac fry stage exhibited the greatest mortality in their study. The No-Observable-Adverse-Effect-Level (NOAEL) for sac fry mortality was 34 pg/g in the egg, while the Lowest-Observable-Adverse-Effect-Level (LOAEL) was 55 pg/g. An LD50 of 65 pg/g was calculated based on sac fry mortality. Sac fry that died were reported to develop subcutaneous yolk sac edema and hemorrhages that morphologically resemble blue sac disease.

Daphnia magna of three different age groups (less than or equal 1 day, 7 days, 21 days) exposed to TCDD concentrations ranging from 200 to 1,030,000 ppq were not adversely affected following 48-hour exposures and a 1-week observation period (Table 3-1) (Adams et al., 1986).

3.2 Effects of Chronic Exposure to TCDD in Water

Yockim et al. (1978) exposed a number of aquatic organisms to TCDD in a recirculating static model ecosystem in which soil was treated with TCDD and flooded with water (Table 3-2). *Daphnia*, snails, and algae were placed in one chamber and mosquito fish in another chamber one day after flooding the soils. Additional mosquito fish were added on day 15 following the death of the first group. All remaining organisms were harvested after 32 days. Channel catfish fingerlings were added on day 32. Water concentrations of TCDD in the model ecosystem tanks ranged from 2,400 to 4,200 ppq TCDD with an average of approximately 3,000 ppq. The authors reported that nasal hemorrhaging and listless swimming accompanied death in exposed mosquito fish; all mosquito fish died within 15 days of exposure. All exposed fingerling channel catfish died after 15 to 20 days of exposure compared to no deaths in the control fish. Erratic swimming, fin necrosis, and anal and lower jaw hemorrhaging were reported to accompany death in the catfish. Algae, *Daphnia*, and snails exposed for 32 days were reported to have no apparent adverse effects, as measured by feeding, growth, and reproductive activity (Yockim et al., 1978).

Juvenile fathead minnows exposed to 1,700 to 63,000 ppq TCDD for 28 days in a static renewal system exhibited increased mortality at all concentrations (Table 3-2) (Adams et al., 1986). The authors reported a 28-day LC50 of 1,700 ppq. The authors noted that the TCDD whole-body residues observed in dead fish ranged from 16.7 μg/kg to 2,042 μg/kg.

Exposure of mosquito larvae to TCDD at an initial water concentration of 200,000 ppq for 17 days produced no effects on pupation (Table 3-2) (Miller et al., 1973). A 36-day exposure of snails to water initially containing 200,000 ppq TCDD resulted in a reduced snail hatch (Miller et al., 1973). No significant differences were observed in the survival of adult or juvenile snails in this study. Miller et al. (1973) exposed adult Oligochaete worms for 55 days at an initial concentration of

200,000 ppq TCDD. The exposure resulted in a significant decrease in number of worms at the end of the exposure period.

In a study of rainbow trout fry exposed to TCDD for 28 days using an intermittent-flow proportional diluter, Mehrle et al. (1988) found that adverse effects were observed at all dose levels (Table 3-2) Significant mortality was observed at concentrations of 176, 382, and 789 ppq TCDD within the 28-day exposure period. Mortality was also significantly increased at lower concentrations of 38 and 79 ppq TCDD during the 28-day depuration phase. The NOEC for this effect was determined to be less than the lowest exposure concentration of 38 ppq TCDD. Mehrle et al. (1988) determined that the control solution contained 1.1 ppq TCDD (as detected by radiometric analysis). Based on the 5% mortality observed in the control group during the exposure phase and much of the depuration phase, the authors suggested that the NOEC for mortality was between 1.1 and 38 ppq TCDD. The authors calculated a 56-day LC50 of 46 ppq based on the combined mortality data for the exposure and depuration phases. Growth was significantly decreased at all TCDD concentrations after 28 days of exposure, resulting in a NOEC less than 38 ppq TCDD. Mehrle et al. (1988) reported behavioral changes in all treatment groups by the end of the 28-day exposure compared to normal behavior of the control fish. The whole-body residue of TCDD in fish exposed to 38 pg/L for 28 days was approximately 980 pg/g.

NCASI (1991) investigated the toxicity of TCDD to rainbow trout using an experimental stream in which exposures from the water column, sediments, and food organisms were considered. The results of this study indicate that the NOECs for cold-water species (including rainbow trout) were on the order of 3.5 ppq TCDD. For warm-water species, NOECs were estimated to be 1.6 ppq TCDD based on long-term survival of juvenile bass (NCASI, 1991). More recent work by NCASI, based on actual effluent levels, resulted in a NOEC of 5.8 ppq for long-term growth and survival of adult largemouth bass and channel catfish (NCASI, 1991). The actual NOECs are probably larger than these levels as NCASI has indicated that these were the highest concentrations tested. The specific methodologies of these studies are not available as NCASI is in the process of preparing their report.

Cook et al. (1991) reported in a manuscript (preprint) that carp and fathead minnows exposed to TCDD for 71 days and observed for an additional 61 days exhibited toxicity (Table 3-2). A dimethylformamide solution of TCDD was continuously fed into the aquaria during the exposure period. During the exposure period, the nominal TCDD water concentration of 200 pg/L in the aquaria decreased to 62 pg/L for exposed carp and 49 or 67 pg/L for exposed fathead minnows. One of the three treatment groups of carp was previously exposed to 1,2,3,4-TCDD, 1,3,6,8-TCDD, and 1,3,7,9-TCDD. The authors reported that both carp and fathead minnows exhibited toxic effects following TCDD exposure. Carp were reported to be more severely affected than fathead minnows even though they showed lower whole-body TCDD concentrations. However the specific incidences of effects in the treatment groups and the control groups were not provided in the manuscript. In addition to mortality, carp reportedly showed signs of overt toxicity including fin darkening, fin erosion, caudal fin deformation, hemorrhages in lateral body wall, lateral line lesions, cranial deformation, edema, difficulty swimming, body wall ulcers, and exopthalmia. Extensive pathology was reported in histological analyses of liver, spleen, gill, fins, and gastrointestinal tract, however, the specific findings were not reported in this manuscript. Carp were reported to have a whole-body concentration of approximately 2,200 pg/g at the end of the exposure period. The nature of the toxic effects observed in fathead minnows in this study was not provided in the manuscript.

3.3 Other Toxicity Studies

Juvenile rainbow trout were exposed to TCDD in their diets at concentrations of 2.3, 2,300, and 2,300,000 pg/g (ppt) of diet for 6 days per week for a total of 105 days resulting in an average intake of 3.2×10^{-8}, 3.6×10^{-5}, and 2.1×10^{-2} µg/g fish, respectively (Table 3-3) (Hawkes and Norris, 1977). No effects on mortality, food consumption, growth, or fin erosion were observed in trout at 2.3 or 2,300 pg/g diet. The highest dose level of 2,300,000 pg/g TCDD in the diet was reported to cause increased mortality, reduced feeding activity and growth, and increased fin erosion and liver pathology. The authors noted that the "no-effect" level for survival, growth, feeding activity, and fin erosion in rainbow trout treated with TCDD orally is between the levels of 2,300 and 2,300,000 pg/g (ppt).

In two separate studies Kleeman and coworkers (1986b, 1988b) examined metabolism and disposition of TCDD in rainbow trout and yellow perch. In both experiments, fingerling fish were fed a diet containing 494 ppt [^{3}H]TCDD for 13 weeks followed by 13 weeks of the same diet without TCDD. Neither rainbow trout or yellow perch showed any evidence of overt toxicity as measured by fin necrosis, reduced growth, cutaneous hemorrhage or an increase in lethality.

Kleeman et al. (1988) determined LD50s at 80 days post-treatment for a number of fish species: rainbow trout - 10 µg/kg, yellow perch - 3 µg/kg, carp - 3 µg/kg, bluegill - 16 µg/kg, largemouth bass - 11 µg/kg, and bullhead - 5 µg/kg (Table 3-3). At the highest dose of 125 µg/kg TCDD, all species showed a latency period of 1 to 4 weeks prior to death. Latency periods were longer at lower lethal doses. All fish species exhibited fin necrosis. Decreases in body weight gain were found to be dependent on the species and the dose. Cutaneous hemorrhage was found only in perch, carp, and bluegill treated with TCDD, while cutaneous hyperpigmentation was observed only in carp and largemouth bass treated with TCDD.

Spitsbergen et al. (1988a) exposed juvenile rainbow trout to TCDD by intraperitoneal injection at doses ranging from 0.1 to 125 µg/kg. A significant depression in the rate of body weight gain was observed at doses of 5 µg/kg and greater. Mortality was increased to 20% at 5 µg/kg but was not affected at 1 µg/kg. The authors reported the 80-day LD50 of TCDD to be 10 µg/kg. Rainbow trout treated with 10 µg/kg exhibited gross and microscopic lesions while trout treated with 1 or 0.1 µg/kg did not exhibit lesions. Morphological lesions included those of the epithelial and lymphomyeloid tissues. Fish treated with 10 µg/kg showed marked leukopenia and thrombocytopenia; fish treated with 1 µg/kg showed a moderate depression of these cell numbers. This finding led the authors to conclude that hematologic parameters may be one of the most sensitive indicators of exposure to TCDD in rainbow trout.

Yellow perch were exposed to TCDD at doses of 1 to 125 µg/kg intraperitoneally (Table 3-3) (Spitsbergen et al., 1988b). A dose-related increase in lethality was observed. At 5 µg/kg, mortality was approximately 80% at 80 days after injection, while fish that received 1 µg/kg did not exhibit mortality. The authors calculated the 80-day LD50 of TCDD to be 3 µg/kg. Significant loss of body weight was observed in perch treated with 5 µg/kg, but was not observed in perch treated with 1 µg/kg. Perch administered 5 µg/kg TCDD or greater exhibited fin necrosis, petechial cutaneous hemorrhage, and ascites. Lymphomyeloid and epithelial tissues were identified as the primary targets for TCDD-induced lesions in yellow perch. The lowest dose which was associated with histopathologic lesions (hepatocyte lipidosis) was 1 µg/kg.

Beatty et al. (1976) exposed tadpoles to 25 to 1,000 µg/kg TCDD intraperitoneally (Table 3-3). No effects on mortality, metamorphosis, or histology were observed at any dose level. Adult bullfrogs treated with TCDD were reported to show no effects on mortality and no significant lesions. Somewhat lessened food intake was observed in frogs receiving 500 µg/kg during the initial part of the study, but food consumption in this treatment group was not different from that of controls by the end of the experiment.

Young coho salmon were exposed to TCDD water concentrations of 0.054 to 54.0 ng/g wet weight fish for 24, 48, or 96 hours (Miller et al., 1979). Food consumption, weight gain and survival were measured during a 114-day post exposure period. Coho salmon exposed to 54.0 ng/g wet weight fish for 96 hours showed a significant difference in feeding 7 days following exposure. Those fish exposed to 54.0 ng/g wet weight fish for 48 hours showed a significant response after 15 days and similarly, the group exposed for 24 hours at 54.0 ng/g wet weight fish showed a significant response 20 days after exposure.

Growth and survival were not significantly influenced by exposure duration. Weight gain decreased with increasing TCDD concentration. Coho salmon exposed to 5.4 ng/g wet weight fish showed significant differences 56 days following exposure. Survival was measured at 60 days and 144 days following exposure. Mortality reached 100% for the high dose group (54.0 ng/wet weight fish) after 60 days and was as high as 85% for the 5.4 ng/wet weight fish dose group. No significant mortality was evident for doses at or below 0.54 ng/g wet weight fish at 60 or 114 days. The threshold response level for growth and survival in young coho salmon for exposure periods up to 96 hours is between 0.54 and 5.4 ng/g wet weight fish. A conversion to a water level was not possible based on the information provided.

Miller et al. (1979) also exposed guppies to concentrations ranging from 0.08 to 80 ng/g wet weight fish for 24 hours. Incidence of fish necrosis was measured for 69 days following exposure. A significant incidence of fin necrosis was observed in fish exposed to 0.8 ng/g wet weight fish or higher 42 days following exposure. Similar to Miller and coworkers' (1979) coho salmon study, TCDD water concentrations were not reported.

3.4 Conclusion

Based on the acute toxicity studies described above, the Lowest-Observed-Effect-Concentrations (LOECs) for short-term exposures to different life stages of fish have been reported to range from 100 to 107,000 ppq (Miller et al., 1973, 1979; Norris and Miller 1974; Helder, 1980, 1981; Branson et al., 1983, 1985; Adams et al., 1986; Cooper et al., 1986; Wisk and Cooper, 1990). The No-Observed-Effect-Concentrations (NOECs) for short-term exposures of fish have been reported to range from 10 to 1,050 ppq TCDD (Miller et al., 1973, 1979; Adams et al., 1986).

For long-term exposures to fish, LOECs have ranged from 38 to approximately 3,000 ppq while NOECs have ranged from 1.1 to approximately 3,000 ppq (Helder, 1980, 1981; Yockim et al., 1978; Mehrle et al., 1988; Adams et al., 1986). The experimental findings of Mehrle et al. (1988) indicate no adverse effects in any of the control rainbow trout which were exposed to a measured TCDD level of 1.1 ppq. The authors concluded that the NOEC was between 1.1 and 38 ppq. A NOEC in this range is supported by recent experimental stream studies conducted by NCASI (1991), which indicate a NOEC of 3.5 ppq for cold-water species and a NOEC of 1.6 ppq for warm-water species. More recent data reported by NCASI (1991) provide a NOEC of 5.8 ppq for warm-water species.

Examination of several of the toxicity studies conducted on TCDD provides information regarding the whole-body concentrations in fish at which toxicity is observed. Carp containing approximately 2,200 pg/g (ppt) of TCDD by the end of a 71-day exposure exhibited increased mortality, signs of overt toxicity, and pathological changes (Cook et al., 1991). Carp chronically exposed to TCDD and containing a whole-body TCDD concentration in excess of 1,000 pg/g (ppt) showed ascites, subcutaneous hemorrhage, and fin necrosis (Cook et al., 1986). Adverse effects on growth, survival, and behavior were observed in rainbow trout swim-up fry that had accumulated 980 pg/g (ppt) at the end of a 28-day exposure (Mehrle et al., 1988). The most sensitive indicators of toxicity in juvenile rainbow trout were leukopenia and thrombocytopenia that occurred following a single dose of 1 μg/kg (1,000 pg/g) (Spitsbergen et al., 1988a).

The available data suggest fish are more sensitive to TCDD than other aquatic biota. Studies conducted by Helder (1980, 1981) show fish eggs to be the most sensitive life stage with a reported acute NOEC of 100 ppq for rainbow trout and pike eggs. Cook et al. (1991) reported a LOAEL of 55 pg/g egg concentration for lake trout. The acute NOEC was *Daphnia* of 1,030,000 ppq TCDD (Adams et al., 1986). Long-term exposure to approximately 3,000 ppq TCDD resulted in no adverse effects in algae, snails, and *Daphnia* (Yockim et al., 1978).

The review of currently available data regarding toxicity suggests that ambient water concentrations of 3.5 to 5.8 ppq TCDD would likely be protective of aquatic organisms. This conclusion is based on the weight of evidence provided by the NCASI (1991) experimental stream studies which reported a NOEC of 3.5 ppq for cold-water species and 5.8 ppq for warm-water species based upon a nominal water concentration. AWQS compliance is determined by a calculated nominal water concentration (i.e. effluent concentration diluted by receiving water body) rather than on an actual measured ambient water concentrations. Laboratory experiments have demonstrated that measured water concentration are consistently lower than nominal concentrations. For example, in the study conducted by Mehrle et al. (1988) a nominal concentration of 115 ppq resulted in a measured concentration of only 38 ppq. Based on this approach, TCDD concentrations higher than 5.8 ppq would likely be protective of aquatic life.

4.0 BIOCONCENTRATION/BIOACCUMULATION OF TCDD IN FISH

In aquatic environments, the primary route of potential human exposure to TCDD is through the ingestion of fish tissue (EPA, 1984). Due to the importance of this pathway, an ambient water quality standard based upon fish ingestion will be more restrictive than those based upon other considerations. When EPA developed its ambient water quality criteria for TCDD (EPA, 1984), it used a bioconcentration factor (BCF) approach to predict how much dioxin a fish will accumulate from its surroundings. The predicted concentration of TCDD in fish, used in conjunction with an estimated rate of fish consumption, provided an estimate of potential human exposure to dioxin via this pathway. The BCF approach, however, addresses only the uptake of dissolved compounds across the membranous gill surfaces (EPA, 1989b). BCFs are calculated by dividing the concentration of a chemical in fish tissue by its dissolved concentration in water (EPA, 1989c). Recently, much scientific discussion has focused on the apparent inappropriateness of using the BCF approach in the ambient water quality equation (Keenan et al., 1990b; Rifkin and LaKind, 1991; LaKind and Rifkin, 1990). Criticism of the BCF is related to the observation that hydrophobic substances like TCDD have extremely low dissolved concentrations in water because of their very strong tendency to sorb to organic matter.

In order to accurately predict how much dioxin a fish will accumulate from its surroundings, it is essential that an appropriate "accumulation factor" be used in the equation for a water quality standard (Rifkin and LaKind, 1991). Understanding what constitutes a suitable factor is fundamental to deriving scientifically-based water quality standards. The ramifications of choosing incorrect factors are significant and will be discussed in the following sections of this chapter.

4.1 Measuring Dioxin Accumulation in Fish

Historically, scientists have used several approaches to predict the uptake and accumulation of chemicals in fish. Two major approaches have been used to estimate the tendency of an animal to accumulate environmental contaminants: bioconcentration and bioaccumulation. Methods for estimating bioconcentration factors (BCFs) and bioaccumulation factors (BAFs) include the use of direct measurement *in vivo,* or the prediction of chemical behavior in a biological system based on physicochemical constants.

Until recently, the development of a BCF has been the most common approach used by scientists to predict the concentrations of environmental contaminants in fish tissues. As discussed earlier, the BCF model addresses only the uptake of a compound by fish via the transfer of a dissolved compound across the membranous gill surfaces (EPA, 1989b). BCFs can be calculated by dividing the concentration of a chemical in the fish tissue by its dissolved concentration in water (EPA, 1989c). Studies conducted in the past few years, however, indicate that this model does not adequately characterize the behavior of lipophilic chemicals like dioxins, PCBs, and other organochlorine compounds. The hydrophobic nature of dioxin, combined with its great affinity for organic carbon, means that the amount of dioxin sorbed to organic matter far exceeds that dissolved in the aqueous environment (Rifkin and LaKind, 1991). A number of considerations, including the cross-sectional size of sorbed dioxin, the molecular weight, and solubility are important in limiting the ability of TCDD to penetrate the gills of aquatic organisms (McKim et al., 1985; Gobas et al., 1987; Rifkin and LaKind, 1991). Therefore, in the natural environment, where an insignificant fraction of dioxin is dissolved, bioconcentration is not the primary route of uptake of strongly hydrophobic chemicals and BCFs are not good predictors of fish tissue levels.

Scientific evidence in recent years indicates that the body burden of dioxin in fish comes primarily from ingestion of food and sediment (Kenaga and Goring, 1980; Spacie and Hamelik, 1982; Rand and Petrocelli, 1985; Gobas et al., 1987; Kuehl et al., 1987b; Cook, 1990). For example, results reported by Cook et al. (1990) demonstrate that sediments and various food sources represent the most significant sources of dioxin found in lake trout from Lake Ontario. This is not surprising given that the majority of dioxin introduced into an aquatic system binds to sediment and is not usually detectable in the water column (Lodge and Cook, 1989). In the EPA's (1984) water quality criteria formula, however, the ingestion route of uptake is not considered. A factor other than the BCF should be incorporated into the equation for deriving a scientifically-based water quality standard. This factor should, ideally, serve two functions:

(1) realistically predict or estimate the accumulation of sorbed dioxin by aquatic organisms; and,

(2) practically serve as an accumulation multiplier which can be implemented in a regulatory context for the purpose of establishing effluent permit limits.

One useful approach for developing an appropriate "accumulation factor" for dioxin and other hydrophobic compounds is the Bioavailability Index (BI). Coined by Kuehl et al. (1987b) and further applied by Goeden and Smith (1989), the BI is defined as the ratio of the concentration of the contaminant in the lipid portion of the fish to the concentration in the organic carbon portion of the sediment (Kuehl et al., 1987b; Goeden and Smith, 1989). The use of the BI in the water quality criteria equation would appear to be suitable for hydrophobic chemicals, like dioxin, where the uptake of the dissolved fraction of the chemical is insignificant. However, the implementation of the BI approach for regulatory purposes will require the development and use of a model to calculate the fate of solids on a site-specific basis (Rifkin and LaKind, 1991). This requirement may prove to be impractical at the present time and, thereby, encourage the development of alternative "accumulation factors" that satisfy both prerequisites mentioned above.

Although field research is still in progress, the bioaccumulation factor (BAF) approach and a variant of the BAF, which we have defined as the Regulatory Bioaccumulation Multiplier (RBM) (Sherman and Keenan, 1991), is the best available method for predicting dioxin uptake by fish while allowing regulatory agencies to directly calculate point source limits. It incorporates oral uptake from sediment, from food-chain sources, and from particulate-bound dioxin suspended in the water column. The bioaccumulation potential of dioxin can be adequately characterized by a BAF because uptake via ingestion and gill transfer, elimination, and changes resulting from fish growth can be incorporated into the model (Gobas et al., 1987, 1988, 1989; Spacie and Hamelik, 1982; Sijm and Opperhuizen, 1988).

4.2 Factors Affecting Accumulation in Fish

There are a number of interdependent factors which influence the potential for various chemicals to accumulate in the tissues of fish. Among these are the physicochemical characteristics of the chemical of concern, species differences, health status, age, sex, size, tissue lipid content, and rate of food intake (Spacie and Hamelik, 1982; Spigarelli et al., 1982; Rand and Petrocelli, 1985; Gobas et al., 1987). One of the most critical factors in evaluating the bioaccumulation potential of dioxin in fish is the lipid content of the species of concern. Consequently, there are several adjustments which must be considered before using laboratory-derived data in environmental modeling. The application of an intraspecies correction factor may be necessary if age, sex, and health data indicate differences in lipid content within the same species of laboratory-raised and naturally-occurring fish. An interspecies correction factor may be needed when extrapolating from one species to another. A correction factor should be used to adjust for the low lipid content of the fillet and the unequal partitioning of TCDD between edible and non-edible tissues.

In general, chemical accumulation in fish tissues and other aquatic organisms is a net balance between the rate of uptake and the rate of elimination/depuration. The rate of chemical uptake is primarily a function of the exposure concentration and the bioavailability of the compound in the environment. The elimination/depuration rate is primarily a time-dependent biological function. The pathways whereby fish or other aquatic organisms accumulate dioxin can be described in the following box model:

sources into the aquatic system —> partitioning within the aquatic system —>

uptake by an aquatic organism —> accumulation in the organism —> elimination by the organism

Fish can assimilate dioxin from three compartments of the aquatic system: through the water column, through incidental ingestion of sediments, and through ingestion of food material containing dioxin (Cook et al., 1990). The importance of each contributing component is, in part, determined by the physical and chemical properties of TCDD.

Once absorbed by the fish, dioxin will partition to various organs or be eliminated through the feces (Kleeman et al., 1986a,b). Due to its lipophilic nature, TCDD readily partitions to those organs with the highest fat or lipid content. The majority of TCDD will concentrate in the visceral fat and cranial fat (Kuehl et al., 1987; Kleeman et al., 1986a, 1986b). Skeletal muscle (fillet tissue) contains a low percentage of lipid and, therefore, accumulates the least amount of TCDD (Kuehl et al., 1987; Kleeman et al., 1986a, 1986b). Since the lipid content of a fish can vary with climate and seasonal water temperatures, cold-water fish generally will have a higher percentage of lipid in their tissues than warm-water fish. Seasonal temperature changes can lead to increased metabolism and reduction of lipid stores. When the fat and its associated dioxin are mobilized, dioxin will re-enter the blood stream and eventually may be eliminated through the excretory system.

According to Cook et al. (1990) uptake and depuration of TCDD can be described by first order kinetics equation:

$$\frac{dC_f}{dt} = k_1C_w - k_2C_f \qquad (1)$$

Where the change in the concentration of the chemical in fish over time is a function of the first order rate constant for bioaccumulation (k_1), first order rate constant for depuration (k_2), chemical exposure concentration (C_w), and the fish tissue concentration (C_f).

Equation (1) can be redefined as:

$$C_f = k_1/k_2 \times C_w \times (1 - e^{-k_2 t})$$

The primary parameter that influences dioxin accumulation (C_f) is the initial exposure concentration (C_w). It is evident from this equation that a decrease in the amount of dioxin which is discharged into the aquatic system will decrease the amount of dioxin available to the fish (C_w). As a result, the balance between uptake and depuration will be shifted and fish tissue dioxin levels would be expected to decrease with time.

The period of time that is necessary to detect a measurable reduction in the concentration of dioxin in fish tissues as a result of a reduction in effluent discharges from a suspected source to a water body is dependent upon several factors. Two factors, the biological half-life of dioxin in fish and the amount of dioxin stored in the various compartments of the aquatic system, are most significant. For example, half-life estimates reported by Kleeman et al. (1986a) ranged from 8 weeks in heart tissue to 15 weeks in skeletal muscle in rainbow trout. When whole-body elimination is considered, the half-life of TCDD has been shown to vary from 8 weeks in rainbow trout (Niimi and Oliver, 1986) to as much as 18 weeks in yellow perch (Kleeman et al. 1986b).

Empirical data on the behavior of chemicals in the environment indicate that a measurable reduction in the levels of dioxin in sediments may take several months after the levels of dioxin in industrial discharges to surface waters have been reduced. Over time, the sediment reservoir will be depleted through physicochemical exchange to the water column or through stochastic events such as spring or storm scouring of the sediments. Natural deposition of new cleaner sediments over older deposits will also reduce the bioavailability of TCDD. Bottom dwelling fish are likely to show the slowest rate of TCDD reduction in their tissues due to their relatively high exposure to sediments.

4.3 Establishing A Regulatory Bioaccumulation Multiplier (RBM)

Bioaccumulation multipliers are derived from a ratio of the concentration of TCDD in the fish to the environmental concentration of TCDD. Oftentimes, when regulatory agencies have used BCFs or BAFs, there is confusion regarding exactly what fish concentration and what environmental concentrations have actually been measured. For example, with respect to the fish concentration (i.e. the numerator in the BAF ratio) one study reported the concentration in whole juvenile fish weighing less than half a gram each (there was no "edible" portion and lipid content was not reported) (Adams et al., 1986). In another study the fish concentration referred to whole fish with 19% lipid (Cook et al., 1986, 1991). Other studies report the dioxin content of edible fish containing 1% lipid. To compare BAF values from different studies, a consistent basis for expressing fish concentrations must be defined.

With respect to the environmental concentration (i.e. the denominator in the BAF ratio) a similar problem is apparent. Many studies use a measured concentration in water. In some cases the measurement is on a "whole" water sample; others are filtered or centrifuged. Sometimes a theoretical calculated "dissolved" concentration is used. Still others have used values based upon the amount of suspended particulate and the concentration of dioxin adsorbed on the particulate. A nominal concentration determined by the total amount of TCDD added to the system is also used. Therefore, to compare BAF values, a consistent basis for expressing the environmental or exposure concentration must also be defined.

The amount of dioxin in the effluent receiving water can be calculated according to the following equation:

$$C_w = C_e \times V_e/V_r \quad (1)$$

where:

C_w = Concentration of TCDD in the ambient water
C_e = Concentration of dioxin in the effluent
Ve = Volume of effluent discharged
V_r= Volume of river flow

Because the maximum acceptable level of dioxin in the receiving water is limited by the water quality criteria (WQS), the following equation is derived:

$$WQC = C_e \times V_e/V_r \quad (2)$$

where the WQC is a function of the total quantity of dioxin in an effluent (dissolved and absorbed) per unit volume of effluent (C_E), the effluent flow (V_E), and river flow (V_R).

A site-specific BAF can be derived using the following ratio:

$$BAF = C_f/CE \quad (3)$$

where the C_f represents the concentration in fish tissue and CE is the environmental concentration of TCDD.

Solving for the environmental concentration:

$$CE = C_f/BAF \quad (4)$$

The environmental concentration is limited by the WQC. Thus,

$$WQC = C_f/BAF \quad (5)$$

This methodology has typically been used to define an acceptable human health based environmental concentration or a water quality criteria.

By combining equations (2) and (5),

$$C_f/BAF = (C_e \times V_e)/V_r \tag{6}$$

Solving in terms of BAF:

$$BAF = \frac{C_f}{C_e \times V_e/V_r} \tag{7}$$

The BAF, when used for regulatory purposes, is defined as the dioxin concentration in the portion of fish consumed by humans (i.e. fish fillet) divided by the total quantity of dioxin (dissolved and adsorbed) added to the water body per unit volume of water containing the fish. We have renamed this regulatory BAF with a new term, the Regulatory Bioaccumulation Multiplier, or RBM (Sherman and Keenan, 1991).

The total quantity of dioxin added (dissolved and adsorbed) per unit volume of water is defined as the "nominal" concentration (C_N) then:

$$\text{Regulatory Bioaccumulation Multiplier} = RBM = \frac{C_f}{(C_E \times V_E / V_R)} = \frac{C_f}{C_N}$$

The derivation of an RBM is not as simplistic as dividing the fish concentration by the nominal river concentration. To properly use this equation to derive a site-specific RBM, the following three criteria must be met.

1. The system must be in equilibrium or quasi-equilibrium.

TCDD concentration in fish are proportional to the environmental concentration (see discussion in Section 4.2), provided a sufficient length of time has elapsed since the last alteration in the environmental concentration, i.e. equilibrium is reached. A linear regression analysis is inappropriate when the aquatic system being investigated is not in equilibrium. This can occur after individual discharges of TCDD have been reduced and fish levels have not reached an equilibrium state with the new environmental concentration.

2. A demonstrated correlation must exist between fish concentration and nominal river concentration.

A correlation is required in order for the slope of the regression line to have any meaning. Often a correlation does not exist when nominal river concentrations are low (i.e. less than 0.5 ppg) or anadromous fish species are sampled.

3. The regression equation must have a positive intercept.

A positive intercept suggests that the background concentration of dioxin is not attributable to pulp and paper mill discharges. This is consistent with the detection of dioxin in fish from rivers with no industrial discharges (Mower, 1990).

If all conditions are met, then the RBM will be equal to the slope of the regression line. This indicates the increase in fish concentration related to the increase in the nominal river concentration.

The use of an RBM based upon the fish fillet and the nominal water concentrations allows regulatory agencies to directly calculate point source limits. This also obviates the need to apportion dioxin into different parts of the ecosystem (e.g. food, suspended sediment and "dissolved" in water).

A wide range of BCFs and BAFs have been reported in the literature. A detailed discussion of these studies is included in Appendix A. These widely varying BCFs and BAFs reported for dioxin in the scientific literature actually fall within a rather narrow range if expressed and compared on a consistent basis as defined by the RBM. Employing these consistent definitions, the RBMs generally fall below 5,000. For example, RBMs can be calculated from the "pure water" studies of Cook et al., (1990; 1991), Mehrle et al., (1988), Adams et al., (1986) and Branson et al., (1985). The average RBM normalizing to a fillet lipid content of 2.5% is 3,600 with a range from 600 to 6,440.

Reanalyzing the BCFs of 66,000 reported for carp (Cook et al., 1991), 128,000 for fathead minnows (Cook et al, 1991) and 1,357 for lake trout (Cook et al., 1990), RBMs of 5,680, 4,880, and 600, respectively, can be derived. Similarly, using the reported BCFs of 39,000 and 9,270 for rainbow trout (Mehrle et al., 1988; Branson et al., 1985) and 7,900 for fathead minnows (Adams et al., 1986), RBMs of 6,400, 970 and 2,820, respectively, can be derived. An average of these estimated RBMs is 3,600.

All of these "pure water" laboratory studies were conducted under 'unnatural' conditions where no sediment was present and only low levels of suspended solids and organic carbon were available in the dilution water. Natural systems include sediment, suspended solids and increased amounts of organic carbon. These are likely to decrease the concentration of dissolved dioxin in the water and thus decrease the uptake of dioxin across gill surfaces while the presence of contaminated food, sediment and suspended particulates may increase the uptake of dioxin via ingestion. In the Cook et al. (1990) simulated field studies, these factors were considered. In two specific experiments, Cook and coworkers exposed lake trout to contaminated food, water and sediment. In the first experiment, TCDD levels approximated those found in Lake Ontario and in the second experiment TCDD concentrations were approximately ten times greater than in Lake Ontario. Results of these studies indicated a BAF of between 7,700 and 11,000, respectively. However, when expressed as a Regulatory Bioaccumulation Multiplier (RBM) with a 2.5% lipid content and nominal water concentrations based on the total added dioxin, the BAFs may be as low as 450 and 310. When only suspended and dissolved dioxin are included in the nominal concentration, the RBMs become 4,580 and 3,210.

4.4 Conclusions

A wide variety of BCFs and BAFs for dioxin have been reported in the literature (Adams et al., 1986; Mehrle et al., 1988; Branson et al., 1985; Cook et al. 1990, 1991). Differences between reported BCFs and BAFs are not surprising as they are due, in part, to a number of environmental factors that affect the fate of dioxin in an aquatic ecosystem and within a fish. These factors include the amount of organic material in the water column and in the sediment, water flow rates, fish lipid content, as well as the age, size, sex, and rate of food intake by each species of concern (Spacie and Hamelik, 1982; Spigarelli et al., 1982; Rand and Petrocelli, 1985; Gobas et al., 1987). Differences in the experimental methodologies used in laboratory or field studies conducted over the past ten years to derive BCFs or BAFs also have added to the wide range of values reported in the literature. Before a definitive accumulation factor can be assigned for dioxin, it is essential that the terminology be defined and standardized for use in a regulatory context.

Although a wide range of accumulation factors have been reported, when these values are re-analyzed using a common methodology to permit comparisons, the reported BCFs and BAFs fall within a narrow range. The Regulatory Bioaccumulation Multiplier (RBM) uses consistent criteria to define exposure concentrations of TCDD, normalizes to a common fish lipid content (in this case, 2.5%) and measures TCDD fish concentrations in the edible portion or fillet tissue. Re-analyzing existing literature values, the calculated RBMs generally fall below the value of 5,000 and do not support a value of 50,000. Therefore, the value of 5,000 constitutes the most scientifically based multiplier for regulatory purposes. Coincidentally, the RBM methodology produces an accumulation factor of equal magnitude to that of the EPA's (1984) recommended ambient water quality criteria value of 5,000; albeit for different reasons and based upon a different rationale. EPA Region III in its approval of Maryland's and Virginia's water quality standards, has affirmed the selection of a value of 5,000 for regulatory purposes.

5.0 FISH CONSUMPTION

The primary route of human exposure to many pollutants occurs through the ingestion of fish obtained from waterbodies containing those compounds (Rifkin and LaKind, 1991). Because of this, the estimation of a representative rate of fish consumption from potentially impacted waterways is important to the derivation of a scientifically-based and health protective water quality standard. Most of the estimates of fish consumption rates that are found in the scientific literature are based either on national surveys or are specific to a particular region of the United States (Puffer et al., 1981; Humphrey, 1978; Javitz, 1980; Rupp et al., 1980). Many of these surveys have either not adequately characterized the types of fish consumed (EPA, 1989c), or no distinction has been made between the consumption of commercially-harvested and recreationally-harvested fish (Javitz, 1980; EPA, 1989c). These factors are important to define in a risk assessment approach to deriving a water quality standard as there may be interspecies differences in potential to bioaccumulate TCDD (Spacie and Hamelik, 1982; Spigarelli et al., 1982; Rand and Petrocelli, 1985; Gobas et al., 1987). In addition, regional variations in consumption of preferred species, availability of these species, access to productive fisheries, length of fishing season and cultural heritage can greatly influence fish ingestion habits.

The EPA has used the value of 6.5 g/day as an estimate of fish consumption in developing its Ambient Water Quality Criteria (AWQC) (EPA, 1984). This value is based on the estimated national per capita rate of fish consumption and includes all commercially-harvested and recreationally-caught freshwater and estuarine fish and shellfish (EPA, 1989a). Although the EPA's estimate may be appropriate for estimating an average consumption rate for the U.S. population as a whole, its ability to predict regional consumption or consumption by recreational anglers or other subpopulations is, at best, coincidental.

An analysis conducted by Rupp et al. (1980) revealed that in addition to regional variations in fish consumption, there are substantial variations in fish consumption patterns among individuals living in the Pacific region of the U.S. The authors reported that only 14.1 percent of the fish consumers surveyed in the Pacific region consumed freshwater fish, whereas 90 percent of those individuals consumed saltwater fish (Rupp et al., 1980). These results clearly suggest that most people do not eat freshwater fish.

When establishing a water quality standard for TCDD it is most accurate to use state- or region-specific data to account for regional and individual differences in fish consumption (EPA, 1989a). In doing this, it is necessary to identify and characterize fish consumption within subpopulations that may consume significantly more fish than the average for the region under consideration. In the Pacific Northwest, Native American tribal members have commercial fisheries and treaty rights to tribal and subsistence catch. Thus, it is possible that they, like the recreational anglers, may consume more fish than the general population. To address these possibilities, additional consumption estimates for these two populations were made. Although it has been claimed that Asian Americans might conceivably eat a greater amount of fish than the general population, a review of the available literature indicates that their consumption is not likely to exceed that of Native Americans or recreational anglers (Parsons et al., 1991; Landolt, 1985). Separate consumption estimates for this subpopulation were not made in the present study.

5.1 General Population

Specific estimates of the consumption of Columbia River fish by the general population of Oregon have not been made and published in the literature. Rupp et al. (1980), estimated that the per capita rate of total freshwater fish consumption in the Pacific region, which includes the state of Oregon, was 0.90 g/day. This estimate was an average over the total population and included individuals that consumed no fish. For adults only, the per capita consumption rate was 1.07 g/day.

According to NMFS (1989), fish consumption increased 16.9 percent between 1970 and 1980 (approximately 1.69 percent per year). Extrapolating this average annual rate of increase to the period between 1974 and 1991, it can be estimated that the rate of consumption increased 28.7 percent. Adjusting the Rupp et al. (1980) estimate to reflect this 28.7 percent increase results in an estimated per capita rate of 1.38 g/day.

The use of the Rupp et al. (1980) study to derive consumption estimates for the Columbia River is limited. The transient presence of anadromous species in the Columbia River at different times of the year confounds estimates of consumption as the anadromous species are not freshwater fish despite the fact that they are obtained from the river. Thus, the Rupp et al. (1980) estimate for freshwater fish consumption may underestimate consumption of Columbia River fish. At the same time, Rupp's consumption estimate for saltwater fish may overestimate consumption due to the inclusion of numerous marine species that would not be found in the river.

There are a number of commercial fisheries on the Columbia River. As a result, the general population may eat a variety of commercially obtained fish species that have been harvested from the river. Based on the reported landings of the commercial fisheries, Beak (1989) calculated per capita consumption rates for salmon, steelhead, and sturgeon from the Columbia River. Because a significant portion of the total commercial catch for each species are distributed to commercial markets outside the study area, the landings were adjusted to account for the percentage of fish retained within the Columbia River Basin (Beak, 1989). The catch retained for sale within the region was then adjusted to derive the total mass of edible fish available, assuming an estimate of 50 percent edible portion (Beak, 1989). This edible mass was then apportioned over the total population living within that area, estimated by Beak (1989) to be 3,390,750 individuals in 1988. This population estimate excluded anglers and their families as well as members of the Native American tribes because separate consumption rates were calculated for those populations (Beak, 1989).

Although Beak (1989) assumed for their calculations that 50 percent of the total fish mass is edible, EPA recommends a 30 percent multiplier to estimate the average edible portion of finfish (EPA, 1989a). Using Beak's estimate of the reported total landings retained within the Columbia River Basin (Table 5-1), and using a 30 percent estimate of the edible portion as recommended by EPA (1989a), a per capita consumption rate of 0.54 g/day can be derived for salmon, sturgeon, and steelhead (Table 5-2).

For species not included in the Beak (1989) study, additional estimates of consumption were made using combined, reported landings by commercial and Native American fisheries on the river as reported by the Oregon Department of Fish and Wildlife and the Washington Department of Fisheries (ODFW/WDF, 1990) (Table 5-1). According to ODFW/WDF (1990), a total of 3,460,400 lbs of smelt, sockeye salmon, chum and shad were landed in 1988 by Indian and non-

Table 5-1. Total Commercial Landings in Pounds

Species	Commercial Total Landings	Commercial Landings Retained	Native American Total Landings	Native American Percent Retained	Total Combined Landings	Total Combined Landings Retained
Chinook	7,248,000	2,174,400[a]	3,290,900	888,543[b]	10,538,900	3,062,943
Coho	2,644,500	793,350[a]	38,000	10,260[b]	2,682,500	803,610
Steelhead	---	---	764,800	688,320[c]	764,800	688,320
White Sturgeon	217,300	108,650[d]	136,600	61,470[e]	353,900	170,120
Green Sturgeon	114,300	57,150[d]	---	---	114,300	57,150
Shad	323,200	323,200[f]	59,000	53,100[c]	382,200	376,300
Smelt	2,867,000	2,867,000[f]	---	---	286,700	2,867
Sockeye	61,400	61,400[f]	119,600	107,640[c]	181,00	169,040
Chum	30,200	30,200[f]	---	---	30,200	30,200
TOTAL	13,505,900	6,415,350	4,408,900	1,809,333	17,914,800	8,224,683

Source: ODFW/WDF, 1990.

a. Assuming 30 percent of the fish sold are retained within the Columbia River Basin (Beak, 1989).

b. Assuming 90 percent of the Native American commercial catch is sold to processors and that 30 percent of the commercially processed fish is retained within the Columbia River Basin (Beak, 1989).

c. Assuming 90 percent of the Native American catch is sold to processors and 100 percent of the commercially processed fish is retained within the Columbia River Basin (Beak, 1989).

d. Assuming 50 percent of the fish sold are retained within the study area (Beak, 1989).

e. Assuming 90 percent of the Native American catch is sold to processors and 50 percent of the commercially processed fish is retained within the Columbia River Basin (Beak, 1989).

f. Assuming 100 percent of the fish sold are retained within the Columbia River Basin.

Table 5-2. Per Capita Consumption Rate

Species	Total Combined Landings Retained (lbs/year)	Edible Fish [a] (lbs/year)	Consumption [b] Rate (lbs/person-year)	Consumption Rate [c] (g/person-day)
Chinook	3,062,943	918,883	0.27	0.34
Coho	803,610	241,083	0.071	0.088
Steelhead	688,320	206,496	0.061	0.076
White Sturgeon	170,120	51,036	0.015	0.019
Green Sturgeon	57,150	17,145	0.005	0.0063
Shad	376,300	112,890	0.033	0.041
Smelt	2,867,000	860,100	0.25	0.32
Sockeye	169,040	50,712	0.015	0.018
Chum	30,200	9,060	0.0027	0.0033
TOTAL	8,224,683	2,467,405	0.72	**0.91**

a. Assuming 30 percent edible portion (EPA, 1989a).
b. Assuming a population within the Columbia River Basin of 3,390,750 (Beak, 1989).
c. Consumption Rate (lbs/person - year) x Conversion Factor [(453.69)/(365 days / yr)]

Indian commercial fisheries. Beak (1989) estimated that 90 percent of the Native American catch was sold to commercial processors, that 50 percent of the whole fish was edible, and that 100 percent of the commercially processed fish was retained in the Columbia River Basin. Based on these assumptions, ChemRisk estimated that an additional 0.37 g/day of freshwater fish are consumed per capita. By summing the consumption rates for commercial landings reported by Beak (1989) and by ODFW/WDF (1990), it can be estimated that in 1988, per capita fish consumption among the general population of the Columbia River Basin was approximately 0.91 g/day (Table 5-2). Because game fish are not available to the general population, they were not included in the estimated consumption rate for the general population.

5.2 Recreational Anglers

If dioxin is present in the tissue of freshwater fish species, then recreational anglers may represent an important receptor population if their rate of intake of freshwater fish is significantly elevated above the norm. Consequently, it is important that the consumption rate of recreationally-caught fish from potentially impacted waterbodies be evaluated when developing a water quality standard.

Rates of freshwater fish consumption by anglers along the Columbia River were estimated in two published studies conducted in the early 1970's. Honstead et al. (1971) conducted a diet recall survey of 10,900 individuals from households in which there was at least one angler who fished the Columbia River in the Tri-City area of Washington. The average size of a fish meal was estimated to be approximately 200 grams per meal and it was reported that individuals ate an average of 14 such meals per year. Thus, the annual average rate of consumption was 2.8 kilograms per year, or 7.7 g/day. The maximum consumption rate for adult anglers eating only freshwater sport fish from the Columbia River was estimated to be 33 kg/year or 90.4 g/day (Honstead et al., 1971).

In a creel survey of recreational anglers who fished in the same area of the Columbia River, Soldat (1970) observed that 15 percent of the anglers surveyed caught 90 percent of the fish. The distribution of species creeled and consumed was similar to that reported in the Honstead (1971) diet recall survey. From the data generated from the Soldat (1970) creel survey, a considerably lower average consumption rate of 1.8 g/day can be estimated. Because it was based on actual landings data rather than recall, it is likely that Soldat's (1970) estimate of 1.8 g/day is more accurate for anglers in the upper reaches of the Columbia River. Soldat (1970) inferred this point via a comparison of consumption estimates that he made. Soldat observed that "extrapolation from the number of fishermen observed on the river bank to a total number of fishing trips made per year yielded a value of 63,200 ($\pm$ 4,030). Direct questioning of the fishermen on the number of trips they thought they made per year, however, yielded a value nearly four times as high or 238,000".

Beak (1989) used available landings information to estimate the average rate of consumption of salmon, sturgeon and steelhead by the angling population. In that estimate, it was assumed that fifty percent of the whole fish was edible. Based on the total number of species-specific fishing tags sold in the study area and the mean family (household) sizes in the states of Oregon and Washington, species-specific average consumption rates per family member were estimated. Upon summing the species-specific consumption rates, a total average consumption rate of 10.7 g/day was estimated (Beak, 1989).

The Beak (1989) analysis was limited in that it assumed that anglers consumed only coho salmon, chinook salmon, steelhead, and white sturgeon. ChemRisk has subsequently conducted a further evaluation of the database used by Beak to derive a more representative estimate of total freshwater fish consumption by Columbia River anglers. In this analysis, a number of additional factors were considered including those pertaining to the diversity of species consumed, fishing success, and edible portion of fish. As a conservative approach, ChemRisk selected and used the 1988 landings dataset for the analysis as total landings for 1988 were higher than those reported for 1989.

In addition to the species reported by Beak (1989), ChemRisk included the reported landings of smelt in deriving a consumption estimate. ODFW/WDF (1990) presented commercial landing data for smelt and reported that the recreational harvest may equal the commercial harvest. To calculate an average smelt consumption rate, it was assumed that the recreational harvest of smelt in 1988 equalled the commercial harvest reported for that year by ODFW/WDF (1990); that 50 percent of salmon-fishing anglers also fish for smelt; and, that all anglers who fished for smelt were successful and consumed their catch. It is likely, however, that many smelt anglers use their catch as bait rather than consuming it.

To upwardly adjust Beak's consumption rates for the other species, it was assumed that only 50 percent of anglers were successful in catching salmon, steelhead, and sturgeon. This success rate is consistent with fishing success rates reported in other studies (Landolt et al., 1985; 1987; ChemRisk, 1991). Additionally, the edible portion multiplier of 50 percent used by Beak was adjusted to 30 percent as recommended by EPA (1989a). These modifications resulted in a lower bound estimate of 5.1 g/day as the mean fish consumption rate for anglers and their families who consume Columbia river salmon, steelhead, and smelt. An upper bound estimate of 19.9 g/day is appropriate for the fraction of anglers and their families who additionally consume sturgeon.

In estimating this mean fish consumption rate, it was assumed that all anglers were equally successful and consumed fish at the same rate. However, it is well documented in the literature that the number of anglers that eat small amounts of fish greatly exceeds the number of anglers that eat large amounts of fish (Soldat, 1970; Landolt et al., 1985,1987; West, 1989; Meunz and Peterson, 1990; ChemRisk, 1991). Soldat (1970) observed that 15 percent of the anglers surveyed caught 90 percent of the fish. In a survey of anglers in Michigan (West, 1989), 59.3 percent of respondents reported eating no fish meals, while only 1.6 percent reported eating more than four meals in a seven-day period. Similar observations were made in a recently completed survey of the fish consumption habits of recreational anglers in the State of Maine (ChemRisk, 1991). Results of the Maine survey indicated that when considering all anglers on all freshwater fisheries, 10 percent of the anglers ate 90 percent of the total freshwater fish consumed. For rivers and streams, the distribution of consumption was more exaggerated; 7 percent of the anglers ate 93 percent of the fish consumed (ChemRisk, 1991). An analysis by Technical Assessment Systems, Inc. (Muenz and Petersen, 1990) also indicated that the consumption of fish is positively skewed, i.e., consumption rates are not symmetrically distributed about an arithmetic mean value. Instead most individuals are clustered at the lower end of the consumption rate scale with only a few individuals having higher consumption rates. A review of the USDA (1983) diet survey indicates that the consumption of many common foods such as bread, pasta, beef, and potatoes, also follows a positively skewed pattern.

In a positively skewed distribution, the exact location of an arithmetic mean value can vary widely, but it is always greater than the median, or 50th percentile value. When information is limited, simulation techniques can be used to model the likely distribution of fish consumption rates across the population of recreational anglers and their families. Computer simulation can identify the location of the "average" value and can provide information about the likelihood of other consumption rates within that population. Using a simulation allows one to incorporate the full range of possible fish consumption rates while taking into considering the frequency with which those consumption rates are likely to occur within the population. Choice of the statistical distribution model must be based on the physical characteristics of the situation and the distribution of the available data.

To date, the Maine study of recreational anglers (ChemRisk, 1991) is the most complete dataset upon which to base a statistical distribution model. Thus, a distribution model based on the Maine data for river and stream anglers was chosen to predict a distribution of fish consumption rates for Columbia River anglers and their families.

A truncated lognormal distribution model best describes and represents the positively skewed Maine fish consumption rates. This distribution model is appropriate for a situation where there are both minimum and maximum bounds and where most observations are not symmetrically distributed about a central value but rather are nearer the minimum than the maximum (i.e., observations are positively skewed). Fish consumption rates are well-suited to this type of model because negative fish consumption rates are not possible (i.e., a minimum of zero is required) and because an upper bound based on total daily food intakes can reasonably be established. Using the truncated lognormal model requires that the arithmetic mean, standard deviation, minimum and maximum bounds be specified.

In addition to the distributional model, an appropriate sampling technique for the simulation must be chosen. The sampling technique defines the process by which values are drawn randomly from the specified distributions; it is the repetition of this random value selection that creates the simulation results. For the ChemRisk analysis, the Latin Hypercube sampling method was chosen (Palisade Corp., 1990). When a truncated lognormal distributional model is used, this Latin Hypercube method requires fewer iterations (i.e. the number of times a value is drawn from the distribution) than other sampling methods while adequately representing the less frequently observed values.

A simulation was conducted to compare the results predicted through application of the distributional model to the Maine data to the actual Maine data. Parameters selected for the 5000-iteration Latin Hypercube sampling of the truncated lognormal model were the mean of 3.653 g/day, the standard deviation of 11.515 g/day, the minimum of 0 g/day, and the maximum of 118.22 g/day observed in the Maine survey.

Table 5-3 compares the actual Maine data to the simulation results, and Figure 5-1 plots the percentiles from the Maine data and from the simulation. As can be seen from Figure 5-1, the simulation generally fit the actual data well. The general shapes of the Maine distribution and the simulation result were similar. There was a tendency to overestimate the upper percentiles of the distribution, but this was not considered a detriment to the use of the model.

Because the simulation was successful in predicting the actual fish consumption pattern observed in the Maine data, the truncated lognormal distributional model was then applied to predict a distribution of fish consumption rates for successful Columbia River anglers and their families. The upper bound average fish consumption rate of 19.9 g/day (based on landings below Bonneville Dam as estimated above) was chosen as the arithmetic mean for the model. A standard

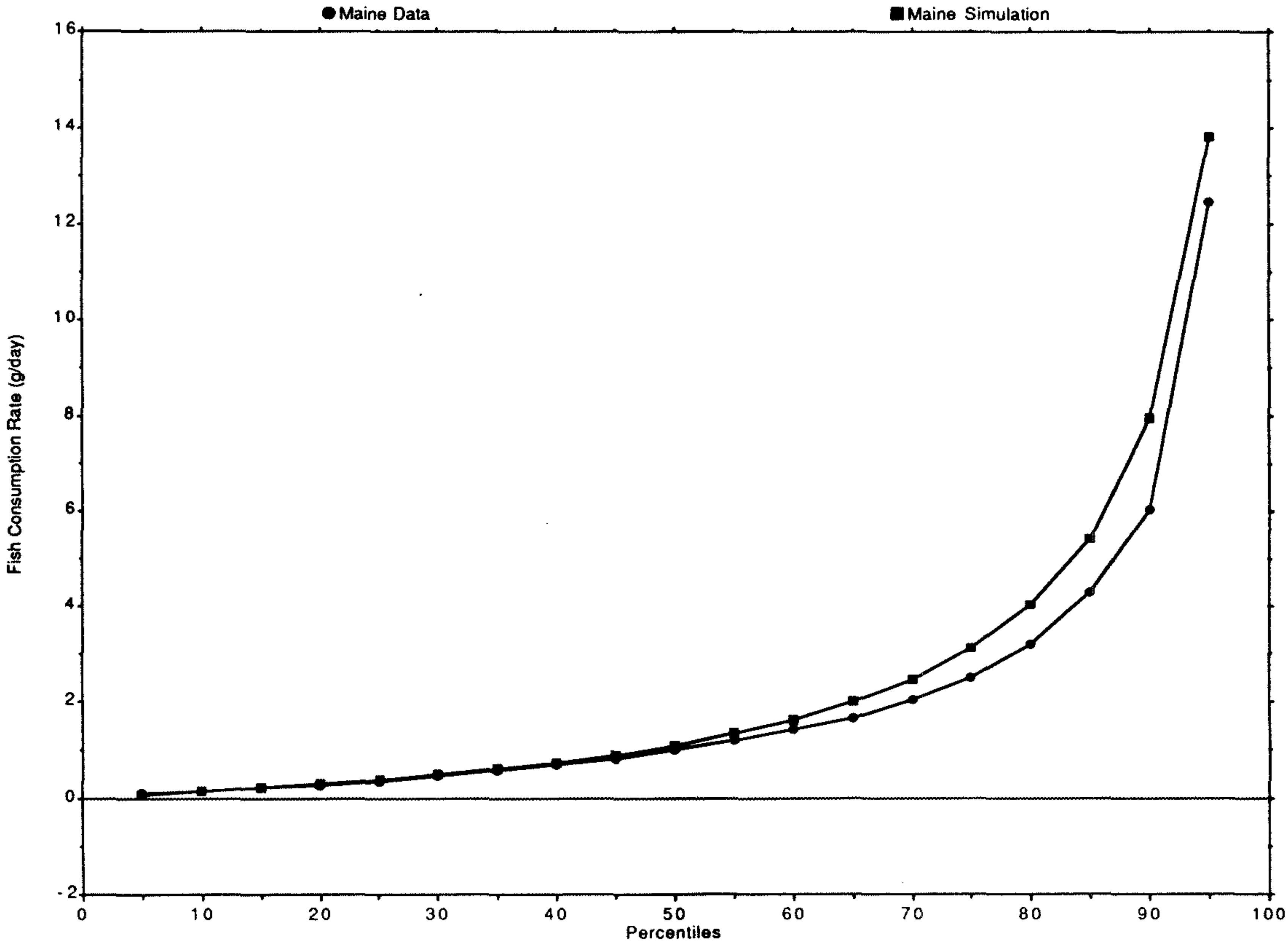
Table 5-3. Comparison of Actual Maine Fish Consumption Data to Simulation Results

	Actual Data[a]	Simulation Results[b]
Minimum	0.0010	0.0038
Median (50th Percentile)	0.99	1.1
75th Percentile	2.5	3.1
Arithmetic Mean	3.6	3.4
Percentile at Mean	81	77
90th Percentile	6.1	7.9
Maximum	118	114

a. All rates are in g/person-day. Based on riverine freshwater fish consumption rates for consuming anglers as presented in ChemRisk, 1991. Percentiles were calculated by rank without any assumption of statistical distribution.

b. All rates are in g/person-day. Results of a 5,000-iteration Latin Hypercube simulation of a truncated lognormal distribution with parameters based on actual Maine data: Arithmetic Mean = 3.653, Standard Deviation = 11.515, Minimum = 0.001, and Maximum = 118.22.

Figure 5-1. Comparison of Simulation of Maine Data with Actual Maine Data



deviation of 63 g/day for the Columbia River simulation was estimated using the standard deviation-to-mean ratio (coefficient of variation) calculated for the Maine study. The coefficient of variation is an important parameter in the simulation because it determines the general shape of the distribution. It was assumed that the distribution of fish consumption rates observed in the Maine study was representative of fish consumption rates for anglers in general. A minimum of 0 g/day and a plausible maximum of 180 g/day were chosen to bound the truncated lognormal distribution. The maximum rate of 180 g/day was based on the EPA's (1989a) selection of this rate as a maximum based on the full substitution of fish for the combined consumption estimates of red meat, poultry, fish, and shellfish in the diet.

The 5,000-iteration Latin Hypercube simulation of fish consumption by Columbia River anglers and their families predicted a median consumption rate of 5.8 g/day (Table 5-4). The mean predicted consumption rate of 15 g/day occurred at the 73rd percentile of the distribution. This mean is within the 5.1 to 19.9 g/day range estimated from the landings data. The 90th percentile of the distribution was 39 g/day. Figure 5-2 presents the distribution of fish consumption rates between 0 and 40 g/day. As expected, most consumption rates were clustered near the low end of the range; the simulation yielded a positively skewed distribution much like the Maine survey results (ChemRisk, 1991) and the earlier observations of other researchers (Soldat, 1970; Landolt et al., 1985; 1987; West, 1989; Meunz and Peterson, 1990).

A second 5,000-iteration Latin Hypercube simulation using a truncated lognormal distributional model was conducted to predict the distribution of consumption rates using the average consumption rate of 1.8 g/day estimated by Soldat (1970) for Columbia River anglers near Hanford. Soldat (1970) reported that spiney ray, bass, and whitefish, rather than salmonids or sturgeon, were the primary species harvested by anglers in this reach of the river. To duplicate the general shape of the Maine distribution, the coefficient of variation from the Maine data was applied to yield a standard deviation of 5.7 g/day. As for the previous simulation, the minimum was set as 0 g/day and the maximum was set at 180 g/day.

Table 5-5 shows the results for the simulation of fish consumption rates for Columbia River anglers based on Soldat (1970). The simulation predicted a median consumption rate of 0.54 g/day. The mean consumption rate was predicted to be 1.8 g/day and occurred at the 78th percentile of the distribution. The 90th percentile of the distribution was 4.0 g/day. Figure 5-3 presents the distribution of fish consumption rates between 0 and 5 g/day. As observed in the Maine data, most consumption rates were clustered near the low end of the range.

5.3 Native Americans

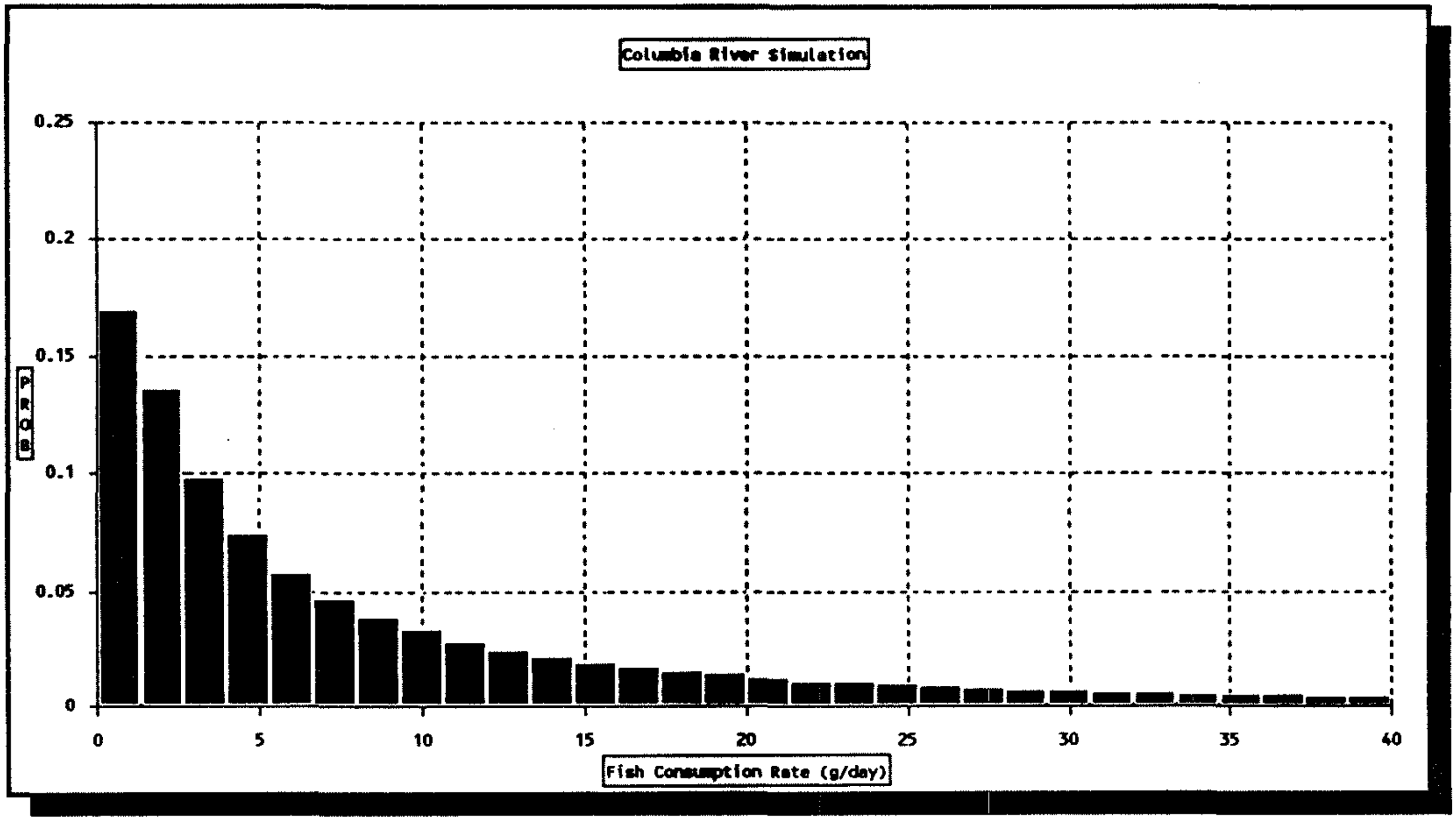
Although a number of researchers have examined the rates of fish consumption by Columbia River anglers (Soldat, 1970; Honstead et al., 1971) the focus of those studies has not been upon fish consumption rates of Native American tribal members. Beak (1989) calculated an average rate of consumption of Columbia River fish by tribal members based on annual commercial fish harvest data. Beak (1989) reported that the 1988 Native American fisheries catch was approximately 147,000 upriver chinook (average weight 22.4 lbs), 78,500 steelhead (average weight 9.7 lbs), 5,200 coho salmon (average weight 7.3 lbs), and 4,100 white sturgeon (average weight 33.3 lbs). Approximately 10 percent of this catch was retained by the tribes for tribal use and the remainder was exported (Beak, 1989). Based on the 10 percent retention rate, the total weight of fish retained by the tribes was estimated to be 422,874 pounds. Beak (1989) used an edible fraction

Table 5-4. Simulation Results for Columbia River Fish Consumption Rates

	Simulation Results[a]
Minimum	0.018
Median (50th Percentile)	5.8
Arithmetic Mean	15
Percentile at Mean	73
75th Percentile	16
90th Percentile	39
Maximum	180

a. All rates are in g/person-day. Results of a 5,000-iteration Latin Hypercube simulation of a truncated lognormal distribution with parameters based on an estimated mean, a plausible maximum, and preserving the mean/standard deviation ratio from the Maine fish consumption data: Arithmetic Mean = 19.9, Standard Deviation = 63, Minimum = 0, and Maximum = 180.

Figure 5-2. Simulation of Columbia River Fish Consumption by Recreational Anglers Below Bonneville Dam



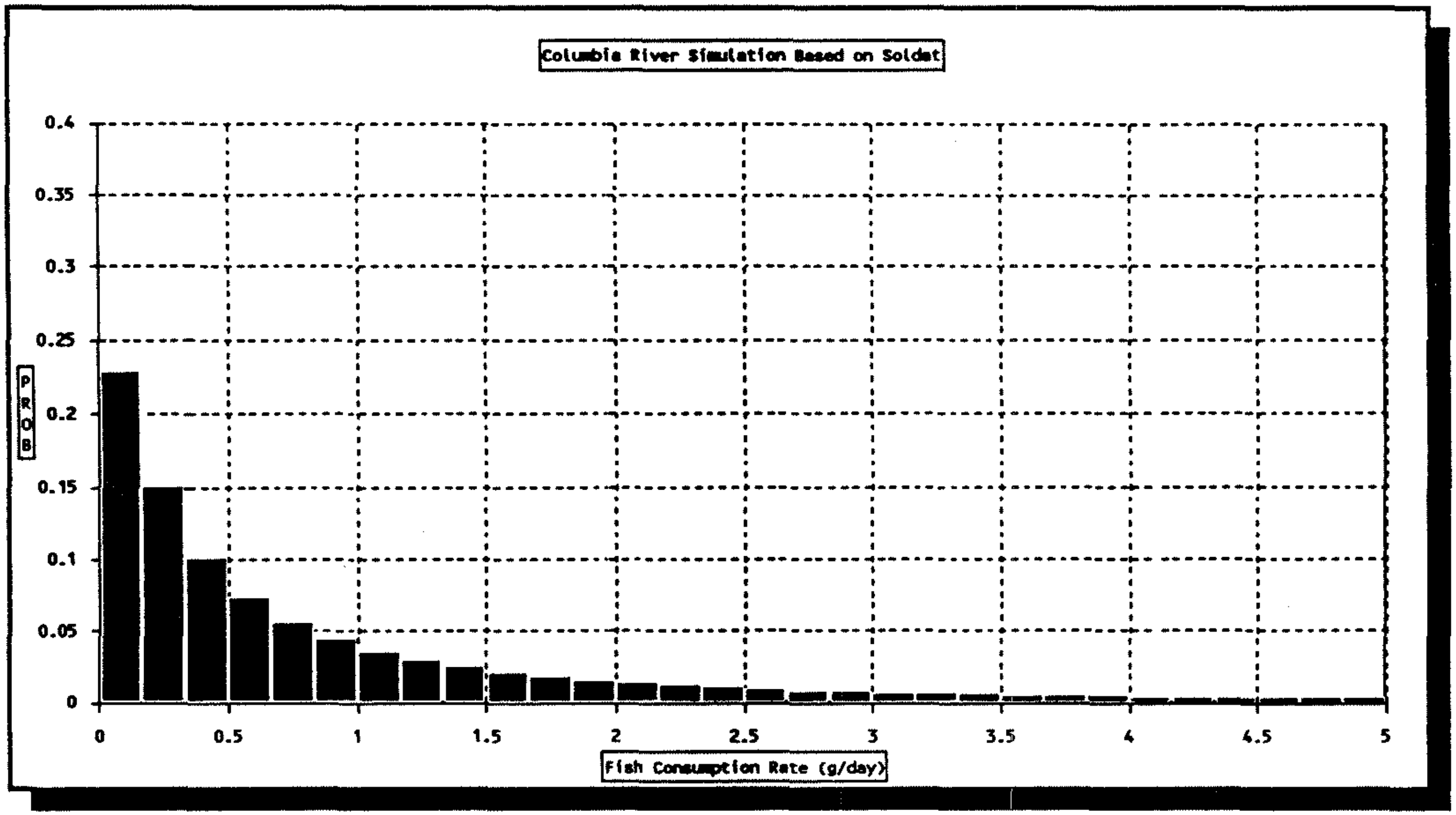
Simulated as Truncated Lognormal Distribution (Mean = 19.9, SD = 63, Min = 0, Max = 180)

Table 5-5. Simulation Results for Columbia River Fish Consumption Rates Based on Soldat (1970)

	Simulation Results [a]
Minimum	0.0069
Median (50th Percentile)	0.54
75th Percentile	1.5
Arithmetic Mean	1.8
Percentile at Mean	78
90th Percentile	4.0
Maximum	160

a. All rates are in g/person-day. Results of a 5,000-iteration Latin Hypercube simulation of a truncated lognormal distribution with parameters based on the mean from Soldat (1970), a plausible maximum, and preserving the mean/standard deviation ratio from the Maine fish consumption data: Arithmetic Mean = 1.8, Standard Deviation = 5.7, Minimum = 0, and Maximum = 180.

Figure 5-3. Simulation of Columbia River Fish Consumption by Recreational Anglers based on Soldat (1970)



Parameters used in the truncated lognormal distribution (Mean = 1.8, SD = 5.7, Min = 0, Max = 180) estimate of 50 percent, and assumed that all tribal members consumed fish at the same rate. In this manner, 211,437 pounds (95,943 kg) of fish were divided among the estimated 16,054 Columbia River Basin tribal members which resulted in a per capita consumption rate of 16.4 g/day (Beak 1989). Lack of data regarding individual consumption rates among tribal members prohibited a more detailed statistical analysis or modeling simulation of fish consumption by Native Americans in the vicinity of the Columbia River.

Beak's (1989) edible yield estimate of 50 percent is higher than the edible portion of 30 percent for finfish that is recommended by the EPA (1989a). The EPA's estimate is based on the assumption that 30 percent of the whole fish is muscle meat and that the muscle meat is the only portion of the fish that is generally consumed. However, communications with tribal representatives have indicated that some tribal members may consume other parts of the fish. Therefore, an edible portion of 50 percent, as used by Beak (1989), may be the most appropriate multiplier for use in estimating average consumption of fish by the Native American population.

5.4 Summary

Fish consumption is an important component of the dioxin ambient water quality standard equation since ingestion of fish is the most likely route of human exposure to TCDD found in aquatic environments (USEPA, 1984; Keenan et al., 1990; Parson et al., 1991; Rifkin and LaKind, 1991). For this reason, it is important to characterize the fish consumption habits of all potentially exposed populations. The Columbia River has been chosen as a representative waterbody in the State of Oregon.

The Columbia River is a unique fishery because it has large numbers of anadromous fish that enter the river to spawn. It is during these spawning runs that large numbers of salmonids are harvested both commercially and recreationally. In addition, the Columbia River tribes are entitled to subsistence and ceremonial catch. For these reasons, three populations have been characterized for the Columbia River: the general population, recreational anglers, and Native Americans.

To estimate consumption by the general population, total landings data for each species were adjusted to reflect the percentage of landings that were retained within the Columbia River Basin. These landings were then adjusted for edible portion and averaged over the population of the Columbia River Basin, resulting in a mean consumption estimate of 0.91 g/day.

For anglers, two separate estimates of consumption were derived. For the reaches of the Columbia River below the Bonneville Dam, a simulation was used to model the distribution of fish consumption rates among the population of recreational anglers in that area. This simulation was based on total landings of salmon, trout, sturgeon and smelt. A truncated lognormal distribution of consumption rates believed to be typical for freshwater recreational anglers, in general and verified in a statewide survey of recreational anglers in Maine (ChemRisk, 1991), was used to model the distribution for Columbia River anglers. Based on the results of that simulation, a median consumption rate of 5.8 g/day was derived.

On the upper reaches of the Columbia River, resident species are caught and consumed in greater numbers than the salmonids (Soldat, 1970; Honstead, 1971). It is likely that this is due to the decreased availability of the anadromous species in those reaches. Using the average consumption rate reported by Soldat (1970), a simulation using the truncated lognormal distribution pattern of consumption rates was conducted. The results of that simulation indicated a median rate of consumption of resident species was 0.54 g/day.

For the Native American population, total landings reported by Beak (1989) were adjusted for the percentage of catch retained by the tribe. An edible portion of 50 percent was assumed. Total edible fish mass retained was averaged over the total population to derive a per capita fish consumption estimate of 16.4 g/day.

Based on the results of this analysis, it appears that the Native Americans are the highest consumers of Columbia River fish. However, the Beak (1989) consumption estimate used was based an estimate of the consumption of salmon and steelhead only. As these species are anadromous, their potential for uptake of dioxin is limited. Approximately 85 percent of anadromous fish sampled in the Columbia River during a recent study had no detectable levels of dioxin, and those with detectable concentrations were at or near "background" levels typical of fish in rivers with no identified point source discharges (ChemRisk 1990; Parsons et al., 1991). Due to the species consumed, it is likely that Native Americans would have low exposure to dioxin in fish.

To estimate potential dioxin exposure for Native Americans consuming Columbia River fish at a rate of 16.4 g/day, a lifetime average daily dose (LADD) can be calculated using the following equation:

$$LADD = Cf \times Fc \times 1/BW \times EDa \times EDy \times 1/L$$

where:

LADD = Lifetime Average Daily Dose (pg/kg-day)
Cf = Concentration of TCDD in fish (pg/g)
Fc = Fish Consumption Rate (g/day)
Bw = Body Weight (70 kg)
EDa = Exposure Duration (365 days/year)
EDy = Exposure Duration (70 years)
L = Lifetime (25,550 days)

Fish tissue levels measured in 1989 (ChemRisk, 1990) can be used to estimate intake of TCDD. The average fish tissue concentrations reported in that analysis were 0.12 pg/g for salmon and 0.07 ppt for steelhead. If it is conservatively assumed that all 16.4 g of fish consumed daily contains an average of 0.12 pg/g of TCDD, the LADD can be estimated to be 0.028 pg/kg-day. This is well below the dose level deemed acceptable by the majority of U.S. federal agencies (FDA 1983; Kimbrough et al., 1984) and by the governments of Western European Nations and Canada (Ontario, 1985; van der Heijden et al., 1982; U.K. 1989).

By contrast, a large percentage of the fish harvested by recreational anglers on the lower Columbia River is sturgeon, a species that has been reported to have higher tissue levels of TCDD (ChemRisk, 1990). As a result, even though the rate of consumption by anglers is lower than that estimated for Native Americans, total average daily intake by anglers may be higher. Calculating a LADD for anglers using the average tissue level of 0.46 pg/g reported for sturgeon (ChemRisk, 1990) results in a LADD of 0.038 pg/kg-day. This indicates that anglers and their families may be the most highly exposed population that consumes fish from the Columbia River.

The EPA has stated recently that it is most appropriate to model exposure to the most exposed population (MEP) rather than to the maximally exposed individual (MEI) (Inside EPA, 1991). Within populations, the distribution of fish consumption rates is positively skewed i.e. most consumers eat small amounts while a few are high consumers (Soldat, 1970; USDA, 1983; Meunz and Peterson, 1990; ChemRisk, 1991). In a skewed distribution of fish ingestion rates, the median is the most accurate descriptor of central tendency as 50 percent of the population consumes less than this value while 50 percent eats more. Thus, selection of the median rate of fish consumption is the most appropriate rate to represent "typical" consumption in a target population. Based on the above LADD calculations, recreational anglers represent the MEP for the Columbia River. Thus, it is most appropriate to select 5.8 g/day, the median rate of fish consumption for the MEP, in deriving a water quality standard for the Columbia River.

6.0 CONSUMPTION OF WATER

At the present time, the EPA (1989c) uses a value of 2.0 L/day to represent the average adult consumption rate of water. This value is based on the daily ration of water required by United States Army field personnel (EPA, 1989c). While this number may be appropriate for a population that has little access to other beverages, it is likely to overestimate actual water consumption by average adults. In addition, due to their increased physical exertion and exposure to the outdoors, Army personnel are likely to require considerably more water in a day than the average individual.

Results of several studies have indicated that the average adult consumption rate for liquids ranges from 0.4 to 2.2 L/day (Pennington, 1983; NAS, 1983; Cantor et al., 1987; Gillies and Paulin, 1983; EPA, 1984; ICRP, 1974). The FDA Total Diet Study (Pennington, (1983) provided estimates, broken down by age and sex, of average daily intakes of a large number of foods and beverages. While the average adult consumes approximately 2 L/day of fluids (1.485 and 2.094 L/day for women and men, respectively), women and men were reported to consume an average of only 0.456 L of water daily. Total water-based beverages (including water alone) consumed were 0.971 and 1.149 L/day for women and men, respectively. The remainder of fluid intake consisted of milk and milk-based drinks and soups; alcoholic beverages including beer, wine, and hard liquor; and carbonated soft drinks. Although alcoholic beverages and carbonated sodas are water-based beverages, it is likely that they are produced and bottled using non-local sources of water.

A number of additional studies have investigated the consumption rate of drinking water by adults. The National Academy of Sciences (NAS, 1983) calculated the average consumption rate of liquids to be 1.63 L/day, based on data obtained in nine studies. Cantor et al. (1987; cited in EPA, 1989c), in an investigation of the relationship between drinking water and bladder cancer conducted for the National Cancer Institute, calculated the average water consumption rate to be 1.39 L/day. Gillies and Paulin (1983; cited in EPA, 1989c) reported a range of 0.26 to 2.80 L/day with a mean intake of 1.256 + or - 0.39 L/day. The EPA (1984) estimated tap water consumption intake levels by age, using data collected by the Department of Agriculture. The daily intake levels for adults ranged from 1.24 to 1.73 L/day. These levels included soft drinks and alcoholic beverages. The International Commission on Radiological Protection (ICRP, 1974) estimated the range of consumption to be 0.4 to 2.2 L/day for adults. In EPA's 1986 " Development of Risk Assessment Methodology for Land Application and Distribution and Marketing of Municipal Sludge", the EPA reports that mean water ingestion rates range from 0.3 to 1.2 liters per day (EPA, 1986).

It is quite evident that the EPA's estimate of 2 L/day overestimates the water consumption rate for the average individual. As indicated by the Pennington (1983) data, a large percentage of intake includes non-water-based as well as water-based beverages from a remote source. The Pennington data suggest that approximately 60% of the total dietary fluid intake by the average adult consists of water or water-based soups or beverages. If a total fluid consumption rate of 2 L/day is reasonable, it can be assumed that 60%, or 1.2 L/day, is water.

7.0 APPROPRIATE FLOW CONDITIONS

Typically, compliance with ambient water quality standards is demonstrated by measuring the concentration of TCDD discharged in the effluent and applying a stream dilution factor. The stream dilution factor is calculated as the flow rate of effluent discharged into the stream divided by the combined effluent and stream flow rate as described in the following equation:

$$C_w = C_e \times V_e/V_r$$

where:

C_w = Concentration of TCDD in the ambient water
C_e = Concentration of dioxin in the effluent
Ve = Volume of effluent discharged
V_r= Volume of river flow

The selection of the appropriate stream flow rate is an important component of water quality regulations. A flow rate should be selected that is logically consistent with the types of health effect studies that form the basis of the regulation. The basis of ambient water quality criteria and standards for TCDD is typically carcinogenicity. When cancer risks are estimated, it is the long-term average exposure to the compound over a lifetime that is of interest. In the case of possible risks due to consumption of fish, the long-term average river TCDD concentrations are the best predictors of fish residue bioaccumulation. Water concentrations representative of long-term exposure are best estimated using long-term average flow conditions, such as the harmonic mean.

For TCDD, long-term average flow conditions would also be appropriate when considering reproductive effects as the toxic endpoint of concern. The flow rate selected should be consistent with the types of studies showing the most critical effects (i.e. the effects observed at the lowest dose), as these studies form the basis of the reference dose. An evaluation of numerous published reproductive toxicity studies indicates that the critical effects have been demonstrated in studies of monkeys fed TCDD in their diet for about 4 years (Bowman et al., 1989b). Since this study is based on long-term exposure, long-term average flow conditions are appropriate when evaluating the potential for reproductive effects in humans consuming fish. Some studies have examined possible reproductive effects of short-term exposure to TCDD. However, these studies show effect levels that are higher than those exhibited in the chronic exposure studies.

The harmonic mean represents long-term, daily exposure and is calculated as the reciprocal of the mean of the reciprocal daily flow values:

$$Q_{hm} = \frac{N}{(1/Q_1 + 1/Q_2 + ... + 1/Q_N)}$$

where:

Q_{hm} = Harmonic mean
N = The number of days
Q = The daily stream flow.

The harmonic mean is generally a more conservative estimator of long-term average flow conditions than the arithmetic mean (EPA, 1988b). The most appropriate stream flow rate for measuring compliance with TCDD water quality standards is the long-term average flow represented by the harmonic mean.

8.0 PERSPECTIVE ON RISK

Risk can be defined as an estimate of the probability that a given exposure to an agent in the environment will result in an adverse health effect. Adverse health effects may include mortality, morbidity, or injury to individuals or a population as a whole (Derby and Keeney, 1981;Graham, 1990). Risk is a function of both hazard and exposure. The innate toxicity of a given compound contributes to its hazard, while the frequency, duration and intensity of contact with the compound defines potential exposure. Risk assessment evaluates both components and characterizes the probability that adverse health effects in humans, domestic animals, wildlife or ecological systems will result from exposures to environmental hazards.

Cancer risks may be expressed as either individual or population risks. An individual cancer risk value is an estimate of the probability that an individual member of a population will develop cancer as a result of a lifetime of exposure to a cancer-causing agent. Given that the background incidence of cancer in the U.S. population is about 30%, or 30 cases of cancer in 100 people (American Cancer Society, 1989), exposure to a chemical resulting in a risk level of 1 in 1,000,000 (10^{-6}) is equivalent to ensuring that the lifetime cancer risk for any person exposed to this level of contamination is not greater than 300,001 in 1,000,000 (30.0001%) rather than 300,000 in 1,000,000. Population risk is expressed as the product of the individual risk and the size of the exposed population. It is measured as an upper-limit estimate of the number of additional incidences of cancer in the exposed population (Travis et al., 1987).

Health risk assessments have become so widely adopted in the United States that their conclusions are now major factors in many environmental decisions. Risk assessment is often used as the basis for deriving ambient standards and target concentrations or cleanup goals which ensure that the estimated plausible risk to humans will be below a specific, established level. The science of risk assessment provides a bridge between scientific research on the health effects of chemicals and the various risk management options that may be considered by regulatory agencies. The risk assessment process has helped reduce unwarranted concern over trivial hazards by helping the public put into proper perspective the magnitude of the risks posed by both naturally occurring toxicants in food, and manmade chemicals (Young, 1987). Risk assessment provides the means whereby those chemical hazards which are significant health risks may be identified and appropriate action be taken to limit exposure.

Putting risks into perspective is an important facet of risk management. Virtually every aspect of human life exposes individuals to health risks (Klaassen et al., 1986). Each day, people take risks or make decisions to avoid risks. Risks associated with common activities may be readily acceptable to individuals. In establishing a regulatory acceptable risk level for the State of Oregon, it is important that one have a perspective of the environmental health risks relative to those voluntary and involuntary risks to which individuals are exposed every day. Furthermore, it is important that state regulators consider previous risk decisions made in their state or region, as well as pertinent existing state and federal regulations, such as drinking water . Risk management decisions should address exposure assessments and the question of acceptable risk on a case-by-case basis.

This chapter addresses the current regulatory status of various federal, regional and state agencies. It presents a perspective on the risk levels that have prompted regulatory action and discusses the selection of an acceptable risk level for the State of Oregon. For the purpose of comparison, various risks that are incurred daily as a result of voluntary and involuntary activities are discussed.

8.1 Regulatory Positions on Risk

Various federal and state regulatory agencies are responsible for establishing regulations and standards which protect the public from exposure to carcinogens and environmental toxins (Travis et al., 1987). An underpinning of regulatory and risk management decisions is the level of cancer risk which is considered to be acceptable or *de minimis*. The term *De minimis* risk is used by risk assessors and regulators to define insignificant risk levels, or those risks that are below regulatory concern (Travis et al., 1987). A common misconception within risk assessment is that all occupational and environmental regulations adopt a theoretical maximum cancer risk of 10^{-6}. When this level of risk is exceeded, the public and the media quite often view the situation as a serious threat to public health. In 1987, the former commissioner of the U.S. Food and Drug Administration (FDA), Dr. Frank Young, discussed this misunderstanding (Young, 1987).

> "The risk level of one in one million is often misunderstood by the public and the media. It is not an actual risk - i.e., we do not expect one out of every million people to get cancer if they drink decaffeinated coffee. Rather, it is a mathematical risk based on scientific assumptions used in risk assessment. FDA uses a conservative estimate to ensure that the risk is not understated. We interpret animal test results conservatively and we are extremely careful when we extrapolate risks to humans. When FDA uses the risk level of one in one million, it is confident that the risk to humans is virtually nonexistent."

Cancer risk levels, which are often perceived to represent trigger levels for regulatory action, frequently represent levels of risk that are so small that they are of negligible concern.

The *de minimis* cancer risk levels adopted by risk managers and regulators are based typically on a range of acceptable risk levels which depend upon a given situation and the size of the population potentially at risk. In addition, the development of an acceptable level of risk often involves consideration of the technological and economic feasibility of risk reduction strategies, as well as the societal costs and benefits of alternative risk levels.

8.1.1 Federal Agencies

Recent reviews indicate that the theoretical cancer risks associated with currently enforced environmental regulations are in the vicinity of 1 in 100,000, not 1 in 1,000,000 (Travis et al., 1987; Travis and Hattemer-Frey, 1987). In a retrospective review of the use of cancer risk estimates in 132 federal decisions, Travis et al. (1987) examined the level of cancer risk that triggered regulatory action. The authors considered three measures of risk: individual risk, the size of the population exposed, and the population risk. The results of the review showed that for exposures resulting in a small-population risk, the level of risk above which agencies almost always acted to reduce risk was approximately 4×10^{-3}. For large-population risks (the entire U.S. population) agencies typically acted on risks of about 3×10^{-4}. For effects on small populations, regulatory action was never taken for individual risk levels below 1×10^{-4}. For large-population effects, the *de minimis* risk level dropped to 1×10^{-6}. Based on the findings of Travis

(1987; Travis and Hattemer-Frey, 1987) and upon further examination of the database, Graham (1990), has suggested using a range of acceptable lifetime cancer risk levels in risk management decisions (1 x 10^{-2} to 1 x 10^{-4} for maximally exposed individuals and 1 x 10^{-4} to 1 x 10^{-6} for the average exposed individuals)

Rodricks et al. (1987) also evaluated regulatory decisions and reached similar conclusions. In decisions relating to promulgation of National Emission Standards for Hazardous Air Pollutants (NESHAPS), the EPA found that the maximum individual risks and total population risks from a number of radionuclide and benzene sources were too low to be judged significant. Maximum individual risks were in the range of 3.6 x 10^{-5} to 1.0 x 10^{-3}. In view of the risks deemed insignificant by EPA, Rodricks et al. (1987) noted that 1 x 10^{-5} appears to be in the range of what EPA might consider an insignificant average lifetime risk, at least where annual aggregate population risk is concerned.

As mandated by the 1986 Safe Drinking Water Act (SDWA), the EPA has established Maximum Contaminant Level Goals (MCLGs) for chemical substances listed under the Act. These non-enforceable goals have been established at levels considered protective of human health (40 CFR 141, July 25, 1990). The EPA has established MCLGs of zero for known or suspected carcinogens that are believed to have no threshold. Recognizing that MCLGs of zero cannot be measured, the SDWA directed that Maximum Contaminant Levels (MCLs) be established as close to the MCLGs as feasible.

> "Based on the statutory directive for setting the MCLs, EPA derives the MCLs based on an evaluation of (1) the availability and performance of various technologies for removing the contaminant, and (2) the costs of applying those technologies. Other factors which are considered in determining the MCL include the ability of laboratories to measure accurately and consistently the level of the contaminant with available analytical methods. For carcinogens, EPA also evaluates the health risks that are associated with various levels of the contaminant with the goal of ensuring that the risks at the MCL fall within the 10^{-4} to 10^{-6} risk range that the Agency considers protective of public health and therefore achieves the overall purpose of the SDWA" (40 CFR 141, July 25, 1990).

A number of the known or suspected carcinogens for which MCLs have been promulgated are listed in Table 8-1. If the estimated lifetime average daily doses, based on 2 l/day drinking water consumption by a 70 kg adult averaged over a lifetime, are multiplied by the cancer potency factor for each contaminant (EPA, 1989e), the incremental risks associated with the EPA MCLs range from 10^{-6} to 10^{-4}. This range is also mentioned in the recently promulgated Hazardous Waste Management System Toxicity Characteristics Revisions (55 FR 11798-11863):

> "For drinking water contaminants, EPA sets a reference risk range for carcinogens at 10^{-6} to 10^{-4} excess individual cancer risk from lifetime exposure. Most regulatory actions in a variety of EPA programs have generally targeted this range using conservative models which are not likely to underestimate the risk."

Final revisions to the National Contingency Plan (NCP) (EPA, 1990c) set the acceptable risk range between 10^{-6} and 10^{-4} at hazardous waste sites regulated under CERCLA. Previously, the range of risks was 10^{-7} to 10^{-4}. Since the NCP revisions, the EPA has selected and promulgated a single risk level of 10^{-5} (1 in 100,000) in the Hazardous Waste Management System Toxicity

Table 8-1. Selected MCLs and Associated Risk Levels

Chemical	USEPA Maximum Contaminant Level (mg/l)	USEPA Carcinogen Classification[d]	Cancer Potency Factor (mg/kg-day)$^{-1}$[d]	Incremental Cancer Risk Associated with Lifetime Exposure to Chemical in Drinking Water[e]
Benzene	0.005 [c]	A	2.9×10^{-2}	4.1×10^{-6}
Carbon Tetrachloride	0.005 [c]	B2	1.3×10^{-1}	1.9×10^{-5}
Chlordane	0.002 [a]	B2	1.3×10^{0}	7.4×10^{-5}
para - Dichlorobenzene	0.075 [c]	B2	2.4×10^{-2}	5.1×10^{-5}
1,2- Dichloroethane	0.005 [c]	B2	9.1×10^{-2}	1.3×10^{-5}
1,1-Dichloroethylene	0.007 [c]	C	6.0×10^{-1}	1.2×10^{-4}
1,2-Dichloropropane	0.005 [a]	B2	6.8×10^{-2}	9.7×10^{-6}
Ethylene dibromide (EDB)	0.00005 [a]	B2	8.5×10^{1}	1.2×10^{-4}
Heptachlor	0.0004 [a]	B2	4.5×10^{0}	5.1×10^{-5}
Hexachlorobenzene	0.001 [b]	B2	1.7×10^{0}	4.9×10^{-5}
Polychlorinated biphenyls	0.0005 [a]	B2	7.7×10^{0}	1.1×10^{-4}
2,3,7,8 - TCDD	5×10^{-8} [b]	B2	1.56×10^{5}	2.2×10^{-4}
Tetrachloroethylene	0.005 [a]	B2	5.1×10^{-2}	7.3×10^{-6}
Toxaphene	0.005 [c]	B2	1.1×10^{0}	1.6×10^{-4}
1,1,2 - Trichloroethane	0.005 [b]	C	5.7×10^{-2}	8.1×10^{-6}
Trichloroethylene	0.005 [a]	B2	1.1×10^{-2}	1.6×10^{-6}
Total Trihalomethanes	0.10 [c]			
Bromodichloromethane[f]		B2	1.3×10^{-1}	3.7×10^{-4}
Dibromochloromethane[f]		C	8.4×10^{-2}	2.4×10^{-4}
Bromoform[f]		B2	7.9×10^{-3}	2.3×10^{-5}
Chloroform[f]		B2	6.1×10^{-3}	1.7×10^{-5}
Vinyl Chloride	0.002 [c]	A	2.3×10^{0}	1.3×10^{-4}

a. EPA 40 CFR 141. May 22, 1989.
b. EPA 40 CFR 141 July 25, 1990.
c. EPA Fact Sheet, Office of Drinking Water, Feb 12, 1988.
d. EPA, 1989g. Health Effects Assessment Summary Tables. Fourth Quarter. OERR 9200.6 - 303 - (89-4).
e. Calculations based on ingestion of 2 liters per day, 365 days per year, for a 70 year lifetime, and a body weight of 70 kg.
f. Assuming single chemical contaminant is responsible for MCL of 0.10 mg/L.

A - Human Carcinogen (Sufficient evidence of carcinogenicity in humans).
B2 - Probable human carcinogen (sufficient evidence of carcinogenicity in animals with inadequate or lack of evidence in humans).
C - Possible human carcinogen (limited evidence of carcinogenicity in animals and inadequate or lack of human data).

Characteristics (TC) Revisions (55 FR 11798-11863). In their justification, the EPA cited the following rationale:

> "The chosen risk level of 10^{-5} is at the midpoint of the reference risk range for carcinogens (10^{-6} to 10^{-4}) targeted in setting MCLs. This risk level also lies within the reference risk range (10^{-6} to 10^{-4}) generally used to evaluate CERCLA actions. Furthermore, by setting the risk level at 10^{-5} for TC carcinogens, EPA believes that this is the highest risk level that is likely to be experienced, and most if not all risks will be below this level due to the generally conservative nature of the exposure scenario and the underlying health criteria. For these reasons, the Agency regards a 10^{-5} risk level for Group A, B, and C carcinogens as adequate to delineate, under the Toxicity Characteristics, wastes that clearly pose a hazard when mismanaged."

8.1.1.1 EPA Records of Decision

This section represents a review of Records of Decision (RODs) issued for sites located in Region 10, which includes the states of Oregon, Washington, and Idaho. RODs specify the remedial measures to be taken at each Superfund site and consider the acceptable level of risk for site-specific cleanup goals. This review demonstrates that a range of risks is typically considered to be acceptable for chemicals in all media. Risks ranging from 10^{-7} to 10^{-4} have been approved by the EPA for Region 10 Superfund sites (Table 8-2). Applicable or Relevant and Appropriate Requirements (ARARs) generally form the basis for requiring treatment of these sites. ARARs are those cleanup standards, standards of control, and other human health and environmental requirements, criteria, or limitations established under state or federal law that address problems or situations sufficiently similar to those encountered at the site that their use is well suited to the particular site.

<u>Western Processing Company, WA 9/85</u>

The Western Processing Company in Kent, Washington, operates a facility to recycle, reclaim, treat and dispose of numerous industrial wastes, including waste oils, electroplating wastes, waste pickle liquor, battery acids, steel mill flue dust, pesticides, spent solvents, and zinc dross. In general, the area around the site is rapidly being developed for commercial and industrial purposes and to a limited amount, for residential or agricultural use. Investigations have found extensive contamination of soil, surface water, and groundwater both on and off-site.

This second remedial action recommends excavation of all soils which exceed the average daily intake level of 1×10^{-5} excess cancer risk level, thereby eliminating the threat of exposure through direct contact, which is the exposure route of concern. On-site soils with known PCB concentrations over 50 ppm and off-site soils contaminated with PCB concentrations exceeding 2 ppm will be excavated and capped. In addition, hot spots will be excavated. For direct contact, a hot spot has been defined as soil with any one compound exceeding the ADI, or with a cumulative cancer risk in excess of 1×10^{-5}, or a PCB concentration above 2 ppm.

The performance standard is to return nearby Mill Creek waters and sediments to ambient water quality criteria levels for aquatic organisms or to upstream background levels, whichever is less stringent. If groundwater can not be returned to MCLs or other health based criteria (e.g.,

Table 8-2. Risk Levels Considered Acceptable in Region X USEPA Records of Decision

Date	Site Name	Chemicals	Media	Clean-up Risk Level
October 1990	Coal Creek (Ross Electric), Washington	PCBs	Soil	Cleanup goals based on 10^{5} cancer risk for PCBs in soil.
September 1990	Fort Lewis, Washington	VOCs	Groundwater	Cleanup levels for groundwater were based on MCLs.
March, 1990	Silver Mountain Mine, WA	Arsenic, cyanide	Soil, groundwater	The action level for the cleanup of soils was established on a 10^{-4} risk level. Cleanup levels for groundwater were based on MCLs.
September, 1989	Northwest Transformer, Washington	PCBs	Soil	The action level for the cleanup of soils was established on a 10^{4} risk level.
September, 1989	Commencement Bay Nearshore/Tideflats, WA	PCBs, PAHs, Arsenic	Sediment	Cleanup goals based on cancer risk range of 10^{6} to 10^{-4}.
September, 1989	Northside Landfill, WA	VOCS	Groundwater	Cleanup levels for groundwater were based on MCLs.
December, 1988	Commencement Bay Tacoma Tar Pits, WA	PCBs, PAHs, lead	Soil	Cleanup goals based on 10^{-6} cancer risk for soil contaminants.
July, 1988	Frontier Hard Chrome, WA	Chromium, VOCs	Groundwater	Cleanup levels for groundwater were based on MCLs.
March, 1988	Commence Bay South Tacoma Channel, WA	VOCs	Groundwater	Cleanup levels for groundwater were based on MCLs.
September, 1987	Colbert Landfill, WA	VOCs	Groundwater	Cleanup levels for groundwater were based on MCLs.
September, 1985	Ponders Corner, WA	VOCs	Groundwater	Cleanup levels for groundwater were established on a 10^{-6} risk level.
September, 1985	Western Processing Co., WA	PCBs	Soil, groundwater	The action level for the cleanup of soils was established on a 10^{-4} risk level. Cleanup levels for groundwater were based on MCLs.
May, 1985	South Tacoma Channel, Well 12A, WA	VOCs	Groundwater	Cleanup levels for groundwater were established on a 10^{-6} risk level.

Table 8- 2. Risk Levels Considered Acceptable in Region X USEPA Records of Decision (cont'd)

Date	Site Name	Chemicals	Media	Clean-up Risk Level
December, 1989	Teledyne Wah Chang Albany, OR	Radionuclides	Sludge	Cleanup levels for sludge were established on a 10^{-6} risk level.
September, 1988	Martin Marietta Reduction Facility, OR	VOCs, metals	Groundwater	Cleanup levels for groundwater were based on MCLs or Alternate Concentration Limits (ACL).
March, 1988	Gould Site, OR	Lead	Soil, groundwater	Cleanup levels for all media were based on MCLs and EP Toxicity sediment standards.
September, 1986	United Chrome Products, OR	Chromium	Groundwater	Cleanup levels for groundwater were based on MCLs.

acceptable excess cancer risk levels or ADIs), alternate concentration limits (ACLs) may be established in a future Record of Decision.

Ponders Corner, WA 9/85

Septic tanks and an open disposal area adjacent to a commercial cleaners were the most probable sources of contamination at the Ponders Corner site. In general, PCE and TCE were considered to be the major contaminants of the groundwater, and PCE was considered as a major contaminant of the soil.

A 10^{-6} risk level, which was the action level established by the Tacoma-Pierce County Health Department currently, this risk level is not exceeded by the existing source-pathway-receptor system of treated drinking water. The treated groundwater, then, did not present a significant exposure route.

Colbert Landfill, WA 9/87

The main contaminants detected in the groundwater at the Colbert Landfill site during the remedial investigation were six VOCs, all chlorinated aliphatic hydrocarbons. The Colbert Landfill, located in Spokane County, Washington, operated as a sanitary landfill receiving both municipal and commercial wastes during its operation. During this time, various organic solvent wastes were disposed of at the site. Sampled residential wells sampled showed contamination of well water exceeding proposed MCL values and ranged from 1 μg/l for PCE to 5600 μg/l for TCA. The contaminated aquifers were classified as current sources of drinking water according to the EPA groundwater classification system.

The selected remedy was designed to prevent a further spread of contaminated groundwater in two aquifers by installing and operating interception wells and treating the extracted groundwater. This remedy also meets all substantive laws and regulations pursuant to the established ARARs. Treatment was intended to reduce contaminant levels in the aquifers and in the wastewater effluent to a level equal to or below performance standards. These performance standards were established to serve both as minimum treatment levels for effluents, and as maximum residual levels for groundwater. These standards have been set as MCLs of 200 μg/l for TCA, 7 μg/l for DCE, and 5 μg/l for TCE. In the case of contaminants for which MCLs have not been determined, a similarly defined health based level derived from a 10^{-6} risk level for carcinogenic constituents was established. These maximum allowable concentrations include 4,050 μg/l for DCA, 0.7 μg/l for PCE, and 2.5 μg/l for methylene chloride.

Commencement Bay / South Tacoma Channel, WA 3/88

Contaminant migration from the industrial and municipal landfill in Pierce County, Washington, affected aquifers supplying drinking water and nearby wetlands. The primary contaminants affecting the groundwater and surface water are VOCs. The VOCs detected in groundwater were benzene at 19 μg/l, toluene at 60 μg/l, vinyl chloride at 80 μg/l, 1,2-dichloroethane at 20 μg/l, methylene chloride at 1300 μg/l, and 1,1-dichloroethane and chloroethane at 42 μg/l and 55 μg/l, respectively. Priority pollutant metals occasionally exceeded MCLs established pursuant to the Safe Drinking Water Act.

The selected remedy included a landfill cap and methane gas extraction system to control the source, and a groundwater extraction and treatment system to control migration of the plume. All extracted water will be treated to specific performance standards, monitored to ensure compliance, and will be properly discharged. Performance standards for discharge to surface water require all contaminants to meet MCLs, which includes 5 µg/l for both benzene and 1,2-dichloroethane, 200 µg/l for 1,1,1-trichloroethane, and 2 µg/l for vinyl chloride. If no MCL was established for a particular contaminant, the ambient water quality criteria for protection of human health for water and fish ingestion was used. These values were 1400 µg/l and 14 µg/l for ethyl benzene and toluene, respectively. In the absence of an MCL or ambient WQC, EPA Region 10 conducted a risk assessment of the chemical in question and provided an appropriate treatment goal for the protection of public health, welfare, and the environment. Based on EPA Region 10 risk assessment at the 10^{-6} risk level, risks included 20 µg/l for chloroethane, 20 µg/l for 1,1-dichloroethane, 10 µg/l for xylenes, and 5 µg/l for methylene chloride.

Commencement Bay - Nearshore/Tideflats, Tacoma Tar Pits, WA 12/88

The Tacoma Tar Pits site is part of the Commencement Bay - Nearshore/Tideflats Superfund site located within the Tacoma Tideflats industrial area. Contaminants are derived from a former on-site coal gasification process. The tar pits lie between two bodies of water which, although not used as a water supply, support extensive fish and shellfish populations. Consequently, concern existed regarding the impact on surface water quality and many local industries that use groundwater from on-site wells. The primary contaminants of concern affecting surface water and soil included benzene, PAHs, PCBs, and lead. Concentrations of PCBs in surface soil were found at levels as high as 204 mg/kg, while lead was found at levels of 10,000 mg/kg in soils.

Surface soils and sediments exceeding the 10^{-6} lifetime cancer risk level, and all soils classified as Extremely Hazardous Wastes (EHW) under state law were excavated. Soils classified as EHW are defined as those soils with PAH levels exceeding 10,000 mg/kg, or 1 percent. PCB materials exceeding 50 ppm were permanently immobilized, consistent with TSCA regulations. Soils and sediments from other areas were excavated to a depth of 3 feet or less in all locations where soils exceeded concentrations defined to have a 10^{-6} lifetime cancer risk. This 10^{-6} risk level translates to 1 mg/kg for PCB, 1 mg/kg for PAHs, and 56 mg/kg for benzene. Surface soil contaminated with lead above the 166 mg/kg level was also excavated and stabilized.

Commencement Bay - Nearshore/Tideflats, WA 9/89

Chemicals of concern at the Commencement Bay - Nearshore/Tideflats (CB/NT) Superfund site in Tacoma, Washington, included PCBs, arsenic, PAHs, and heavy metals. Exposure to chemicals in fish and sediments were the pathways of concern. The average concentration of each detected chemical in English sole was used to calculate exposure. Based on these calculations, six chemicals were predicted to result in a risk greater than 10^{-6} at the maximum fish consumption rate of 1 pound per day, and only PCBs and arsenic predicted risk levels greater than 1×10^{-4}. At a fish consumption rate of 1 pound per month, only PCBs and arsenic exceeded the 10^{-6} risk level.

Evaluation of the data indicated that a PCB sediment cleanup level of 150 μg/kg would result in an average post-cleanup sediment concentration of 30 μg/kg for the CB/NT site in general. This cleanup goal would be expected to result in a mean fish concentration of 37 μg/kg, or less than 2% of the FDA action level of 2,000 μg/kg for PCBs. This would result in attainment of fish PCB levels similar to those found in reference areas. The potential health risks attributable to seafood consumption from remediated waterways was estimated at about 4×10^{-5} for a seafood consumption rate of 12.3 grams per day, and corresponds to the risks found in reference areas.

Northwest Transformer (Mission/Pole), WA 9/89

The Northwest Transformer site in Whatcom County, Washington, poses a threat to on-site workers and to nearby residents due to the presence of contaminated groundwater migrating off-site. The site was used primarily for the storage and salvage of transformers prior to final disposal or sale for scrap. Groundwater sampling has indicated the presence of PCBs at levels associated with an excess lifetime cancer risk of 10^{-3}. Low levels of penta- through octachlorinated dibenzodioxins and/or furans were found in burn pit soil samples.

The remedial option for this site achieves both the TSCA soil cleanup objectives of removing or treating soils contaminated with more than 10 ppm PCB, and reducing the potential for direct contact with residual PCB levels (below 10 ppm) by covering with clean soil. The ROD required that excavated soils be treated using in situ vitrification (ISV) to reduce the remaining residual concentration of PCBs to less than 1 ppm. A two-foot clean soil cover was required to reduce exposure to residual contamination. The two-foot depth for clean fill was derived from the recommended tilling depths for common root crops and is considered protective for both residential and agricultural future uses.

The ISV technology and the two foot clean fill cover was deemed protective of human health and the environment by eliminating PCB contamination above the 10 ppm level from the site and by creating a barrier between any remaining low level contamination and the existing ground surface. Resulting excess lifetime cancer risks would be within the range of 10^{-5} to 10^{-4}.

Teledyne Wah Chang Albany, OR 12/89

The preliminary assessment for the sludge pond unit at the Teledyne Wah Chang Albany Superfund site in Millersburg, Oregon was directed by the nature of the contaminants. Sludge was sampled and contains metal compounds produced by the various on-site processing units, including cyanide, zirconium, hafnium, chromium, mercury, nickel, uranium, and radium. The most prevalent organic compound was hexachlorobenzene, which may be a byproduct of the plant operations.

The selected remedy included the excavation of contaminated sludge to be mixed with a solidification agent and relocated to an off-site permitted solid waste disposal site. Due to the presence of radioisotopes (i.e., radium), the nature of the sludge makes treatment by reducing toxicity or volume impractical. The risk reduction by this interim action was from an estimated 3 excess cancers in a population of 1000 without any future control actions (assuming an extreme residential use scenario of the actual sludge pond area), to 1×10^{-6} by permanently removing the routes of exposure.

Silver Mountain Mine, WA 3/90

The ROD for the Silver Mountain Mine Superfund site in Okanogan County, Washington stated that arsenic and cyanide contribute 95% of the current and future excess lifetime cancer risk to humans. The Silver Mountain Mine site is characterized by an abandoned mine dump where a heap leaching operation resulted in cyanide and arsenic contamination. The site consisted of a leach heap of mined material, a trench remaining from the abandoned cyanide heap leaching operation, and a larger pile of unprocessed mined material. The risk assessment determined that the media of concern were limited to soil and groundwater due to the levels of arsenic, cyanide, and a few other heavy metals.

The selected remedy for soil cleanup of the site was to grade and cap the leach heap while at the same time implementing institutional controls. The action level for the cleanup of contaminated soils was established based on a 10^{-4} risk level and a hazard index of 1.0. Cleanup standards were set at 200 mg/kg for arsenic and 95 mg/kg for cyanide.

Using reasonable maximum exposure assumptions, arsenic, antimony, and cyanide were identified as the contaminants of concern in water. Nitrate/nitrite and lead were each present in a single groundwater sample at concentrations above established criteria; however, these samples were considered unlikely to be representative of overall site conditions. Cleanup goals for groundwater contaminants were set at 6 µg/l for arsenic based on a 10^{-4} cancer risk, and 154 µg/l for cyanide based on its health advisory. Cleanup levels of 20 µg/l for lead and 10 mg/l for combined nitrate and nitrite were based on federal MCLs.

Fort Lewis, WA 9/90

In the remediation of the VOC-contaminated groundwater at the Fort Lewis Superfund site in Pierce County, Washington, it was required that contaminants be cleaned up to reach their federal MCLs. Groundwater contamination was detected in off-site wells, thereby affecting the drinking water supplies of nearby residents. Analyses of the soil, groundwater, surface water, and sediments indicated that groundwater contamination was the principal threat at the site.

Extraction and treatment of the contaminated groundwater via air stripping was selected as the remedial option in order to protect human health and the environment. The ROD stipulated that the process should comply with applicable emissions regulations. Extraction of the VOC-contaminated groundwater would eliminate potential exposures via ingestion or inhalation of contaminated groundwater. The primary goal of this remediation is to restore groundwater to its beneficial use as a source of drinking water. The groundwater would be restored to levels consistent with state and federal ARARs which result in a cumulative excess cancer risk not to exceed 10^{-4}. By extracting the contaminated groundwater and treating it by air stripping, the cancer risk would be reduced to 5×10^{-5} and the hazard index decreased to 0.91.

The baseline risk assessment indicated that the levels of residual soil contamination correspond to a carcinogenic risk of 10^{-5} and a noncarcinogenic hazard index of 0.06. According to the ROD, this baseline risk for soil is within the acceptable exposure levels (i.e., 10^{-7} and 10^{-4}) that are protective of human health as promulgated by federal standards. Therefore, remediation of soil is not included as part of the selected remedy.

Coal Creek (Ross Electric), WA 10/90

Polychlorinated biphenyls (PCBs) represented the majority of the carcinogenic risk presented at the Coal Creek site. The action level for the cleanup of PCB-contaminated soil was established based on a 10^{-5} level of risk. This risk level was selected because it fell within the cancer risk range (10^{-7} to 10^{-4}) determined by the EPA to be protective of human health. It was concluded that the cleanup of PCBs to this level would adequately protect human health and the environment by reducing the risks associated with all soil contaminants.

In accordance with TSCA requirements, the remediation of this site required that all soils, sediments, and mixed debris in the fill mound with PCB concentrations greater than 50 ppm be excavated and incinerated on site. Treatment residues were not permitted to contain greater than 1 ppm PCBs or greater than 1 ppb total TCDD equivalents. All soils and sediments with PCB concentrations greater than 1 ppm were to be contained on-site under an engineered cap. This remediation goal of 1 ppm was based on risk calculations and corresponds to an excess lifetime cancer risk level of 10^{-5} for persons exposed under the residential exposure scenario, and complies with the State of Washington's Model Toxics Control Act cleanup standards. Groundwater emanating from the fill mound after remediation was required not to exceed the federal MCL for PCBs and lead, nor exceed the secondary MCL for copper. For residential exposures, the excess lifetime cancer risk was reduced to 1×10^{-5}. For industrial or recreational exposures, the corresponding risk was reduced to 2×10^{-6}.

Summary

A review of the RODS issued in Region X indicates that the EPA's position on the acceptable risks associated with the remediation of Superfund sites has varied depending upon the chemicals on-site and a number of site-specific factors. Clean-up goals associated with risks as high as 10^{-4} have been approved at some sites while risk levels of 10^{-6} have been used to determine clean-up goals elsewhere. In other situations, technology-based criteria (MCLs and analytical quantitative limits) have been used to establish cleanup goals which result in estimated health risks between 10^{-4} to 10^{-6}.

8.1.2 State Agencies

The states of Alabama, Georgia, South Carolina, Virginia, Maryland, Michigan, Minnesota, Ohio, Maine, and Wisconsin have used or propose to use a 10^{-5} risk level in their risk management decisions. Similarly, a lifetime incremental cancer risk of 10^{-5} is used by the Commonwealth of Massachusetts as a cancer risk limit for exposures to substances in more than one medium at hazardous waste disposal sites (Mass DEQE, 1988). This risk limit represents the total cancer risk at the site associated with exposure to multiple chemicals in all contaminated media. The State of California has also established a risk criterion of 10^{-5} for use in determining levels of chemicals and exposures that pose "no significant risk" of cancer under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) (CCR Section 12703) (California, 1987).

The following sections summarize Oregon State policies on acceptable risk levels which are used in setting ambient air and drinking water standards or guidelines, and cleanup goals at hazardous waste sites.

Water Quality Criteria

Water quality standards for the State of Oregon are based on criteria developed by EPA that were developed for the protection of human health and based on the ingestion of drinking water and/or fish. In 1987, the Oregon Environmental Quality Commission (EQC) adopted a water quality standard of 0.013 pg/L for TCDD in waters with designated beneficial uses for fish consumption and water ingestion. This standard was adopted for the protection of human health at a risk of 1 x 10^{-6} and directly corresponds to the EPA water quality criteria for TCDD (EPA, 1984).

Sediment Quality Standards

No numerical standards have been adopted by the State of Oregon. At present, the DEQ uses a tiered approach based on a combination of historical information, physical, chemical, and biological parameters to establish guidelines for sediment quality. EPA interim sediment criteria values (EPA, 1988c) have been used as a basis for the established guidelines.

The DEQ does not recommend that sediment quality standards be adopted into Oregon Administrative Rules at this time. Instead, the DEQ recommends that an advisory committee be formed to review the development of these standards. Current guidelines are intended to be used for evaluating sediments for appropriateness of in-water disposal. It is recommended that chemical trigger points be evaluated on a regular basis by the scientific review panel (EQC, 1990).

Groundwater Quality Criteria

Maximum Contaminant Levels (MCLs) established under the Federal Safe Drinking Water Act have been used by the State of Oregon to determine when groundwater may not be suitable for human consumption. For a 70 kg adult who ingest 2L/day of drinking water over lifetime, the risk levels associated with federal MCLs range from 10^{-6} to 10^{-4}.

Ambient Air Standards

DEQ currently uses federal standards to regulate air pollutants. For toxics which do not have federal cleanup levels, the state may develop cleanup goals considered to be at least as stringent as those promulgated by the Clean Air Act. These are based on Maximum Achievable Control Technology with the goal of achieving a lifetime risk of less than 1 x 10^{-5} for the most exposed individual

Hazardous Waste Cleanup Goals

The Environmental Cleanup Division (ECD) of the DEQ performs oversight of hazardous waste substances site investigations. The remedial action shall attain the background level of the hazardous substances, unless the Director determines that background level does not satisfy the feasibility requirements set forth in OAR 340-122-090(1)(b), in which case the Director shall select a remedial action that attains the lowest concentration level of the hazardous substances that satisfies the protection and feasibility requirements set forth in OAR 340-122-090(1).

Endangerment assessments often involve the establishment of risk based detection limits. Upper lifetime risks and hazard indices can be calculated by assuming that concentrations of the contaminants of concern in water, soil, and air are at their respective detection limits and by using toxicity values and exposure assumptions developed by EPA.

The RI/FS policy utilizes the equations and exposure default values described in EPA Risk Assessment Guidance for Superfund (1989d) and EPA Region 10. Detection limit goals for risks and hazard indices are 10^{-7} and 0.1, respectively. If the risk and hazard index goals for proposed analytical method detection limits are exceeded, justification must be provided to DEQ supporting the proposed detection limits for the project. Oregon is currently proposing soil cleanup levels which would correspond to federal MCLs or to a 1×10^{-6} excess lifetime cancer risk.

8.1.3 Summary

The risk level of 1×10^{-5} for a TCDD water quality standard has considerable justification both in regulatory precedent and in arguments based on fundamental principles of risk management. EPA suggests that the range of 10^{-6} to 10^{-4} is appropriate for setting water quality standards. This is consistent with the trend of state and federal regulatory decisions regarding water pollutants. The selection of a 10^{-5} level of risk represents the center of the range of risks that attempt a balance between protection of the individual and unreasonable overregulation.

8.2 Comparison of Risks

Quantitative cancer risk estimates can be more readily understood when placed in perspective with health risks associated with familiar activities, occupations, or commodities. Comparisons are made between cancer risk estimates and everyday risks. Most of the risk values cited in this section are annual risk estimates, or reflect mortality rates during any given year. The examples used in this section are summarized for the purpose of providing a conceptual yardstick for measuring the magnitude of a risk.

8.2.1 Commonplace Risks

Many common human activities entail risks greatly in excess of one in one million (Table 8-3). For example, although risks are inherent in various modes of transportation, people generally accept those risks. Driving a car not only subjects the driver and passengers to the risk of an accident, but also poses a risk to pedestrians. The total annual risk of dying in a car accident is

Table 8- 3. Commonplace Risks[a]

Action	Annual Risk
Travel	
Motor vehicle accidents	2.4×10^{-4}
Collisions with pedestrians	4.2×10^{-5}
Frequent airline passenger (4 hrs per week)[b]	1.0×10^{-5}
Bicycling	1.0×10^{-5}
Housing	
Home accidents (all causes)	1.1×10^{-4}
Natural background radiation (sea level)	2.0×10^{-5}
Living in a natural stone or brick building	1.0×10^{-5}
Average diagnostic medical x-rays in U.S.	2.0×10^{-5}
Air pollution	2.4×10^{-4}
Sports	
Boating	5.0×10^{-5}
Hunting	3.0×10^{-5}
Swimming	3.0×10^{-5}
Football[b]	4.0×10^{-5}
Smoking	
Smoking, all effects (1 pack per day)	3.6×10^{-3}
Person sharing room with smoker	1.0×10^{-5}

a. Wilson and Crouch, 1987.

b. Hutt, 1978 as cited in Rodericks and Taylor, 1983.

about 2 in 10,000 (2.4×10^{-4}). The risk to a pedestrian dying in a motor vehicle accident is approximately 4 in 100,000 (4.2×10^{-5}). This equates to a lifetime risk of dying in a motor vehicle accident of approximately 7 in 1,000. An airline passenger that flies an average of four hours per week has an annual risk of 1 in 100,000 (1.0×10^{-5}) (Wilson and Crouch, 1987). An average bicyclist also has an annual risk of dying of 1 in 100,000 (Hutt, 1978; as cited in Rodricks and Taylor, 1983).

In general, accidents occurring in the home pose an annual risk of about 1 in 10,000 (1.1×10^{-4}). This overall risk is comprised of risks from falls, drowning, fires, inhalation and ingestion of objects, firearms, accidental poisoning and electrocution (Crouch and Wilson, 1982). Living in an average stone or brick building for about 20 months increases an individual's risk of cancer caused by natural radioactivity by 1 in 100,000 (1.0×10^{-5}) (Allman, 1985).

Exposures to radiation, either natural background radioactivity or radiation for medical purposes, increases the chances of cancer. Average diagnostic medical chest x-rays have been reported to increase the risk of cancer by 2 in 100,000 (2.0×10^{-5}) annually. Exposure to natural radiation at sea level (excluding radon) poses a similar level of risk (2.0×10^{-5}). Exposure to air pollution in the eastern United States poses an even greater risk of 2 in 10,000 (2.0×10^{-4}) annually (Wilson and Crouch, 1987). Furthermore, Gough (1990) estimates that between 2 and 3 percent of all cancers are associated with environmental pollution, while between 3 and 6 percent of all cancers may be attributed to total radiation sources.

Numerous popular sporting activities pose an increased potential risk of dying due to accidents. Boating, hunting, swimming and football pose an annual risk level of between 3 and 5 in 100,000 (3.0 to 5.0×10^{-5}) (Crouch and Wilson, 1982). Other sports that were not included in Table 8-3 have even higher levels of risk such as flying amateur aircraft (3 in 1,000), mountaineering (6 in 10,000) and scuba diving (4 in 10,000) (Crouch and Wilson, 1982).

Cigarette smoking has been suggested to increase one's annual average risk of cancer and other health effects by more than 1 in 1,000. Chronic exposure to secondary tobacco smoke has been estimated to increase individual's risks of health problems associated with tobacco smoke by 1 in 100,000 or 1.0×10^{-5} (Crouch and Wilson, 1982).

8.2.2 Occupational Risks

Many common occupations pose risks to individuals on the order of 10^{-6} or greater. For example, working in manufacturing or farming industries may increase an individual's risk of death during any year by 8×10^{-5} or 4×10^{-4}, respectively (Crouch and Wilson, 1982). Workers at gas stations are exposed to benzene vapors from volatilizing fuel levels ranging up to 32 $\mu g/m^3$ (API, 1986). Assuming that a worker is exposed to this maximum concentration during one-half of his occupational lifetime (20 hours/week, 240 days/year, 45 years), an associated lifetime cancer risk of about 3×10^{-5} can be calculated. That risk is expected to be much higher if the attendant is also exposed to additional vapors when gasoline is used to clean automobile parts in the workshop.

In the dry cleaning industry, workers are exposed daily to levels of tetrachloroethylene ranging from 10,000 to 20,000 $\mu g/m^3$ (Wallace, 1990). The risk associated with exposure to a midrange level of 15,000 $\mu g/m^3$ for a worker's occupational lifetime can be calculated to be approximately 3 x 10^{-3}. Occupational exposure limits established by OSHA may also be associated with relatively high risk values. Several OSHA time-weighted-average threshold limit values (OSHA, 1989) for carcinogens are associated with 10^{-3} risks (acrylamide and epichlorohydrin) and 10^{-2} risks (carbon tetrachloride, chlordane, and chloroform) to workers, assuming that a 70 kg worker inhales 10 m^3/day for 240 days/year over a 45-year occupational duration. Additional occupations that pose 10^{-5} and 10^{-4} risks to individuals are listed in Table 8-4.

8.2.3 Dietary Risks

Dietary factors, such as alcohol consumption and a high fat diet, have been implicated in many studies as a major contributor to cancer deaths (Ames et al., 1987; Scheuplein, 1990). In addition, people are exposed to risks every day by ingesting natural carcinogens in food (Scheuplein, 1990; Ames et al., 1987). Dr. Robert Scheuplein, Director of the Office of Toxicological Sciences at the FDA, estimated the risk of dying from cancer from dietary exposure to natural and man-made carcinogens is about 7 in 100 (7.7 x 10^{-2}). Of this, about 98% of the cancer risk in the diet may be attributable to natural carcinogens in food (Scheuplein, 1990). Diet contributes approximately 35% of the total human cancer risk, and smoking, the other major risk factor for cancer, accounts for another 30% (Doll and Peto, 1981).

Ames (1983), estimated that the daily intake of natural carcinogens in traditional food may exceed several grams. Scheuplein (1990) more conservatively assumed that of 1,000 grams of solid food consumed per day, approximately 0.1% or one gram of food per day consists of carcinogens. Table 8-5 lists intake and risk estimates for various food categories containing carcinogenic substances. This analysis clearly indicates that the risks from natural carcinogens are much greater than those posed by traces of pesticide residues or contaminants (Scheuplein, 1990). Methods of storing, preparing and consuming food as well as dietary patterns (protein to fat ratios) also contribute to the high cancer risks.

Table 8-6 lists some of the naturally-occurring carcinogens in food. Natural carcinogens in food and those produced during food preparation have been shown to occur in amounts that exceed environmental exposure levels. For example, certain molds in foods synthesize toxins that are mutagenic or carcinogenic, e.g. aflatoxin, which is found in nuts (peanut butter), wheat, and corn and which appears in cow's milk through food chain exposure (Ames et al., 1987). Consumption of as little as 40 tablespoons of peanut butter has been reported to increase the chance of liver cancer caused by aflatoxin by 1 in a million (Covello, 1989).

Large amounts of hydrazine, a known carcinogen and mutagen, have been found in most edible mushrooms. The most common commercial mushroom (*Agaricus bisporus*) contains about 300 mg of a hydrazine derivative per 100 grams of mushrooms. Formaldehyde is a natural carcinogen that is ubiquitous in foods. Daily consumption of shrimp, bread, cola, and beer in various combinations could result in significant exposure to formaldehyde (Ames et al., 1987).

Cooking of food generates a variety of carcinogenic substances. Carcinogens formed during food processing include: ethyl carbamate (fermentation), nitrosamines (curing, frying, salting, pickling), polynuclear aromatics (broiling meat, smoking), and heterocyclic amines and nitropyrenes (grilling and charring of fish or meat) (Scheuplein, 1990). Intake of nitropyrenes from grilled chicken has been estimated to be much higher than that from air pollution (Sugimura et al., 1986; Kinouchi et

Table 8-4. Occupational Risks of Death

Occupational or Industry	Annual Risk Per Person at Risk
Manufacturing	8.2×10^{-5}
Trade	5.3×10^{-5}
Service and government	1.0×10^{-4}
Transport and public utilities	3.7×10^{-4}
Agriculture (Includes transporation-related accidents)	6.0×10^{-4}
Construction	6.1×10^{-4}
Mining and quarrying	9.5×10^{-4}
Farming	3.6×10^{-4}
Tractor fatalities per tractor	8.8×10^{-5}
Metal mining and milling	9.4×10^{-4}
Nonmetal mining and milling	7.1×10^{-4}
Policeman	2.2×10^{-4}
Railroad employees	2.4×10^{-4}
Fire fighter	8.0×10^{-4}

Adapted from Crouch and Wilson, 1982.

Table 8-5. Risk Estimates of Various Food Categories Containing Carcinogenic Substances

Food Category	Amount of Food Consumed	(Estimated) Amount of Carcinogen Consumed	Risk
Traditional food	1,000 g	1,000 mg	7.61×10^{-2}
Spices and flavors	1.0 g	10 mg	7.61×10^{-4}
Indirects	20 mg	2 mg	1.52×10^{-4}
Pesticides and contaminants	200 µg	0.1 mg	7.61×10^{-6}
Animal drugs	1.0 mg	0.1 mg	7.61×10^{-6}
Food preparation (charred protein only)	1.0 g	0.1 mg	7.61×10^{-6}
Mycotoxins	10 µg	0.001 mg	7.61×10^{-8}
		Total Risk =	7.7×10^{-2}

Adapted from Scheuplein, 1990.

Table 8-6. Naturally Occurring Carcinogens in Food[a]

Food	Carcinogen
Apples	Patulin
Mushrooms	Hydrazines
Parsnips, celery[b]	Psoralens
Cereals, corn, seeds, nuts	Aflatoxins
Plants (herbal teas)	Pyrrolizidine alkaloids
Spinach, beets, lettuce, radishes	Nitrates --> nitrosamines
Phytoplankton (fish and shellfish)	Polyaromatic hydrocarbons
Garlic[b]	Alkyl isothiocyanate
Chilies[b]	Capsaisin
Oranges[b]	d-limonene
Spices:[b]	
Mustard	Allylisothiocyanate
Pepper, nutmeg	Safrole
Cinnamon	Cinnamaldehyde
Smoke	Nitrosamines
Marjoram	Carvacrol
Tarragon	Estragole

a. Compiled from Scheuplein, 1990; Cheeke and Shull, 1985.

b. Foodstuffs or spices with known or suspected carcinogenic activity.

al., 1986). In fact, according to Ames (1983), the amount of burnt material eaten in a typical day is at least several hundred times more than that inhaled from severe air pollution.

Currently, safety information on direct food additives is more available than for most dietary categories because of consumer concern. Direct food additives are not approved by the FDA unless they are either non-carcinogenic or *de minimis* in animal tests; the *de minimis* risk in this context is 10^{-6}. However, saccharin is an exception to this rule because of a Congressional moratorium of an FDA regulation banning its use (Scheuplein, 1990). According to another study (Wilson, 1979), drinking a 12-ounce can of diet soda containing saccharin every day of the year results in an annual cancer risk of 1 in 100,000 (1.0×10^{-5}).

In summary, potential cancer risks are associated with intake of foods containing carcinogenic substances that are naturally occurring, or are formed during cooking and preparation. Comparison of these risk values for common, everyday exposures with proposed acceptable levels of risk, such as 10^{-5} and 10^{-6}, is an effective means of placing risks in perspective.

8.3 The Cost of Compliance with a 10^{-6} Risk Limit

A range of risk levels has been used in U.S. federal and state regulatory decisions. Although, an incremental risk level of 10^{-5} rather than 10^{-6} has often been used by the EPA to protect public health (EPA, 1990d; Rodricks et al., 1987; 55FR 11798-11863), the 10^{-6} risk level is frequently proposed as a universal acceptable level of risk which is protective of human health. Under certain circumstances, the application of an overly conservative risk level may necessitate the implementation of new, expensive technologies and substantially increase the cost of compliance.

When selecting an acceptable level of risk, regulatory officials must take into account the number of people exposed to the risk in question. This principle is a fundamental component public health evaluation. For instance, the currently popular 1×10^{-6} risk standard was originally intended to be protective of the entire U.S. population from exposure to cancer causing contaminants in the food supply. Yet, when localized populations are exclusively exposed to a risk, as is the case with dioxin-contaminated fish, a less stringent numerical standard is adequate to protect the public health. When choosing appropriate risk levels, regulators should also weigh the economic costs and benefits that may be associated with risk reduction. Although some environmental laws try to restrict economic considerations, common sense and studies of regulatory behavior indicate that economic factors play a critical role in environmental decision making. The economic consequences of regulatory decisions must be heeded so that public health is not adversely affected. Public health professionals have recognized for decades that reducing family income impairs public health. The costs of environmental regulation may reduce real family income by increasing the prices of goods and services that all of us purchase, which ultimately causes a reduction in real family incomes. Subsequently, when families have less income, they have less money available for everything from preventive checkups to smoke detectors. If regulatory costs are excessive, the regulator may inadvertently cause more harm to the health status of families than will be prevented.

As a case in point, consider the chlorination of public drinking water supply by municipalities. As a direct result of chlorination, a number of potentially harmful compounds known as trihalomethanes are produced. Most notable of these is chloroform. Based on exposure calculations which assume that the average 70 kg adult ingests 2 liters of water per day (EPA, 1989e), the dose of individual trihalomethanes received in water is associated with risk levels ranging from 1.7×10^{-5} to 3.7×10^{-4} (Table 8-1). In order to comply with a 10^{-6} risk level, treatment systems would have to be modified in order to reduce the levels of these compounds in finished water. Implementation of an activated charcoal filter system is one method which would reduce trihalomethane levels sufficiently to bring the risk associated with these compounds in drinking water into compliance. The life of a charcoal bed and, thus, the cost of system maintenance, is highly dependent upon the level of organic matter entering the treatment system. In a worst-case estimation in which the bed life is only 30 days, use of the charcoal filter water treatment system would raise the cost of municipal drinking water by $1.562 per 1,000 gallons (Adams and Clark, 1989). For a 1,000,000 gallon per day facility supplying water to 3,000 to 4,000 homes, this would result in an added water treatment plant operating cost of $1,562 daily or $570,130 yearly. In an optimal situation in which the water entering the system is low in organic material, a bed life of 730 days would result in a daily system cost of $417 ($152,205 annually) for the same size plant (Adams and Clark, 1989). These costs, as well as costs in the range of $100,000 for the initial installation of the system, would have to be met by municipalities and passed on to the consumers. If an acceptable risk level of 10^{-6} were applied to this industry, municipalities would be faced with a dilemma. Since shutting down the public water treatment facility is not an option, each town and city would need to make costly process changes or apply to the state for an exemption from this regulation.

As a second example of the significant costs of implementing an across-the-board limit of risk, consider the changes that will be required at every gasoline station in the state. In order to reduce occupational exposures to benzene fumes from gasoline to the proposed 10^{-6} risk level, retrofitting of all pump nozzles and underground storage tanks would be required to recover vapors. According to a study conducted by the American Petroleum Institute in 1988 (personal communication, H. Thompson, API, 1990), the cost of retrofitting the average 6 nozzle service station with a vapor collection system ranges from $2,582 to $2,795 per nozzle. These costs would be passed on to the consumer in the form of increased gasoline prices. Likewise, similar types of costly vapor recovery systems would most likely be required at dry cleaning facilities in order to comply with a 10^{-6} risk level.

The food industry provides a final example of the costs of compliance. Based on the discussion presented on risks associated with common activities and consumption of natural carcinogens in food and beverages, many areas could be affected by a universal acceptable risk level of 10^{-6}. The risks associated with exposure to naturally-occurring carcinogenic substances in a number of foods and spices exceed the 10^{-6} level (Table 8-6). The costs of bringing these products into compliance with a 10^{-6} risk level would be high. For example, the aflatoxin mold is a carcinogenic substance which is associated with high moisture crops like peanuts and corn. When crops are subjected to the warm, moist, dark environments which are created during storage and transport, the spore is released and the mold grows. Reduction of aflatoxin levels for the purpose of compliance with a 10^{-6} risk level would require major changes in the technologies involved in storage and transport of fresh crops. Crops would need to be quickly and carefully dried and stored in cool environments in order to prevent release of the spore. Methods of transport to other parts of the country would need to be modified in order to reduce the amount of time the crops are subjected to a moist, warm environment. Without major changes in the way the crops are handled, high percentages of these crops would not be permitted to be sold to consumers, and would need to be discarded. The cost to the consumer would be decreased availability and higher prices. The cost to the farmer or transporter would be significant financial loss.

Based on the approaches taken by the federal and state governments toward regulating chemicals in the environment, the adoption of a single acceptable risk level of 10^{-6} for all substances in all media is excessively conservative and may be technologically, economically and practically infeasible under certain circumstances. Acceptable risk levels need to be based on social, economic and policy issues which are likely to vary by site and by substance.

8.4 Conclusions

The EPA has stated that it is most appropriate to model exposure to the most exposed population (MEP) rather than the most exposed individual (Inside EPA, 1991). As a result, it is population risk, as well as individual risk, that needs to be considered when establishing regulatory standards and cleanup goals. The population risk is the product of the individual risk and the size of the impacted population. When the size of the impacted population is small, the use of a less stringent risk level results in the same net population risk as that derived using a more stringent risk level and a larger population size. To arbitrarily use a 10^{-6} risk level for a small impacted population is overly conservative and not in keeping with regulatory precedents.

The use of the 10^{-6} level of risk has not been a consistent practice at either the federal or state level in risk management decision making. In fact, as has been clearly shown in the preceding discussion, risk management decisions made by the EPA, as well as numerous state agencies, have generally used considerably lower risk levels. It is reasonable that the Oregon risk assessment policies be consistent with and reflect currently accepted practices.

Major business enterprises may be impacted by the establishment of a stringent acceptable risk level, should this risk level be applied to their industry. These industries could then find it necessary to either close their doors or apply for an exemption to the rule. Likewise, municipalities may be required to seek alternate methods to maintain a potable water supply for the general public as an alternative to chlorination which would result in an unacceptable increase in cancer risk. Limits for the acceptable concentrations of hazardous contaminants in groundwater used for human consumption frequently exceed the 10^{-6} risk level.

Imposed unilaterally as a management guideline, a 10^{-6} risk level would be imprudent. The more appropriate approach to risk management decision making should address the issue of acceptable risk on a case-by-case basis.

9.0 RECOMMENDATION FOR A SCIENTIFICALLY SUPPORTABLE WATER QUALITY STANDARD

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) is regulated under the Clean Water Act (CWA). The federal government has mandated that by 1992, all states establish ambient water quality standards for TCDD as one of the 126 "priority pollutants" listed under Section 307(a) of the CWA. One option available to states is to adopt the EPA Ambient Water Quality Criteria (AWQC) as enforceable water quality standards. A number of state agencies have taken this generic approach and have adopted the default values proposed in the EPA's 1984 document, *Ambient Water Quality Criteria for 2,3,7,8-Tetrachlorodibenzo-p-dioxin.*

A second option, as referenced by Section 304(a)(1) of the CWA, is the development of a water quality standard based on the latest scientific knowledge regarding the effects of TCDD on human health and the environment. This option is particularly relevant in light of the recent announcement by EPA Administrator William Reilly that the EPA will conduct a year-long study to reevaluate the risks associated with dioxin exposure (EPA, 1991). In his announcement, Administrator Reilly stated, "our efforts to reduce risk must be based on the best available scientific information" (EPA, 1991).

A number of states including New Hampshire, Virginia, New York, Tennessee, South Carolina, Georgia, Alabama, Arkansas, Texas, Florida and Maryland have chosen to use this approach in developing state-specific standards. New Hampshire and New York have adopted water quality standards of 1 ppq. EPA has recently approved the 1.2 ppq standards for TCDD adopted by Maryland and Virginia. These state-specific standards are substantially different from the 0.013 ppq standard proposed in EPA's "Gold Book".

The EPA AWQC for dioxin (EPA, 1984) for bodies of water from which fish and water are consumed were calculated using the following equation:

$$WQS = (ADI \times BW) / [(BCF \times FCR) + WCR]$$

Where:

WQS	=	Water quality standard (pg/L)
ADI	=	Acceptable daily intake (pg/kg-day)
BW	=	Body weight (kg)
BCF	=	Bioconcentration factor (L water/kg fish)
WCR	=	Water consumption rate (L/day)
FCR	=	Fish consumption rate (kg/day)

When deriving their AWQC for the ingestion of fish and water, the EPA assumed that the maximum allowable dose for humans was 0.006 pg/kg-day based on a linear, non-threshold model. They also assumed a fish consumption rate of 6.5 g/day, a water consumption rate of 2 L/day, a BCF of 5,000, and a human body weight of 70 kg. Using these assumptions, an AWQC of 0.013 pg/L (ppq) was derived.

Since that time, however, considerably more has been learned about the behavior of dioxin. Our scientific understanding of the behavior of TCDD in the environment, in fish, and in humans has evolved to the degree that it would be imprudent for regulators and risk assessors to ignore these factors when establishing health-based regulatory standards. Only through a critical evaluation of these key variables can one derive a reasonable human health-based ambient water quality standard for dioxin.

There have been considerable advances in understanding the mechanism of dioxin's toxicity that have changed the way scientists view its potential effects on human populations. Recent scientific thought indicates that dioxin acts via a threshold mechanism and that its carcinogenic hazard has been overstated. Thus, acceptable dose levels of between 1 and 80 pg/kg-day have been proposed by various state agencies and by the governments of Canada and several western European nations (FDHRS, 1991; WDH, 1991; Ontario, 1985, van der Heijden et al., 1982; NCASI, 1987; UK, 1989; Tollefson, 1991). These dose levels are orders of magnitude greater than the EPA's earlier estimate of 0.006 pg/kg-day. Based on the most current scientific evidence, an ADI of 1 to 10 pg/kg-day is protective of human health. In developing a conservative and health protective water quality criterion, ChemRisk has chosen to use an allowable daily intake level of 1 pg/kg-day.

The rate of fish consumption is an important consideration in developing a water quality standard because the primary route of human exposure to TCDD in aquatic environments is through the ingestion of fish tissue (EPA, 1984). The Columbia River is a unique area due to the large numbers of migratory species that can be obtained commercially and recreationally. The migratory behavior and lipid contents of these fish influence the extent to which TCDD may accumulate in those species. Thus, not only is it important to obtain a rate of fish consumption for the populations of interest, but it is also critical that the particular species of fish consumed by each population be evaluated in the development of a standard.

It appears that Native Americans consume more fish on a daily basis than do recreational anglers. However, because of the species consumed, Native Americans are likely to be exposed to lower amounts of dioxin than are the recreational anglers. Thus, the median consumption rate for recreational anglers, 5.8 g/day, should be used to derive a standard for the State of Oregon.

When EPA (1984) developed its AWQC for TCDD, it used a BCF of 5,000 as a representative multiplier to predict how much dioxin aquatic organisms will accumulate from their surroundings. The BCF approach, however, addresses only the uptake of dissolved compounds across the membranous gill surfaces (EPA, 1989b). Recently, much scientific discussion has focused on the apparent inappropriateness of using the BCF approach in the AWQC equation. Attention has been placed on defining a factor, other than the BCF, which should be used in its place. Ideally, this "accumulation factor" should serve two functions:

(1) realistically predict or estimate the accumulation of sorbed dioxin by aquatic organisms; and,

(2) practically serve as an accumulation multiplier which can be implemented in a regulatory context for the purpose of establishing effluent permit limits.

An empirical approach to develop an accumulation factor that meets these two requirements has resulted in the definition of a Regulatory Bioaccumulation Multiplier or RBM (Sherman and Keenan, 1991). The RBM uses consistent criteria to define exposure concentrations of TCDD, normalizes to a common fish lipid content, and measures TCDD fish concentrations in the edible portion or fillet tissue. The use of the RBM allows regulatory agencies to directly calculate point source limits and obviates the need to apportion dioxin into different parts of the ecosystem (e.g. food, suspended sediment, and dissolved in water) via elaborate modelling techniques. Furthermore, the wide range of reported values for accumulation factors in the literature generally fall below a value of 5,000 when reanalyzed and reported as RBMs. Therefore, an RBM value of 5,000 constitutes the most scientifically-based estimate of bioaccumulation for regulatory purposes in the AWQC equation.

An estimate of 1.2 L/day for water consumption is an appropriate estimate of daily consumption of Columbia River water. Although fluid ingestion rates of 2 L/day were used by the EPA in developing their AWQC, a review of the literature indicates that 2 L/day overestimates consumption by the average individual as it assumes that individuals consume water from a single impacted source for an entire lifetime. There is no consideration of other non-water or bottled beverages consumed or of water consumed from non-impacted sources.

Upon consideration of each of these factors, and an evaluation of the weight of scientific evidence supporting their selection, a scientifically-based and health-protective standard for dioxin can be proposed, using the following equation:

$$WQS = \frac{ADI \times BW}{(RBM \times FCR) + WCR}$$

Where:

WQS	=	Water quality standard (ppq)
ADI	=	Allowable daily intake (pg/kg-day)
BW	=	Body weight (kg)
RBM	=	Regulatory Bioaccumulation Multiplier (l/kg)
FC	=	Fish consumption (kg/day)
WCR	=	Water consumption rate (L/day)

Based on a conservative and health-protective exposure level of 1.0 pg/kg-day, an RBM of 5,000, a fish consumption rate of 5.8 g/day for the "typical" recreational angler, and a water consumption rate of 1.2 L/day, the scientific evidence is supportive of a water quality criterion of 2.3 ppq for the State of Oregon. This represents a scientifically supportable criterion that is fully protective of public health. As it has been shown that NOECs for aquatic species range from 3.5 to 5.8 ppq, this proposed water quality criterion will also be protective of freshwater fish and other aquatic organisms.

10.0 REFERENCES

Adams, W.J., G.M. DeGraeve, T.D. Sabourin, J.D. Cooney and G.M. Mosher. 1986. Toxicity and bioconcentration of 2,3,7,8-TCDD to fathead minnows (Pimephales Promelas). *Chemosphere* 15(9-12): 1503-1511.

Adams, J.Q. and R.M. Clark. 1989. Cost estimates for GAC treatment systems. *J Amer. Water Works Assoc.* 81(1):35-42.

Allen, J.R., J.P. Van Miller and D.H. Norback. 1975. Tissue distribution, accumulation and biological effects of [C14] tetrachlorodibenzo-p-dioxin in rats. *J. Food. Cosmet. Toxicol.* 13: 501-505.

Allen, J.R., D.A. Barsotti, L.K. Lambrecht and J.P. van Miller. 1979. Reproductive effects of halogenated aromatic hydrocarbons on nonhuman primates. *Ann. NY Acad. Sci.* 320: 419-425.

Allman, W.F. 1985. Staying alive in the 20th century: We have nothing to fear. *Science* 6(8):31-41.

AMA. 1984. *The Health Effects of "Agent Orange" and Polychlorinated Dioxin Contaminants: An Update.* American Medical Association, Council on Scientific Affairs Advisory Panel on Toxic Substances, Chicago, IL. Updated 05-29-85.

American Cancer Society. 1989. Cancer Facts and Figures.

Ames, B.N. 1983. Dietary carcinogens and anticarcinogens. *Science* 221:1256-1264.

Ames, B.N., R. Magaw and L.S. Gold. 1987. Ranking possible carcinogenic hazard. *Science* 236: 271-279.

API. 1986. Benzene in Florida Groundwater: An Assessment of the Significance to Human Health. Florida Petroleum Council: A Division of the American Petroleum Institute. October.

Atkinson, C. 1990. Personal communication regarding state of Connecticut hazardous waste site cleanup goals and regulations.

Axelson, O., L. Sundell, K. Anderson, C. Edling, C. Hogstedt and M. Kling. 1980. Herbicide exposure and tumor mortality. *Scand. J. Work Environ. Health* 6: 73-79 (cited in NCASI, 1987).

Barsotti, D.A., L.J. Abrahamson and J.R. Allen. 1979. Hormonal alterations in female Rhesus monkeys fed a diet containing 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Bull. Environ.. Toxicol.* 21: 463-469.

Beak Consultants, Inc. 1989. Human Consumption Rates of Fish from the Columbia River, Project #73296. Prepared for Northwest Pulp & Paper Association. Bellevue, WA., December.

Beatty, P.W., M. A. Holscher and R.A. Neal. 1976. Toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in larval and adult forms of *Rana catesbeiana. Bull. Env. Cont. Toxicol.* 16(5): 578-581.

Birnbaum, Linda. 1990. Consensus at Banbury DIOXIN Conference. United States Environmental Protection Agency. Health Effects Research Laboratory Research Triangle Park, North Carolina.

Bleiberg, J., M. Wallen, R. Brodkin and I.L. Applebaum. 1964. Industrially acquired porphyria. *Arch. Dermatology* 89: 793-797.

Bond, G.G., K.M. Bodner and R.R. Cook. 1989. Phenoxy herbicides and cancer: Insufficient epidemiologic evidence for a causal relationship. *Fund. Appl. Toxicol.* 12: 172-188.

Borton, D. 1991. Memo to W. Gillespie, National Council of the Paper Industry for Air and Stream Improvement (NCASI), regarding: Evaluation of data used by EPA to support a bioconcentration factor (BCF) for 50,000 for 2,3,7,8-TCDD. February 5, 1991.

Bowman, R.E., S.L. Schantz, M.L. Gross and S.A. Ferguson. 1989a. Behavioral effects in monkeys exposed to 2,3,7,8-TCDD transmitted maternally during gestation and for four months of nursing. *Chemosphere* 18(1-6) :235-242.

Bowman, R.E., S.L. Schantz, N.C.A. Weerasinghe, M.L. Gross and D.A. Barsotti. 1989b. Chronic dietary intake of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) at 5 or 25 parts per trillion in the monkey: TCDD kinetics and dose-effects estimate of reproductive toxicity. *Chemosphere 18*(1-6): 235-242.

Branson, D.R. 1983. Letter to C.E. Stephan. Dow Chemical U.S.A., Midland, MI. September 20. (cited in EPA, 1984).

Branson, D.R., I.T. Takahashi, W.M. Parker and G.E. Blau. 1985. Bioconcentration kinetics of 2,3,7,8-tetrachlorodibénzo-p-dioxin in rainbow trout. *Environ. Toxicol. Chem.* 47: 79-788.

Bruzzi, P. 1983. Birth defects in the TCDD polluted area of Seveso: Results of a four-year follow-up. In: *Accidental Exposure to Dioxins, Human Health Aspects.* F. Coulston and F. Pochiari(eds.) Academic Press. New York. 271-280.

California. 1987. Notice of Public Interest: Health and Welfare Agency the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65). State of California, Health and Welfare Agency, Office of the Secretary.

Cantor, K.P., R. Hoover, P. Hartge et al. 1987. Bladder cancer, drinking water source, and tap water consumption: A case-control study. *National Cancer Institute* 79(6): 1269-1279. In: EPA, 1989d.

CDC. 1984. Centers for Disease Control. *Morbidity and Mortality Weekly Report* 33: 54-61 (cited in Kimbrough and Houk, 1987).

CDC. 1990. *The Association of Selected Cancers with Service in the U.S. Military in Vietnam. I. Non-Hodgkin's Lymphoma.* Selected Cancers Cooperative Study Group. March 29, 1990.

Cheeke, P. R. and L. R. Shull. *Natural Toxicants in Feeds and Poisonous Plants.* AVI Publishing Company, Inc. Westport, Connecticut. 1985.

ChemRisk. 1990. Assessment of the Human Health Risks Related to the Presence of Dioxins in Columbia River Fish. ChemRisk™, A Division of McLaren/Hart, Portland, ME. January 8.

ChemRisk. 1991. Consumption of freshwater fish by Maine anglers. ChemRisk™, A Division of McLaren/Hart. March 26, 1991.

CMA. 1988. Chemicals in the Community: Methods to Evaluate Airborne Chemical Levels. Chemical Manufacturers Association, Washington, D.C. May.

Cook, P.M., A.R. Batterman, B.C. Butterworth, K.B. Lodge, and S.W. Kohlbry. 1990. *Laboratory Study of TCDD Bioaccumulation by Lake Trout from Lake Ontario Sediments, Food Chain and Water*. Ch. 6. United States Environmental Protection Agency, Environmental Research Laboratory, Duluth, MN.

Cook, P.M., M.K. Walker, D.W. Kuehl and R.E. Peterson. 1991. Bioaccumulation and toxicity of 2,3,4,8-tetrachlorodibenzo-p-dioxin and related compounds in aquatic ecosystems. Preprint.

Cooper, K.R., J. Schell, P. Kahn and M. Gallo. 1986. The effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on the development and survival of the Japanese Medaka (Oryzias latipes). Abstract No. 108. In: *The Toxicologist* Abstracts of the 25th Anniversary Meeting of the Society of Toxicology. Vol. 6 (1), March.

Cooper, K.R. 1989. Effects of Polychlorinated Dibenzo-p-Dioxins and Polychlorinated Dibenzofurans on Aquatic Organisms. Reviews in Aquatic Sciences 1(2):227-242.

Covello, V.T. 1989. Communicating right-to-know information on chemical risks. *Environ. Sci. Tech.* 23(12): 1444-1449.

Crow, K.D. 1981. Chloracne and its potential clinical implications. *Exper. Dermatol.* 6243-257.

Crouch, E.A.C. and R. Wilson. 1982. Risk/Benefit Analysis. Ballinger Publishing Company. Cambridge, MA.

Dean, J. and R. Kimbrough. 1986. *Immunotoxicity of the Chlorinated Dibenzodioxins and Dibenzofurans. In Report of the Dioxin Update Committee. Convened by EPA Office of Pesticides and Toxic Substances.* Dioxin Update Conference, July 1-2.

Derby, S.L. and R.L. Keeney. 1981. Risk analysis: Understanding 'How safe is safe enough?' *Risk Anal.* 1(3): 217-224.

DHHS. 1989. *Fifth Annual Report on Carcinogens Summary 1989.* U.S. Department of Health and Human Services, Public Health Service. Washington, DC.

Doll, R and R. Peto. 1981 *J. Natl. Cancer Inst.* 66:1193-1308 (as cited in Gough, 1989).

Endicott, D.D., W.L. Richardson and D.M. Di Toro. 1988. Lake Ontario TCDD modeling report. U.S. Environmental Protection Agency, Washington, DC.

EPA. 1983. Dow Chemical Company - Midland Plant Wastewater Characterization Study. Preliminary summary of results. U.S. EPA Region V, Environmental Sciences Division, Eastern District Office. March 28. (as cited in EPA, 1984).

EPA. 1984. *Ambient Water Quality Criteria for 2,3,7,8-tetrachloro-dibenzo-p-dioxin*. EPA 440/5-84-007. Office of Water Regulations and Standards, U.S. Environmental Protection Agency. Washington, D.C.

EPA. 1985. *Health Assessment Document for Polychlorinated Dibenzo-p-dioxins.* Office of Health and Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC. EPA/600/8-84/014F. September.

EPA. 1986. *Development of Risk Assessment Methodology for Land Application and Distribution and Marketing of Municipal Sludge.* Prepared by Environmental Protection Agency. EPA/600/8-86/018A. June.

EPA. 1988a. *A Cancer Risk-Specific Dose Estimate for 2,3,7,8-TCDD.* U.S. EPA, Office of Health and Environmental Assessment, Washington, DC. EPA 600/6-88/007A. June.

EPA. 1988b Harmonic Mean Design Flows. Memorandum from Lewis A. Rossman to the record, December 9. U.S. Environmental Protection Agency Office of Research and Development, Risk Reduction Engineering Laboratory.

EPA. 1988c. *Interim Sediment Criteria Values for Nonpolar Hydrophobic Organic Contaminants.* U.S. Environmental Protection Agency. May.

EPA. 1989a. *Assessing human health risks from chemically contaminated fish and shellfish - A guidance manual.* U.S. Environmental Protection Agency, Office of Water Regulations and Standards. EPA 503/8-89-002. September.

EPA. 1989b. *Interim Procedures for Estimating Risks Associated with Exposure to Mixtures of Chlorinated Dibenzo-p-Dioxins and Dibenzofurans (CDDs and CDFs) a 1989 Update.* Risk Assessment Forum. U.S. Environmental Protection Agency, Washington, DC. EPA/625/3-89/016.

EPA. 1989c. *Exposure Factors Handbook.* U.S. Environmental Protection Agency, Office of Health and Environmental Assessment. EPA/600/8-89/043. July.

EPA. 1989d. *Risk assessment guidance for Superfund. Volume I: Human health evaluation manual (Part A).* Interim Final. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. EPA/540/1-89-002. December.

EPA. 1989e. *Risk Assessment Guidance for Superfund. Volume II: Environmental Evaluation Manual.* U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. EPA 540/1-89/001. March.

EPA. 1989f. *Health Affects Assessment Summary Tables.* Fourth Quarter. U.S. Environmental Protection Agency.

EPA. 1990a. *Risk Assessment for 2,3,7,8-TCDD and 2,3,7,8-TCDF Contaminated Receiving Waters From U.S. Chlorine-Bleaching Pulp and Paper Mills.* U.S. Environmental Protection Agency. August 1990.

EPA. 1990b. Technical support document for EPA's September 12, 1990 Approval/Disapproval of Maryland's Water Quality Standards revision. U.S. Environmental Protection Agency.

EPA. 1990c. Red Border Review of Proposed Revisions to National Contingency Plan. U.S. Environmental Protection Agency.

EPA. 1990d. *Reducing risk: setting priorities and strategies for environmental protection. Science Advisory Board.* SAB-EC-90-021. U.S. Environmental Protection Agency. Washington, D.C. September.

EQC. 1990. Authorization for rulemaking hearing: Proposed amendments to water quality standards as part of the triennial review required by the Clean Water Act. Environmental Quality Commission, State of Oregon. November 2.

Eriksson, J., L. Hardell, N. Berg and et. al. 1981. Soft-tissue sarcomas and exposure to chemical substances; a case-reference study. *Br. J. Indus. Med.* 38: 27-33.

Evans, R.G., K.B. Webb, A.P. Knutsen, S.T. Roodman, D. Roberts, J. Bagby, W.A. Garrett and J.S. Andrews. 1987. A medical follow-up of the health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Seventh International Symposium of Chlorinated Dioxins and Related Compounds. Las Vegas, NV.

Faccetti, S., A. Fornari, M. Montagna. 1981. Distribution of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the tissues of a person exposed to the toxic cloud of Seveso. *Forens. Environ. Appl.*. 1: 1405-1414. (as cited in WDH, 1991).

FDA. 1983. Statement by Sanford A. Miller, Ph.D., Director, Bureau of Foods, Food and Drug Administration, before the subcommittee on Natural Resources, Agriculture, Research and Environment, Committee on Science and Technology, U.S. House of Representatives. June 30.

Fingerhut, M.A., W.E. Halperin, D.A. Marlow, L.A. Piacitelli, P.A. Honchar, M.H. Sweeney, A.L. Greife, P.A. Dill, K. Steenland and A.J. Suruda. 1991a. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *N.Eng. J. Med.* 324(4): 212-218.

Fingerhut, M.A., W.E. Halperin, D.A. Marlow, L.A. Piacitelli, P.A. Honchar, M.H. Sweeney, A.L. Greife, P.A. Dill, K. Steenland and A.J. Suruda. 1991b. *Mortality among U.S. workers employed in the production of chemicals contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD).* U.S. Department of Health and Human Services, National Institute for Occupational Safety and Health. January.

Fishbein, L. 1987. Health-risk estimates for 2,3,7,8-tetrachlorodibenzodioxin: An overview. *Tox. and Ind. Health* 3(1): 91-134.

Gallo, M. 1990. Statement on the outcome of The Banbury conference. "Biological Basis for Risk Assessment of Dioxins and Related Compounds".

Gammage, R.B. 1990. Exposure to formaldehyde in indoor air. *Risk Anal.* 10(1): 77-83.

Gasiewicz, T.A., J.R. Olson, L.E. Geiger and R.A. Neal. 1983. Absorption, distribution and metabolism of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in experimental animals. In: *Human and Environmental Risks of Chloroinated Dioxins and Related Compounds.* R.E. Tucker, A.L. Young and A.P. Gray(eds.) Plenum Press. New York. 495-525.

Gillies, M.E. and H.V. Paulin, 1983. Variability of mineral intakes from drinking water: A possible explanation for the controversy over the relationship of water quality to cardiovascular disease. *International Journal of Epidemiology* 12(1): 45-50. In: EPA, 1989c.

Gobas, F.A.P.C., W.Y. Shu and D. Mackay. 1987. *Factors Determining Partitioning of Hydrophobic Organic Chemicals in Aquatic Organisms.* D. Reidel Publishing Company. New York.

Gobas, F.A.P.C., Derek C.G. Muir and Donald Mackay. 1988. Dynamics of dietary bioaccumulation and faecal elimination of hydrophobic organic chemicals in fish. *Chemosphere* 17(5): 943-962.

Gobas, Frank A.P.C., Kathryn E. Clark, Wan Ying Shu and Donald Mackay. 1989. Bioconcentration of polybrominated benzenes and biphenyls and related superhydrophobic chemicals in fish: Role of bioavailability and elimination into the feces. *Environ. Tox. Chem.* 8: 231-245.

Goeden, H.M. and A.H. Smith. 1989. Estimation of human exposure from fish contaminated with dioxins and furans emitted by a resource-recovery facility. Risk Analysis 9(3): 377-383.

Goldstein, B.D. and N. Kim. 1989. Letter to Dr. Raymond C. Loehr, Chairman, Executive Committee of the Science Advisory Board. November 28. U.S. EPA, Washington, D.C.

Gough, M. 1990. How much cancer can EPA regulate away? *Risk Analysis.* 10(1): 1-6.

Gough, M. 1989. Estimating Cancer Mortality. Environ. Sci. Technol. 23(8): 925-930.

Graham, J.D. 1990. Letter to Dean C. Marriott. Commissioner, Department of Environmental Protection for the State of Maine. October.

Greenlee W.F., T.R. Skopek, K. Gaido and C. Walker. 1990. Comparative genetic mechanisms of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)-induced tumors. In: Mouse Liver Carcinogenesis: Mechanisms and Species Comparison D.E. Stevenson, J.A. Pop, J.M. Ward, R.M. McClain, T.J. Slaga, H.C. Pitot (eds). Alan R. Liss, Inc. NY, NY.

Greenwald, P., B. Kovasznay, D. Collins and G. Therriault. 1984. Sarcomas of soft tissue after Vietnam service. *JNCI* 73: 1107-1109.

Grieg, J.B. and F. Dematteis. 1973. Effects of TCDD on drug metabolism and hepatic microsomes in rats and mice. *Environ. Health Perspect.* 5: 211-219. (as cited in WDH, 1991).

Hardell, L., M. Eriksson, P. Lenner and E. Lundgren. 1981. Malignant Lymphoma And Exposure To Chemicals, Especially Organic Solvents, Chlorophenols And Phenoxy Acids: A Case-Control Study. *Br. J. Cancer* 43: 169-176.

Hardell, L. and A. Sandstrom. 1979. Case-control study: Soft-tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. *Br. J. Cancer* 39: 711-717.

Hawkes, C.L. and L.A. Norris. 1977. Chronic oral toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) to rainbow trout. *Trans. Am. Fish. Soc.* 106(6): 641-645.

Helder, T. 1980. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on early life stages of pike (Esox lucius L.). Sci. Total Environ. 14(3): 255-265.

Helder T. 1981. Effects of 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD) on early life stages of rainbow trout (Salmo gairdneri Richardson). Toxicol. 19: 101-112.

Hoar, S., A. Blair, F. Holmes, C. Boysen, R. Robel, R. Hoover and J. Fraumeni. 1986. Agricultural herbicide use and risk of lymphoma and soft-tissue sarcoma. *JAMA* 256(9): 1141-1147.

Hobson, L.B. 1984. Human effect of TCDD exposure. *Bull. Environ. Contam. Toxicol. 33*:696-701.

Hoffman, R.E., P.A. Stehr-Green, K.B. Webb, R.G. Evans, A.P. Knutsen, W.F. Schramm, J.L. Staake, B.B. Gibson and K.R. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *JAMA* 255: 2031-2038.

Holloway, M. 1990. A Great Poison. Science and the Citizen. *Sci. Am.* November, 1990.

Honstead, J.F., T.M. Beetle and J.K. Soldat. 1971. A Statistical Study of the Habits of Local Fishermen and Its Application to Evaluation of Environmental Dose, A Report to the Environmental Protection Agency by Battelle Pacific Northwest Laboratories, Richland, WA 99352. (cited in TetraTech, 1986).

Humphrey, H.E.B. 1978. Personal communication. (as cited in Rupp, 1980).

Hutt, et al. 1978. (as cited in Rodericks and Taylor, 1983).

IARC. 1987. Evaluation of Carcinogenic Risks to Humans. In: supplement 6. Volumes 1 to 42. International Agency for Research on Cancer. Lyon, France.

ICRP. 1974. Report of the Task Group on Reference Man. International Commission on Radiological Protection.

Inside EPA. 1991. New, Less Conservative EPA Risk Model Could Spawn Less Stringent Results. Inside EPA Weekly Report. Volume 12(13): 1. March 29.

Javitz, H. 1980. Seafood consumption data analysis. SRI Internatinal. Final report prepared for EPA Office of Water Regulations and Standards. EPA Contract 68-01-3887.

Jirasek, L., J. Kalensky and K. Kubec. 1973. Acne chlorina and porphyria cutanea tarda during the manufacture of herbicides. *Cesk. Dermatol.* 48: 306-317. (as cited in UAREP, 1988).

Jirasek, L. J. Kalensky, K. Kubec, J. Pazderove and E. Lukes. 1974. Acne chlorina, porphyria cutanea tarde and other manifestations of general poisoning during the manufacture of herbicides. II. *Cesk. Dermatol.* 49: 145-157. (as cited in UAREP, 1988).

Kang, H.K., L. Weatherbee, P. Breslin, Y. Lee and B.M. Shepard. 1986. Soft-tissue sarcomas and military service in Vietnam: A case comparison group analysis of hospital patients. *J. Occupational Med.* 28: 1215-1218.

Keenan, R.E., R.J. Wenning, A.H. Parsons and D.J. Paustenbach. 1990a. A re-evaluation of the tumor histopathology of Kociba et al. (1978) using 1990 criteria: Implications for the risk assessment of 2,3,7,8-TCDD using the linearized multi-stage model. Proceedings Dioxin '90. Tenth International Conference on Organohalogen Compounds, Volume 1: EPRI Seminar Toxicology-Environment, Food, Exposure-Risk, ed by O. Hutzinger and H. Fiedler, pp. 549-554. Ecoinforma Press, Bayreuth, FRG.

Keenan, R.E., A.H. Parsons, E.S. Ebert, R.J. Wenning, and D.J. Paustenbach. 1990b. Setting rational health-based water quality standards for dioxin risk assessment for the Columbia River. Proceedings, 1990 TAPPI Conference.

Keenan, R.E., D.J. Paustenbach, R.J. Wenning and A.H. Parsons. 1991a. A re-evaluation of the tumor histopathology of Kociba et al. (1978) using 1990 criteria: Implications for the risk assessment of 2,3,7,8-TCDD using the linearized multi-stage model. *Chemosphere* (Submitted).

Keenan, R.E., D.J. Paustenbach, R.J. Wenning and A.H. Parsons. 1991b. A pathology re-evaluation of the Kociba et al. (1978) bioassay of 2,3,7,8-TCDD. Implications for risk assessment. Submitted to *J. Tox. Env. Health* November 27, 1990.

Kenaga, E.E. 1980. Correlation of bioconcentration factors of chemicals in aquatic and terrestrial organisms with their physical and chemical properties. *Amer. Chem. Society* 14(5): 553-556.

Kenaga, E.E. and C.A.I. Goring. 1980. Relationship between water solubility, soil sorption, octanol-water partitioning, and concentration of chemicals in biota. In: *Aquatic Toxicology* J.C. Eaton, P.R. Parrish and A.C. Hendricks (eds). American Society for Testing and Materials. p. 78-115.

Kimbrough, R., H. Falk, P. Stehr and G. Fries. 1984. Health implications of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) contamination of residential soil. *J. Toxicol. Environ. Health* 14: 47-93.

Kimbrough, R.D. 1990. How toxic is 2,3,7,8-tetrachlorodibenzodioxin to humans? *J. Tox. Environ. Health* 30: 261-271.

Kimbrough, R.D. 1991. Examining and communicating risk from dioxin exposure. Proceedings, 1991 Rifkin Conference, Washington D.C. May 9-10.

Kimbrough, R.D. and V.N. Houk. 1987. Effects of Chlorinated Dibenzodioxins. In: *Solving Hazardous Waste Problems*. American Chemical Society(eds.) Washington, DC. 68-79.

Kinouchi, T., H. Tsutsui, Y. Obnishi. 1986. *Mutat. Res.* 171: 105. (as cited in Ames et al., 1987).

Klaassen, C.D., M.O. Amdur and J. Doull. 1986. Casarett and Doull's Toxicology. MacMillan Publishing Company, New York.

Kleeman, J.M., J.R. Olson, S.M. Chen and R.E. Peterson. 1986a. Metabolism and disposition of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rainbow trout. Toxicol. & Appl. Pharm. 83: 391-401.

Kleeman, J.M., J.R. Olson, S.M. Chen and R.E. Peterson. 1986b. 2,3,7,8-Tetrachlorodibenzo-p-dioxin metabolism and disposition in Yellow Perch. Toxicol. & Appl. Pharm. 83: 402-411.

Kleeman, J.M., J.R. Olson and R.E. Peterson. 1988. Species differences in 2,3,7,8-tetrachlorodibenzo-p-dioxin toxicity and biotransformation in fish. *Fund. Appl. Tox.* 10: 206-213.

Kociba, R. and B. Schwetz. 1982. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Drug Metab. Rev.* 13(3): 387-406.

Kociba, R.J. 1984. Summary and Critique of Rodent Carcinogenicity Studies of Chlorinated Dibenzo-p-dioxins. In: *Public Health Risks of the Dioxins*. W.W. Lowrance (ed.) William Kaufmann, Los Altos. 77-98.

Kociba, R. and O. Cabey. 1985. Comparative toxicity and biologic activity of chlorinated dibenzo-p-dioxins and furans relative to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Chemosphere* 14(6/7): 649-660.

Kociba, R.J., D.G. Keyes, J.E. Beyer, R.M. Carreon, C.E. Wade, D.A. Dittenber, R.P. Kalnins, L.E. Frauson, C.N. Park, S.D. Barnard, R.A. Hummel and C.G. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicol. Appl. Pharmacol.* 46: 279-303.

Kuehl, D W., P. M. Cook, A. R. Batterman, D Lothenbach and B. C. Butterworth. 1987. Bioavailability of polychlorinated dibenzo-p-dioxins and dibenzofurans from contaminated Wisconsin River sediment to carp. *Chemosphere* 16(4): 667-678.

Lakind, J. and E. Rifkin. 1990. Current method for setting dioxin limits in water requires reexamination. *Environ. Sci. Technol.* 24(7): 963-965.

Landolt, M.L., F.R. Hafer, A. Nevissi, G. van Belle, K. Van Ness, and C. Rockwell. 1985. Potential toxicant exposure among consumers of recreationally caught fish from urban embayments of Puget Sound. NOAA Technical Memorandum NOS OMA 23. National Oceanic and Atmospheric Administration, Rockville, MD.

Landolt, M.L., D.L. Kalman, A. Nevissi, G. van Belle, K. Van Ness, and F.R. Hafer. 1987. Potential toxicant exposure among consumers of recreationally caught fish from urban embayments of Puget Sound. NOAA Technical Memorandum NOS OMA 33. National Oceanic and Atmospheric Administration, Rockville, MD.

Lathrop, G.D., W.H. Wolfe, S.G. Machado, J.E. Michalek, T.G. Karrison, J.C. Miner, W.D. Grubbs, M.R. Peterson and W.F. Thomas. 1987. *Air Force Health Study: An Epidemiologic Investigation of Health Effects in Air Force Personnel Following Exposure to Herbicides.* Science Applications International Corporation, VA and Epidemiology Division, United States Air Force. October.

Lehnert, V.G. and D. Szadkowski. 1986. The Carcinogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in humans: Evaluation of liability. *Arbeitsmed. Sozialmed. Praventivmed.* 21: 153-175 (cited in UAREP, 1988).

Leung, H.W., D.J. Paustenbach, F.J. Murray, M.E. Anderson. 1990. A physiological pharmacokinetic description of the tissue distribution and enzyme induction properties of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the rat. *Toxicol. Appl. Pharmacol*. 103: 399-410.

Lodge, K.P. and P.M. Cook. 1989. Partitioning studies between the sediment and water: The measurement of Koc for Lake Ontario sediment. *Chemosphere* 19(1-6): 439-444.

Maine-DHS. 1988. Policy for Identifying and Assessing the Health Risks of Toxic Substances. Maine Department of Human Services, Environmental Toxicology Program, Division of Disease Control, Bureau of Health. 1: 310.1012. February.

Maronpot, R.R., C.A. Montgomery Jr., G.A. Boorman and E.E. McConnell. 1986. National Toxicology Program nomenclature for hepatoproliferative lesions of rats. *Toxicol. Path.* 14(2): 263-273.

Mass DEQE. 1988. Massachusetts Contingency Plan Fact Sheet Waiver of Department Approvals for Non-Priority Disposal Sites (310 CMR 40.533). Commonwealth of Massachusetts, Executive Office of Environmental Affairs, Department of Environmental Quality Engineering, Division of Hazardous Waste. April.

Mastroiacovo, P., A. Spagnolo, E. Marni, L. Meazza, R. Bertollini and G. Segni. 1988. Birth defects in the Seveso area after TCDD contamination. *JAMA* 259(11): 1668-1672.

Mausner, J.S. and S. Kramer. 1985. *Epidemiology.* W.B. Saunders Company. Philadelphia, PA. 361 p.

McConnell, E.E., H.A. Solleveld, J.A. Swenberg and G.A. Boorman. 1988. Guidelines for combining neoplasms for evaluation of rodent carcinogenesis studies. In: *Carcinogenicity: The Design, Analysis and Interpretation of Longterm Animal Studies. ILSI Monographs.* H.C. Grice and J.L. Cimineri(eds.) Springer-Verlag. New York, NY. 183-196.

McKim, J., P. Schmeider and G. Veith. 1985. Absorption dynamics of organic chemical transport across trout gills as related to octanol-water partition coefficient. *Tox. Appl. Pharm.* 77: 1-10.

McNulty, W.P. 1984. Fetotoxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) Rhesus macaques (Macaca mulatta). *Am. J. Primatol.* 6: 41-47.

Mehrle, P.M., D.R. Buckler, E.W. Little, L.M. Smith, J.D. Petty, P.H. Peterman, D.L. Stalling, G.M. De Graeve, J.J. Coyle and W.J. Adams. 1988. Toxicity and bioconcentration of 2,3,7,8-tetrachlorodibenzodioxin and 2,3,7,8-Tetrachlorodibenzofuran in rainbow trout. *Environ. Tox. Chem.* 7: 47-62.

Meunz, L.R. and B. Peterson. 1990. Final report on the analysis of fish consumption data. Technical Assessment Systems, INC. Prepared for U.S. Environmental Protection Agency. August 3, 1990.

Miller, R.A., L.A. Norris and C.L. Hawkes. 1973. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in aquatic organisms. Environ. Health Perspect. 5: 177-186.

Miller, R.A., L.A. Norris and B.R. Loper. 1979. The response of coho salmon and guppies to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in water. *Trans. Am. Fish. Soc.* 105: 401-407.

Moore, L.W., H. Matheny, T. Tyree, D. Sabatini and S.J. Klaine. 1988. Agricultural runoff modeling in a small west Tennessee watershed. *J. WPCF* 60(2): 242-249.

Mower, B. 1990. Maine's Dioxin monitoring program. 1988-1990. December.

Murray, F.J., F.A. Smith, K.D. Nitschke, C.G. Humiston, R.J. Kociba and B.A. Schwetz. 1979. Three-generation reproductive study of rats given 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the diet. *Toxicol. Appl. Pharmacol.* 50: 241-252.

Murphy, M. 1990. Personal communication regarding state of Massachusetts regulations.

NAS. 1983. *Risk Assessment in the Federal Government: Managing the Process.* National Academy Press. Washington, DC.

NCASI. 1987. *Dioxin: A Critical Review of its Distribution, Mechanism of Action, Impacts on Human Health, and the Setting of Acceptable Exposure Limits.* National Council of Paper Industry for Air and Stream Improvement, Inc., New York. NCASI Technical Bulletin No. 524.

NCASI. 1991. Attached submittal to EPA of information derived from the NCASI experimental streams program on estimated 'No Effect' concentrations of TCDD/TCDF on fish. Memorandum from W.J. Gillespie to Corporate Dioxin Contacts Operating Committee. National Council of the Paper Industry for Air and Stream Improvement, Inc. January 4.

Nebert, D.W. and N.M. Jensen. 1979. The Ah locus; genetic regulation of the metabolism of carcinogens, drugs, and other environmental chemicals by cytochrome P-450-mediated monooxygenases. *CRC Crit. Rev. Biochem.* 6:401-437. (as cited in WDH, 1991).

Neely, W. B. 1979. Estimating rate constants for the uptake and clearance of chemicals by fish. *Environ. Sci. Technol.* 13(12): 1506-1510.

Neely, W.B. 1983. Letter to C.E. Stephan. Dow Chemical U.S.A. , Midland, MI. June 10. (as cited in EPA, 1984).

Nessel, C.S., M.A. Amoruso, T.H. Umbreit and M.A. Gallo. 1990. Hepatic Aryl hydrocarbon hydroxylase and cytochrome P450 induction following the transpulmonary absorption of TCDD from intratracheally instilled particles. *Fund. Appl. Toxicol.* 15(3): 500-509.

Niimi, A.J. and B.G. Oliver. 1986. Biological half-lives of chlorinated dibenzo-p-dioxins and dibenzofurans in rainbow trout. Environ. Toxicol. Chem. 5: 49-53.

Nisbet, I.C.T. and M.B. Paxton. 1982. Statistical aspects of three-generation studies of the reproductive toxicity of TCDD and 2,4,5-T. *Am. Stat.* 36(3): 290-298.

NMFS. 1989. *Fisheries of the United States, 1988.* National Oceanic and Atmospheric Administration National Marine Fisheries Service. Current Fishery Statistics No. 8800. U.S. Department of Commerce, Washington, D.C. May.

Norris, L.A. and R.A. Miller. 1974. The toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in guppies (poecilia retiulatus peters). *Bull. Environ. Contamin. Tech.* 12(1): 76-80.

Nygren, M., C. Rappe, G. Lindstrom, M. Hansson, P-A. Bergqvist, S. Marklund, L. Domellof, L. Hardell and M. Olsson (1986). Identification of 2,3,7,8-substituted polychlorinated dioxins and dibenzofurans in environmental and human samples. In: Chlorinated Dioxins and Dibenzofurans in Perspective. C. Rappe, G. Choudhary, L.H. Keith, eds. Lewis Publishers, Inc., Chelsea, Michigan.

ODFW/WDF. 1989. Status Report: Columbia River Fish Runs and Fisheries, 1960-89. Oregon Department of Fish and Wildlife and Washington Department of Fisheries, August.

ODFW/WDF. 1990. Status Report: Columbia River Fish Runs and Fisheries, 1960-89. Oregon Department of Fish and Wildlife and Washington Department of Fisheries, December.

Olson, J.R., T.A. Gasiewicz and R.A. Neal. 1980. Tissue distribution, excretion, and metabolism of 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD) in the Golden Syrian hamster. *Toxicol. Appl. Pharmacol.* 56: 78-85.

Ontario Ministry of the Environment. 1985. *Polychlorinated Dibenzo-p-Dioxins (PCDDs) and Polychlorinated Dibenzofurans (PCDFs).* Intergovernmental Relations and Hazardous Contaminants Coordination Branch. Scientific Criteria Document for Standard Development No. 4-84. September.

OSHA. 1989. OSHA-final rule air contaminants-permissible exposure limits (Title 29 Code of Federal Regulations Part 1910.1000). Am. Ind. Hyg. Assoc.

Palisade Corp. 1990. @Risk. Risk Analysis and Simulation Add-In for Mircrosoft Excel. Windows or Apple Macintosh Version. Palisade Corporation. December 1.

Parsons, A.H., S.L. Huntley, E.S. Ebert, E.R. Algeo and R.E. Keenan. 1991. Risk Assessment for dioxin in Columbia River Fish. *Chemosphere* (submitted).

Patterson, D.G. Jr., L. Hampton, C.R. Lapeza Jr., W.T. Belser, V. Green, L. Alexander and L.L. Needham. High-resolution gas chromatographic/high-resolution mass spectrometric analysis of human serum on a whole-weight and lipid basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Anal. Chem.* 59: 2000-2004.

Paustenbach, D.J. 1989a. Health risk assessments: Opportunities and pitfalls. *Columbia J. Environ. Law* 14: 379-410.

Paustenbach, D.J. 1989b. Important recent advances in the practice of health risk assessments: Implications for the 1990s. *Reg. Tox. Pharm.* 10: 204-243.

Pazderova-Vejlupkova, J., M. Nemcova, J. Pickova, L. Jirasek and E. Lukas. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxins in men. *Arch. Environ. Health* 36(1): 5-11.

Pearce, N.E., A.H. Smith and D.O. Fisher. 1985. Malignant lymphoma and multiple myeloma linked with agricultural occupations in a New Zealand Cancer Registry-based study. *Amer. J. Epidemiology* 121: 225-237.

Pearce, N.E, A.H. Smith, J.R. Howard, R.A. Sheppard, H.J. Giles and C.A. Teague. 1986. Non-Hodgkin's lymphoma, and exposure to phenoxy herbicides, chlorophenols, fencing work and meat works employment: A case control study. *Br. J. Ind. Med.* 43: 75-83.

Pennington, J.A.T. 1983. Revision of the total diet study food list and diets. J. Amer. *Dietetic Assoc.* 82(2): 166-173.

Poland, A.P., E. Glover, A.S. Kende, M. DeCamp and C.M. Giandomenico. 1976. 3,4,3',4'-tetrachloro azoxybenzene and azobenzene: Potent inducers of aryl hydrocarbon hydroxylase. *Science* 194: 627-630.

Poland, A.P. and J.C. Knutson. 1982. 2,3,7,8-Tetrachlorodibenzodioxin; rates of volatilization and photolysis in the environment. *Environ. Sci. & Tech.* 20: 490-492.

Poland, A.P., D. Smith, G. Metter and P. Possick. 1971. A health survey of workers in a 2,4-D and 2,4,5-T plan with special attention to chloracne, porphyria cutanea tarda, and psychological parameters. *Arch. Environ. Health* 22: 316-327.

Poland A.P., J. Knutson, and E. Glover. 1985. Studies on the mechanism of action of halogenated aromatic hydrocarbons. *Clin. Physiol. Chem.* 3: 157-174.

Poland, A. P., P. Greiger and E. Glover. 1990. Factors affecting the elimination rate of [I125I] -2-iodo-3,7,8-trichlorodibenzo-p-dioxin in mice as determined by whole body counting. (Manuscript in prep.)

Puffer, H.W., S.P. Azen, M.J. Duda and D.R. Young. 1981. Consumption rates of potentially hazardous marine fish caught in the metropolitan Los Angeles area. University of Southern California School of Medicine for Environmental Research Laboratory, U.S. Environmental Protection Agency. Grant No. R. 807 120010.

PWG. 1990a. *Pathology Working Group Report on 2,3,7,8-Tetrachlorodibenzo-p-dioxin Chronic Toxicity/Carcinogenicity Study in Sprague-Dawley Rats.* Prepared by R.M. Sauer, PWG Chairperson, PATCHO, INC. and submitted to R.A. Michaels, Chairperson, Maine Scientific Advisory Panel. March 13.

PWG. 1990b. *Hepatotoxicity in Female Sprague-Dawley Rats Treated with 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD).* Prepared by R.M. Sauer, PWG Chairperson, and D.G. Goodman, PATHCO, INC. and submitted to R.A. Michaels, Chairperson, Maine Scientific Advisory Panel. April 27.

Rand, G.M. and S.R. Petrocelli. 1985. *Fundamentals of Aquatic Toxicology*. Hemisphere Publishing Corp., New York, NY.

Reggiani, G. 1978. Medical problems raised by the TCDD contamination in Seveso, Italy. *Arch. Toxicol.* 40: 161-188.

Reggiani, G. 1980. Acute human exposure to TCDD in Seveso, Italy. *J. Toxicol. Environ. Health* 6(10):27-43.

Rifkin, E. and J. Lakind, 1991 Dioxin Bioaccumulation: Key to a sound risk assessment methodology. *J. Toxi col. Env. Health.* (submitted).

Roberts, L. 1991. Flap erupts over dioxin meeting. *Science* 251: 866-867.

Rodricks, J.V. and M.R. Taylor. 1983. Role of risk assessment to food safety decision making. *Reg. Tox. Pharm.* 3:275-284, 302-307.

Rodricks, J.V., S.M. Brett and G.C. Wrenn. 1987. Significant risk decisions in federal regulatory agencies. *Reg. Tox. Pharm.* 7:307-320.

Rodricks, J.V. and M.R. Taylor. 1989. Comparison of risk management in U.S. regulatory agencies. *J. Hazmat* 21:239-253.

Rupp, Elizabeth M. 1980. Age Dependent Values of Dietary Intake for Assessing Human Exposures to Environmental Pollutants. *Health Physics 39*:151-163.

Rupp, E.M., F.L. Miller and I.C.F. Baes. 1980. Some results of recent surveys of fish and shellfish consumption by age and region of U.S. residents. *Health Physics 39*:165-175.

Ryan, J.J., A. Schecter, R. Lizotte, W. Sun and L. Miller. 1985. Tissue distribution of dioxins and furans in humans from the general population. *Chemosphere 14*(6/7):929-932.

Safe, S.H. 1986. Comparative toxicology and mechanism of action of polychlorinated dibenzo-p-dioxins and dibenzofurans. *Annu. Rev. Pharmacol. Toxicol.* 26:371-399. (as cited in WDH, 1991).

Schantz, S.L., D.A. Barsotti and J.R. Allen. 1979. Toxicological effects produced in nonhuman primates chronically exposed to 50 part per trillion 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Abstract # 360, In: *Abstracts of the Eighteenth Annual Meeting*, Society of Toxicology Applied Pharmacology.

Schantz, S.L., N.K. Laughlin, H.C. Van Valkenberg and R.E. Bowman. 1986a. Maternal care by Rhesus monkeys of infant monkeys exposed to either lead or 2,3,7,8-tetrachlorodibenzo-p-dioxin. *NeuroToxicology* 7(2):637-650.

Schantz, S.L., R.E. Bowman, S.A. Ferguson, M.C. VanValkenberg and E.M. Boehm. 1986b. Discrimination-reversal learning in offspring of rhesus monkeys exposed to low levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Soc. for Neurosci. Abstracts 12* (November):

Scheuplein, R.J. 1990a. Statement on the outcome of The Banbury Conference"Biological Basis for Risk Assessment of Dioxins and Related Compounds".

Scheuplein, R.J. 1990b. Perspectives on Toxicological Risk: An Example: Food-Borne Carcinogenic Risk. Food and Drug Administration.

Sherman, W. 1990. Personal communication. Maine Science Advisory Panel.

Sherman, W.R.and R.E. Keenan. 1991. A comparison of pure water bioconcentration factors, field simulated bioaccumulation factors and field estimed bioaccumulation factors for dioxin and the relationship between these values. (To be submitted).

Shu, H., D. Paustenbach and F.J. Murray. 1987. A critical evaluation of the use of mutagenesis, carcinogenesis, and tumor promotion data in a cancer risk assessment of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Reg. Toxicol. Pharm.* 7:57-88.

Sijm, D.T.H.M. and A. Opperhuizen. 1988. Biotransformation, Bioaccumulation and Lethality of 2,8-Dichlorodibenzo-p-dioxin: A Proposal To Explain the Biotic Fate and Toxicity of PCDD's and PCDF's. *Chemosphere 17*(1): 83-99.

Silbergeld, E.K. and T.A. Gasiewicz. 1989. Dioxins and the Ah receptor. *Amer. J. Indust. Med.* 16:455-474.

Smith, A.B., J. Schloemer, L.K. Lowry, A.W. Smallwood, R.N. Ligo, S. Tanaka, W. Stringer, M. Jones, R. Hervin and C.J. Glueck. 1982. Metabolic and health consequences of occupational exposure to polychlorinated biphenyls. *Brit. J. Ind. Med. 39*361-369.

Smith, A.H., D.O. Fisher, N. Pearce and C. Chapman. 1982a. Congenital defects and miscarriages among New Zealand 2,4,5-T sprayers. *Arch. Environ. Health. 37*(4):197-200.

Smith, A.H., D.O. Fisher, N. Pearce and C.A. Teague. 1982b. Do agricultural chemicals cause soft tissue sarcoma? Initial findings of a case-control study in New Zealand. *Community Health Studies 6*(2):114-119.

Smith, A.H. and N.E. Pearce. 1986. Update on soft tissue sarcoma and phenoxyherbicides in New Zealand. *Chemosphere 15*(9-12):1795-1798.

Smith, F.A., B.A. Schwetz and K.D. Nitschke. 1976. Teratogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in CF-1 mice. *Toxicol. Appl. Pharmacol. 38*517-532.

Smith, R.M., P.W. O'Keefe, K.M. Aldous, D.R. Hilker and J.E. O'Brien. 1983. 2,3,7,8-Tetrachlorodibenzo-p-dioxin in sediment samples from Love Canal storm sewers and creeks. *Environ. Sci. Technol. 17*(1):6-10.

Smith, L.M., T.R. Schwartz and K. Feltz. 1990. Determination and occurrence of AHH-active polychlorinated biphenyls, 2,3,7,8-tetrachloro-p-dioxin and 2,3,7,8-tetrachlorodibenzofuran in Lake Michigan sediment and biota. The question of their relative toxocilogical siginficance. *Chemosphere* 21(9): 1063-1085.

Soldat, J.K. 1970. A Statistical Study of the Habits of Fishermen Utilizing the Columbia River Below Hanford. Chapter 25. In: *Environmental Surveillance In the Vicinity of Nuclear Facilities: Proceedings of a Symposium Sponsored by the Health Physics Society*. January 24-26, 1968. William C. Reinig (ed.) Springfield, IL, Charles C. Thomas. 302-308.

Spacie, A. and J.L. Hamelik. 1982. Alternative Models for Describing the bioconcentration of organics in fish. *Environ. Toxicol. Chem. 1*:309-320.

Spigarelli, S.A., M.M. Thommes and A.L. Jensen. 1982. Prediction of Chemical Accumulation by Fish. Ecological Sciences Section Radiological and Environmental Research Division, Argonne National Laboratory. PB824-156918. January 1982.

Spitsbergen, J.M., K.A. Schat, J.M. Kleeman, and R.E. Peterson. 1987. Interactions of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) with immune response of rainbow trout. Vet. Immunol. Immunopathol., 12:263. In: Cooper, 1989.

Spitsbergen, J.M. , J.M. Kleeman and R.E. Peterson. 1988a. Morphologic lesions and acute toxicity in rainbow trout (*Salmo gairdneri*) treated with 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. *J. Tox. Env. Health* 23: 333-358.

Spitsbergen, J.M. , J.M. Kleeman and R.E. Peterson. 1988b. 2,3,7,8-tetrachlorodibenzo-*p*-dioxin toxicity in yellow perch (*Perca flavescens*). *J. Tox. Env. Health* 23: 359-383.

Squire, R.A. and M.H. Levitt. 1975. Report of a workshop on classification of specific hepatocellular lesions in rats. *Cancer Research 35*3214-3223.

Squire, R.A. 1990. Letter to LaJuana S. Wilcher, Assistant Administrator, Environmental Protection Agency. May 24.

Squire, R.A. 1991. *An Assessment of Potential Carcinogenic Risk from 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)*. May.

Sugimura T. et al. 1986. In: *Genetic Toxicology of the Diet*. I. Knudsen, Ed. Liss, New York. pp. 85-107 (as cited in Ames et al., 1987).

Suskind, R.R. 1983. Long-term health effects of exposure to 2,4,5-T and/or its contaminants. *Chemosphere 12*:79.

Suskind, R.R. and V.S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *JAMA 251*(18):2372-2380.

Suskind, R.R. 1985. Chloracne, the hallmark of dioxin intoxication. *Scand. J. Work Environ. Health. 11*165-171.

Theiss, A.M., R. Frentzel-Beyme and R. Link. 1982. Mortality study of persons exposed to dioxin in a trichlorophenol process accident that occurred in the BASF AG on November 17, 1953. *Am. J. Ind. Med. 3*179-189 (cited in NCASI, 1987).

Thomas, N.A. 1983. Memorandum to C.E. Stepan, U.S. EPA Duluth, MN. July 22. (as cited in EPA, 1984).

Tollefson, L. 1991. Use of epidemiology data to assess the cancer risk of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Reg. Tox. & Pharm. 13*:150-169.

Travis, C.C., S.A. Richter, E.A. Crouch, R. Wilson and E. Wilson. 1987. Cancer Risk Management. A review of 132 federal regulatory decisions. *Environ. Sci. Technol.* 21(5):415-420.

Travis, C.C. and H. A. Hattemer-Frey. 1987. Human exposure to 2,3,7,8-TCDD. *Chemosphere* 16(10-12): 2331-2342.

UAREP. 1988. *Human Health Aspects of Environmental Exposure to Polychlorinated Dibenzo-p-dioxins and Polychlorinated Dibenzofurans.* Universities Associated for Research and Education in Pathology, Inc. June.

UK. 1989. *Dioxins in the Environment.* United Kingdom. Pollution Paper No. 27.

USDA. 1983. Food Consumption: Households in the United States, Seasons and Year 1977-1978. U.S. Department of Agriculture. Report # H-6. June.

van der Heijden, C.A., A. Knapp, P. Kramers, M. Van Logten. 1982. Evaluation of the carcinogenicity and mutagenicity of 2,3,4,8-tetrachlorodibenzo-1,4-dioxin (TCDD) classification and no-effect level. State Insitute of National Health. Bilthoven, The Netherlands.

van der Heijden, C.A. 1990. Statement on the outcome of the Banbury Conference "Biological Basis for Risk Assessment of Dioxins and Related Compounds".

Veith, G.D. and P. Kosian. 1983. Estimating bioconcentration potential from octanol/water partition coefficients. In: *PCBs in the Great Lakes.* D. Mackay, R.Patterson, S. Eisenreich and M. Simmons (eds) Ann Arbor Science Publishers. (as cited in EPA, 1984).

Veith, G.D., K.J. Macek, S.R. Petrocelli and J. Carroll. 1980. An evaluation of using partition coefficients and water solubility to estimate bioconcentration factors for organic chemicals in fish. *Aquatic Toxicol*: 116-129. (as cited in EPA, 1984)

West, P., J.M. Fly, R. Marans and F. Larkin. 1989. Michigan sport anglers fish consumption survey. Supplement I - Non-response bias and consumption suppression effect adjustments, A report to the Michigan Toxic Substance Control Commission. Natural Resource Sociology Research Lab Technical Report #2. September.

Wallace, L. 1990. Major sources of exposure to benzene and other volatile organic chemicals. *Risk Anal.* 10(1): 59-64.

WDH. 1991. Health Implications of PCDD and PCDF Concentrations Reported from Lake Roosevelt Sport Fish. Washington State Department of Health. April.

WHO. 1990. Press release: Consultation on tolerable daily intake from food of PCDDs and PCDFs.

Wiklund, K. and L-E. Holm. 1986. Soft tissue sarcoma risk in Swedish agricultural and forestry workers. *JNCI* 76(2):229-234.

Wilson, R. and E.A.C. Crouch. 1987. Risk assessment and comparisons: An introduction. *Science* 236: 267-270.

Wilson, R. 1979. Analyzing the daily risks of life. *Tech. Rev.* 81(4): 41-46.

Wisk, J.D. and K.R. Cooper. 1990. The stage specific toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in embryos of the Japanese medaka (*Oryzias latipes*). *Env. Tox. Chem.* 9: 1159-1169.

Yockim, R.S., A.R. Isensee and G.E. Jones. 1978. Distribution and toxicity of TCDD and 2,4,5-T in an aquatic model ecosystem. *Chemosphere* 3: 215-220.

Young, F.E. 1987. Risk assessment: The convergence of science and the law. *Reg. Tox. Pharm.* 7:179-184.

Zack, J.A. and W.R. Gaffey. 1983. A mortality study of workers employed at the Monsanto Company plant in Nitro, West Virginia. *Environ. Sci. Res.* 26: 575-591.

Zack, J.A. and R.R. Suskind. 1980. The mortality experience of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident. *J. Occup. Med.* 22(1): 11-15.

Zingeser, M.R. 1979. Anomalous development of the soft palate in rhesus macaques (Macaca mulatta) prenatally exposed to 3,4,7,8-tetrachlorodibenzo-p-dioxin. Oregon Regional Primate Research Center, Beaverton, OR.

Zober, A., P. Messerer and P. Huber. 1990. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. *Int. Arch. Occup. Environ. Health* 62: 139-157.

APPENDIX A

Review of Reported Fish Bioaccumulation/Bioconcentration Factors

APPENDIX A

Review of Reported Fish Bioaccumulation/Bioconcentration Factors

The bioconcentration of TCDD has been evaluated in a number of studies, based on both predictive and measured data. Several studies have developed equations for predicting the BCF for an organic chemical based on its octanol-water partition coefficient, K_{ow} (Kenaga and Goring, 1980; Veith et al., 1980; Veith and Kosian, 1983; cited in EPA, 1984). Several K_{ow} values may be found in the literature for a given chemical, since factors such as pH, temperature, purity of the chemical, purity of the solvents, time of phase separation, and time of mixing may influence the results (Kenaga and Goring, 1980). For many chemicals, K_{ow} values are not available, and must therefore be predicted. For TCDD, octanol-water partition coefficients have been measured (Neely, 1979, 1983; Kenaga, 1980; Branson, 1983; cited in EPA, 1984). Using the measured partition coefficient, 6.15, in various equations (Kenaga and Goring, 1980; Veith et al., 1980; Veith and Kosian, 1983), the predicted BCFs range from 3,000 to 68,000.

In its AWQC document for dioxin (EPA, 1984), the EPA recommended a BCF of 5,000 on the basis of several studies. In one field study, a whole-body BCF of 2,000 was reported for channel catfish kept in a cage in a discharge plume of a river for 28 days (EPA, 1983; Thomas, 1983; cited in EPA, 1984). In a laboratory study the steady-state whole-body BCF in rainbow trout was projected to be 5,450 if growth dilution was not taken into account, and 9,270 if a correction is made for growth dilution (Branson et al., 1983; cited in EPA, 1984).

Cook et al. (1990) conducted laboratory experiments using contaminated food, sediment, and water to simulate exposure to lake trout from the Lake Ontario. These researchers verified TCDD concentrations and carefully accounted for losses through sorption processes, water outflow and fish uptake. The precision of their analyses, exemplified by comparing duplicate tanks results in which all but one duplicate produced TCDD concentrations within 7.5% of the mean, adds to the reliability of the data. The results of Cook et al. (1990) showed a whole-body BAF range of 1,860 - 22,700 (median = 6,660) with seven of nine exposure groups resulting in BAF values less than the mean of 7,230. If the 0.5 correction factor suggested by EPA (1990a) to compensate for the unequal partitioning of contaminants between the edible and inedible fish tissues is used, then the mean BAF for TCDD would be 3,615 (range: 930 - 11,350).

Additional field sampling also was conducted to verify the data collected in the laboratory. Because TCDD cannot be detected in the water of aquatic ecosystems, even when biota are highly contaminated (Cook et al., 1990, 1991), modeling was required to estimate the dissolved water concentration of TCDD in Lake Ontario. Based on this, Cook et al. (1990) reported a BAF of 140,000. It is likely, however, that this modeled BAF considerably overestimated the actual BAF as the model used (Endicott et al., 1988) predicted that 80% of the TCDD was dissolved in the water column. This is an unreasonably high percentage due to the superhydrophobic characteristic of TCDD. Cook and coworkers (1990) have attributed the differences between the laboratory values and the field values to two factors: 1) the technical inability to accurately measure dissolved TCDD concentrations in Lake Ontario, and 2) TCDD adsorption to suspended solids in laboratory experiments.

William Sherman, a member of the Maine Scientific Advisory Panel, recently reevaluated the model (Endicott et.al., 1988) used by Cook et al. (1990) to develop a BAF of 140,000 for Lake

Ontario. The Lake Ontario model (Endicott et al., 1988) predicts a TCDD input of 1,000 g/yr into Lake Ontario (Borton, 1991). The measured flow rate of Lake Ontario is 7,100 m^3/sec. Using this information a nominal TCDD concentration of 4.5 ppq can be calculated. Sherman (1990) derived a BAF based on the nominal concentration, a lipid correction from 18% to 2.5%, and a correction factor of 0.5 to convert from whole body to fillet concentrations. In his reanalysis, Sherman (1990) derived a BAF of approximately 5,000.

It has been suggested that the BCF should be increased to 50,000 based on a previously unpublished BCF study of fathead minnows and carp conducted in 1986 by Cook et al. (1991). Cook et al. (1991) cited that study, as well as the study by Mehrle et al. (1988), as supporting an increase in the BCF (normalized to 7 % lipid) to 51,000. However, it is critical to note that, in these studies, the concentrations of dioxin used produced toxicity in the test animals. Mehrle et al. (1988) noted in their report that BCF determinations should only be estimated in fish at exposure levels that do not induce toxic responses.

There are several additional points of concern which may influence application of the Cook et al. (1991) data for regulatory purposes. First, carrier solvents were used to enhance the solubility of TCDD in both the Mehrle et al. (1988) and Cook et al. (1991) studies. Cook et al. (1991) recommends that future investigations avoid using this technique with superhydrophilic compounds such as TCDD.

The BCF values estimated in the 1986 study cited by Cook et al. (1991) were based on two exposure treatments for fathead minnows and three exposure treatments for young carp. One of the carp exposure groups had been previously exposed for 105 days to a mixture of 1,2,3,4-, 1,3,6,8- and 1,3,7,9-TCDD. Despite the large number of fish in each exposure group, only a single aquarium (experimental unit) was used for each treatment level in both studies. Such a small number of exposure groups precludes one's ability to apply any parametric statistical test of significance. Furthermore, due to mortality associated TCDD toxicity, the experiment was terminated earlier than originally scheduled. As a result, only two samples were collected during the depuration phase of the experiment. The combination of toxic effects, which likely altered depuration rates, and the small number of sample points used to calculate the BCF limited the conclusions that can be drawn from these two studies and therefore limit its usefulness in a regulatory context.

Lower BCF values have been reported in the scientific literature. Adams et al. (1986) report a whole-body BCF of 7,900 for fathead minnows. In several rainbow trout studies, whole-body BCF values were reported to range from 9,270 to 39,000 (Mehrle et al., 1988; Branson et al., 1985).

A reanalysis of the data reported by Mehrle et al. (1988) indicates that the steady-state correlation in fathead minnows may have occurred at the lowest exposure level (38 pg/L) between 14 and 21 days when the calculations are based on the TCDD concentrations measured in the water rather than on average values. Using the actual data, the BCF was 22,647 at 14 days, 24,146 at 21 days, and 22,273 at 28 days. If steady-state occurred at 21 days in the lowest exposure group, then the steady-state BCF would be approximately 24,000.

An Assessment of Potential Carcinogenic Risk

from 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)

by

Robert A. Squire, D.V.M., Ph.D.

May, 1991

Robert A. Squire, D.V.M., Ph.D.

I. Introduction

The regulation of TCDD and most other animal carcinogens in the United States is based on the assumption that there is no safe or threshold level of exposure. This conservative policy was originally derived from the theory of radiation-induced carcinogenesis. It was considered prudent since the limited evidence available indicated that chemical carcinogens may act through direct DNA damage similar to radiation. This policy resulted in the use of non-threshold, linearized mathematical models for low-dose extrapolation from animal data to predicted human risk. Such models assume some degree of risk at all doses above zero.

It is important to emphasize that the use of linearized models is a default position which resulted from the absence of scientific evidence that thresholds did exist. As stated in the Office of Science and Technology Policy Guidelines, "When relevant biological evidence on mechanisms of action (e.g. pharmacokinetics, target organ dose) exists, the models or procedures employed should be consistent with the evidence. However, when data and information are limited, and when much uncertainty exists regarding the mechanisms of carcinogenic action, models or procedures which incorporate low-dose linearity are preferred when compatible with the limited information"[1].

It is true that, until recently, there was very little good scientific evidence indicating how chemicals actually cause cancer, and a uniform conservative regulatory policy was appropriate. However, duing the last decade carcinogenic mechanisms have been studied extensively and there is widely accepted scientific evidence that thresholds exist, at least for many non-genotoxic carcinogens. Based upon this evidence, low-dose exposures to TCDD that do not trigger critical cellular events are not expected to increase cancer risks in any species, including humans.

II. Reevaluation of The Animal Evidence.

The basis for the present regulation of TCDD is primarily a study conducted by Dr. R. Kociba, et al. of Dow Chemical Company, which was published in 1978[2]. At the request of The U. S. Environmental Protection Agency (EPA), I reevaluated all of the histologic specimens from the Kociba study, and my findings of liver tumors in female rats, the most sensitive end-point, have

[1]Federal Register, Thursday, March 14, 1985, pages 10371-10442.

[2]Kociba, R. et al. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8,-tetrachlorodibenzo-p-dioxin in rats. Toxicol. Appl. Pharmacol. 46: 279-303, 1978.

served as a basis for EPA regulation. My diagnoses were based upon criteria developed in a National Cancer Institute (NCI) workshop held in 1975, which I organized and chaired[3].

Extensive carcinogenesis research and testing have continued under the auspices of The National Toxicology Program (NTP) since the NCI workshop, and pathologic criteria for evaluating rat liver tumors have changed based upon new scientific evidence[4]. The rat liver lesions from the Kociba study were, therefore, recently reevaluated by me and, subsequently, at my suggestion, by a pathology working group (PWG) of well recognized experts in rat liver pathology representing academia, government and industry[5]. The PWG examined the slides "blind", i.e. without knowledge of experimental group, which was not done in the original examinations, and their findings are, therefore, not only based upon the most current scientific evidence, but also represent the most objective analysis.

---

[3]Squire, R. and Levitt, M. Report of A Workshop on Classification of Specific Hepatocellular Lesions in Rats. Cancer Research 35: 3214-3223, 1975.

[4]Maronpot, R. R. et al. National Toxicology Program Nomenclature for Hepatoproliferative Lesions of Rats. Toxicol. Pathol. 14 (2): 263-273, 1986.

[5]Under the auspices of Pathco, Inc., 10075 Tyler Place, Suite 16, Ijamsville, Md. 21754. PWG members were: R. Sauer (Chairman), W. R. Brown, R. R. Maronpot, P. M. Newberne, J. A. Popp, J. M. Ward, and D. G. Goodman.

The PWG concluded, and I agree, that there were fewer tumors than originally reported in TCDD treated female rats. The two most important findings that emerged from the PWG were that the tumors were mostly benign, with very few malignant carcinomas, and that tumor rates were increased in treated rats only at doses that also induced extensive liver damage, i.e. hepatotoxicity. This clearly disputed the view previously held that TCDD was a potent animal carcinogen. The criteria for considering a chemical a potent carcinogen include the induction of mainly malignant tumors, at relatively non-toxic doses, in both sexes, and in relatively short periods. By contrast, TCDD required a lifetime of hepatotoxic doses to induce primarily benign tumors, and only in females. Another feature that characterizes potent carcinogens is that they invariably are genotoxic, whereas TCDD has been shown to be non-genotoxic. The PWG concluded that TCDD was a weak animal oncogen.

III. Evidence for a TCDD Threshold

There are two possible mechanisms which, theoretically, may result in non-thresholds in carcinogenesis:

a) Tumors are presumed to start in a single altered cell, and a genotoxic chemical (or metabolite) may damage DNA in a single cell even at very low doses through a single "hit".

b) If two or more carcinogens act through a common mechanism, the effect may be additive and result in low-dose linear response.

TCDD does not fall into either category. It is not genotoxic and a single hit mechanism is not plausible. Moreover, its mechanism of action is very specific and requires interaction with a cellular AH receptor, followed by a complex series of intracellular events which, together, would not yield a linear low dose-response. The receptor role was recently further confirmed by a study which showed that ovarian hormones are necessary for hepatocarcinogenesis in rats[6]. Overall, there is no evidence for direct DNA damage or additivity with other carcinogens that would lead to linear dose-response.

TCDD enhances tumor rates in experimental animals by acting as a tumor promoter rather than initiator. This has been confirmed in two-stage, initiation-promotion studies with laboratory rats, and it was shown that doses below 0.1 ug/kg/day had no effect on liver tumor development[7]. In fact, at low doses, TCDD inhibited the effects of a potent initiator

---

[6]Lucier, G. W. et al. Ovarian hormones enhance 2,3,7,8-tetrachlorodibenzo-p-dioxin-mediated increases in cell proliferation and preneoplastic foci in a two-stage model for rat hepatocarcinogenesis Cancer Research 51: 1391-1397, 1991.

[7]Pitot, H. et al. Quantitative Evaluation of the Promotion by 2,3,7,8-tetrachlorodibenzo-p-dioxin in hepatocarcinogenesis from diethylisitrosamine Cancer Res. 40: 1616-1620, 1980.

carcinogen[8]. These findings are consistent with the earlier results in the Kociba study, and also with our understanding of tumor promotion mechanisms, since the weight of scientific evidence indicates that tumor promoters have thresholds[9].

Even if one rejects the concept of thresholds or no-effect levels and the receptor mechanism argument, the scientific evidence indicates that low-dose response would not be linear, and that linearized mathematical models will greatly overestimate risk. TCDD was carcinogenic in animals only at dose-levels that also induced marked hepatotoxicity, which invariably results in regenerative cell proliferation. It is now well recognized that increased cell proliferation contributes to tumor development[10]. Therefore, tumor development at low, non-toxic levels would not be linearly related to toxic, high-dose effects. This is true irrespective of the precise carcinogenic mechanism. Thus, even if one holds the conservative view that TCDD might pose some level of carcinogenic risk at low doses, the EPA linearized model estimates are still exaggerated and misleading.

---

[8]Ibid.

[9]Weisburger, J. H. and Williams, G. M. The Distinct Health Risk Analyses Required for Genotoxic Carcinogens and Promoting Agents. Environ. Health. Perspect. 50: 233-245, 1983.

[10]Cohen, S. and Ellwein, L. B. Cell Proliferation and Carcinogenesis. Science 249: 1007-1011, 1990.

There is a strong historical and biological basis for applying safety factors to no observed adverse effect levels (NOAEL) in animal studies in order to protect against potential human risk. The usual safety factor is 100X, but for added safety, some have recommended 1000X for irreversible effects such as cancer. The latter, i.e. 1000X, exceeds the widest positive dose response range ever reported for a chemical toxin or carcinogen. The NOAEL level in rat livers in the Kociba study was 0.001 ug/kg/day. Applying a 1000X safety factor results in an acceptable daily human intake (ADI) of 0.000001/ug/kg/day, or 1.0 pg/kg/day, and, added to this safety factor, is the evidence that rats are far more susceptible to TCDD toxicity than are humans[11].

IV. Conclusion

In a reevaluation of animal test findings, TCDD was found by a panel of experts to be a weak rather than potent animal carcinogen. Moreover, extensive scientific research regarding the mechanism of TCDD toxicity indicates it is receptor-mediated, and a threshold or no-effect level would be expected. However, even if one rejects the threshold concept, the level of toxicity that was required to increase cancer rates in rats indicates that

---

[11]Kimbrough, R. D. How Toxic is 2,3,7,8-tetrachlorodibenzo-p-dioxin to humans? Jour. Toxicol. Environ. Health (in press).

linearized low-dose extrapolation models are inappropriate and will overestimate human risk. Application of a conservative 1000X safety factor to the animal data is a sound alternative, and this results in an ADI of 1.0 pg/kg/day. The weight of scientific evidence clearly indicates that this level will not pose a cancer risk to humans.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
REGION III
841 Chestnut Building
Philadelphia, Pennsylvania 19107

SEP 12 1990

Honorable Martin W. Walsh, Jr.
Secretary
Maryland Department of the Environment
2500 Broening Highway
Baltimore, Maryland 21224

Dear Mr. Walsh:

The Environmental Protection Agency (EPA) has completed its review of the revisions to the Maryland Department of the Environment (MDE) Water Quality Standards adopted March 21, and effective April 16, 1990, including the hearing record and responsiveness summary. EPA has conducted its review pursuant to Sections 303(c)(1) and 303(c)(2)(B) of the Clean Water Act (CWA), and at this time, EPA is approving the Standards with the exception of Code of Maryland Regulations (COMAR) 26.08.02.05 Mixing Zone Policy. EPA is conditionally approving COMAR 26.08.02.04 Antidegradation Policy. For the next triennial review, or such earlier time as may be required, the State will need to consider additional information that becomes available through sources such as the Toxics Release Inventory System (TRIS). This additional information should be used in expanding the list of chemicals for which criteria are adopted as well as for possible revisions to these criteria.

The Antidegradation Policy section is conditionally approved contingent upon adoption of revisions which were proposed by MDE on May 4, 1990 and also pending a satisfactory demonstration that existing uses (i.e., uses existing on or following November 28, 1975) are protected in MDE's Water Quality Standards (as requested by letter from Alvin R. Morris, Director Water Management Division, EPA Region III on July 12, 1990). A specific schedule for implementation of these changes should be submitted within thirty (30) days and should provide for completion of the above conditions within sixty (60) additional days, unless for good cause shown, the time is extended.

EPA does not approve the Mixing Zone Policy because provisions were not specified to ensure that lethal conditions for aquatic life would be prevented when diffusers are used. As is evident in

EPA guidance on mixing zones, it is EPA's longstanding position that state water quality standards provide inadequate protection of aquatic life uses, and are therefore inconsistent with the CWA, if lethality is allowed in mixing zones. In revising the mixing zone policy the State may use EPA guidance in the EPA Water Quality Standards Handbook, the 1985 Technical Support Document for Water Quality-based Toxics Control (TSD) or the current draft TSD, or may develop a policy which adequately describes conditions which will ensure that lethality will be prevented in mixing zones, including the zone of initial dilution.

Although we realize that Maryland is reluctant to rely on draft guidance (e.g., draft TSD) in developing a mixing zone policy, it is our position that the draft TSD constitutes the best information currently available and therefore may be used if the State so chooses in developing a mixing zone policy. As we previously indicated, EPA will assist the State in order to help Maryland in its desire to ensure consistency with acceptable mixing zone policies adopted by other States. When revising the policy, Maryland could also modify COMAR 26.08.02.03-2, which requires that acute aquatic life criteria be applied at the end of the outfall. As described in the draft TSD, EPA believes that state standards are adequately protective of aquatic life uses, and therefore consistent with the CWA, if they allow for an initial zone of dilution prior to achieving acute criteria if it can be demonstrated that exposure time in that initial zone is so short as to protect aquatic organisms from lethality.

As you are aware, the scientific knowledge and data concerning toxics is rapidly expanding. As new information becomes available, EPA will be advising states concerning any adjustments to the water quality criteria which may be necessary. We would like to assure Maryland that EPA is working to finalize relevant water quality standards and NPDES permitting guidance and regulations as quickly as possible. In the interim, we again offer our assistance in addressing remaining water quality standards related issues, including development of State or area-specific fish consumption rates.

If you have any questions please call me at (215) 597-9814 or have your staff contact Dr. Morris, at (215) 597-9410.

Sincerely,

Edwin B. Erickson

Edwin B. Erickson
Regional Administrator

United States
Environmental Protection
Agency

Region III
841 Chestnut Building
Philadelphia, Pennsylvania 19107

(215)597-4825

Official Business
Penalty for Private Use
$300

EPA Environmental News

Contact: Ruth Podems
(215) 597-4164
90-221, September 14, 1990

U.S.ENVIRONMENTAL PROTECTION AGENCY APPROVES REVISIONS OF MARYLAND'S WATER QUALITY STANDARDS

PHILADELPHIA -- The U.S. Environmental Protection Agency (EPA) Region III has approved revisions to Maryland's water quality standards, with the exception of the mixing zone policy. In addition, the State's antidegradation policy was conditionally approved.

Water quality standards designate intended uses for state waters and establish the level of water quality necessary to protect those uses. Every three years each state must review and, if appropriate, revise its water quality standards. These revisions are subject to EPA approval.

A mixing zone refers to an area in a river or stream where treated wastewater rapidly mixes with the receiving water body. EPA is working with the Maryland Department of the Environment to ensure that mixing zones are defined such that aquatic life passing through them is adequately protected.

-more-

Maryland's water toxics regulations -- including the mixing zone policy -- are being challenged in the Circuit Court of Baltimore by industrial and utility companies for being too stringent.

Antidegradation refers to a policy of maintaining at least the present water quality and highest beneficial uses achieved since 1975 in each body of water. Categories of such uses include fishing, reproduction of fish and other aquatic life, swimming, drinking water and agricultural irrigation. EPA is requesting clarifications and new regulatory language to ensure that all such uses and water quality are and will remain protected.

The 1987 amendments to the Clean Water Act required that all states adopt limits for toxic pollutants during their next triennial review. Maryland addressed these requirements of the Act by assessing current levels of toxic pollutants in state waters and setting standards for those pollutants which were found to impair or potentially impair water quality. Maryland now has water quality standards for 27 toxic pollutants, including limits for certain heavy metals, pesticides and other organic chemicals.

Among the limits approved by EPA is Maryland's water quality standard of 1.2 parts per quadrillion (ppq) for dioxin, a toxic byproduct of the paper bleaching process and probable human carcinogen. EPA has an obligation to approve water quality standards that are scientifically defensible. Maryland's method of deriving its water quality standards is defensible and, therefore, the standards have been approved by EPA.

The Agency will continue to examine the factors used in the calculation of the water quality criteria, or EPA's recommended levels, for toxics and will advise Maryland and all other states to make appropriate adjustments to their standards, as updated scientific information becomes available.

EPA's decision does not affect Maryland's ability to continue issuing National Pollutant Discharge Elimination System (NPDES) permits, which limit discharges into State waterways. Maryland officials have informed EPA that they will issue these permits using the strong biomonitoring requirements and toxics restrictions that were already in place.

# # #

Pollution Prevention Tip: Recycling laser printer toner cartridges can save! Not only can we reduce waste, but recharged cartridges, at $39, save $50 from the new cartridge cost of $89.

TECHNICAL SUPPORT DOCUMENT FOR EPA'S SEPTEMBER 12, 1990 APPROVAL/DISAPPROVAL OF MARYLAND'S WATER QUALITY STANDARDS REVISIONS

TABLE OF CONTENTS

TECHNICAL SUPPORT DOCUMENT FOR EPA'S SEPTEMBER 12, 1990 APPROVAL/DISAPPROVAL OF MARYLAND'S WATER QUALITY STANDARDS REVISIONS

This document summarizes certain EPA considerations and conclusions in approving/disapproving revisions to Maryland's water quality standards adopted March 21, 1990, and effective April 16, 1990. EPA's decision is based on a review of all documents in the administrative record, including, but not limited to, the submission of the revisions and supporting documentation from Maryland, EPA's criteria documents issued pursuant to Section 304(a) of the Clean Water Act (CWA), and a number of comments and petitions from the public -- some of which have been submitted in connection with other states' water quality standards but raise issues relevant to the Maryland submittal.

Section 303(c) of the CWA requires the states to adopt water quality standards, and review and update the standards at least once every three years. Water quality standards include the designated uses for the navigable waters and water quality criteria based upon such uses. The standards are to protect the public health or welfare, enhance the quality of the water and serve the purposes of the Act. Section 303(c)(2)(B) specifically requires states reviewing water quality standards to adopt numeric criteria for all toxic pollutants listed pursuant to Section 307(a)(1) of the CWA for which criteria have been published under Section 304(a), the discharge or presence of which in the affected waters could reasonably be expected to interfere with designated uses of the states' waters.

The states must submit the revised or newly adopted standards to the Regional Administrator of EPA for review and approval. See 40 C.F.R. § 131.20(c). EPA's review includes, among other, things a determination of whether the State has adopted an adequate antidegradation policy, whether the State has adopted water uses which are consistent with the requirements of the CWA, and whether the State has adopted criteria that protect the designated water uses. See 40 C.F.R. §§ 131.5 and 131.6. The Regional Administrator has 60 days from the date the submittal is deemed complete to notify the State that the revisions are approved or, alternatively, 90 days to notify the state that the revisions are disapproved. See 40 C.F.R. § 131.21.

This document summarizes certain EPA considerations and conclusions in approving/disapproving the water quality standards revisions submitted by Maryland. Maryland has 90 days from the date of receiving EPA's determination to adopt the changes specified.

I. GENERAL PROVISIONS OF THE REVISED WATER QUALITY STANDARDS

EPA finds that all of the revised general provisions of the Maryland water quality standards meet the applicable requirements set forth in 40 C.F.R. §§ 131.5 and 131.6, with the following exceptions.[1]

Mixing Zone Policy

Mixing zones (limited areas or volumes of water where initial dilution of a discharge occurs) may be allowed at State discretion. By way of example, use of a mixing zone may allow a permittee to measure the concentration of a particular pollutant for compliance with the chronic criterion for aquatic life at the edge of the mixing zone rather than at the outfall. When mixing zone provisions are part of the State standards, methodologies and procedures used for defining the area of the mixing zone should be included. See 40 C.F.R. § 131.13. This type of information is used by EPA and the State to support regulatory actions and issue permits.

EPA believes that, in order to adequately protect designated aquatic life uses consistent with the Clean Water Act, conditions lethal to aquatic organisms that may pass through mixing zones must be prevented. Although the concentration of a pollutant within

---

[1] The Maryland standards provide that human health criteria are to be applied in permitting decisions based on mean annual flow of the receiving streams. COMAR § 26.08.02.06(a)(iii). EPA has issued draft guidance recommending use of harmonic mean flow when implementing criteria designed to protect against long-term health effects. U.S. EPA, Technical Support Document for Water Quality-based Toxics Control (DRAFT), April 23, 1990. EPA is reviewing comments received on the draft and expects to finalize its guidance in the near future. Since EPA has not yet made a final decision on this issue, it is appropriate for Maryland to use mean annual flow. See Technical Support Document for Water Quality-based Toxics Control, September 1985.

the zone of initial dilution (ZID) may exceed the acute criterion for aquatic life, the mixing zone, including the ZID, must be sized such that the period of exposure for aquatic life passing through the mixing zone will not be long enough to cause lethality.[2] Maryland has not demonstrated how its Mixing Zone Policy would provide for this protection. Therefore, EPA cannot approve the Mixing Zone Policy until the standards define the limits of the mixing zone, including the ZID, to ensure that lethal conditions for aquatic life would be prevented.

Antidegradation Policy

EPA's water quality standards regulations provide that states may not remove designated uses if they are existing uses (40 C.F.R. § 131.10(h)) and that existing uses must be maintained and protected (40 C.F.R. § 131.12(a)(1)). Existing uses are those uses actually attained in the water body on or after November 28, 1975, whether or not they are included in the water quality standards. 40 C.F.R. § 131.3(e).

Maryland's revised regulation provides that the determination of the designated use of a water body shall include consideration of the existing conditions. See COMAR § 26.08.02.02(A)(2)(a). The Maryland Antidegradation Policy delimits when downgrading of the

---

[2] Guidance on mixing zones is provided in the EPA Water Quality Standards Handbook, EPA's 1985 Technical Support Document for Water Quality-based Toxics Control (TSD) and the April 1990 draft revised TSD.

designated use may be allowed. See COMAR § 26.08.02.04(C). In correspondence to EPA, Maryland stated that their regulations provide for protection of existing conditions and that the term "existing conditions" is broader in scope than the term "existing uses". Even if the term "existing conditions" encompasses the term "existing uses", Maryland still needs to clarify what is meant by the statement that existing conditions will be taken into consideration in the determination of the designated use of a water body. Before EPA grants full approval of the Antidegradation Policy, further clarification is requested to ensure that Maryland's regulations provide protection of existing uses and are, therefore, consistent with the CWA.

On May 4, 1990, Maryland proposed to adopt the language noted below as a revision to COMAR § 26.08.02.04(C)(3) under its Antidegradation Policy concerning situations where downgrading of any stream may be considered. The current language which is proposed to be replaced is shown in brackets.

Downgrading may only be considered if:

(1)-(2) (text unchanged)

(3) [Substantial and widespread adverse social and economic impacts will result from maintaining the designated use.] <u>Controls more stringent than the effluent limitations and national performance standards mandated by the Federal Act would result in substantial and widespread economic and social impact.</u>

EPA believes that this modification is necessary because the current language permits downgrading a water body, which is already attaining the designated use, for economic considerations. EPA's regulations require that, in allowing the downgrading of a water body, the State assure water quality adequate to protect existing uses fully. 40 C.F.R. § 131.12(a)(2).

Based on the above considerations, EPA conditionally approves Maryland's Antidegradation Policy contingent upon adoption of revisions which were proposed by Maryland on May 4, 1990, and also pending a satisfactory demonstration that existing uses (i.e., uses existing on or following November 28, 1975) will be fully protected.

II. NUMERIC WATER QUALITY CRITERIA

Where waters are designated for use by humans for such purposes as swimming, boating, fishing, and/or public water supply, or for use by aquatic organisms, the water quality criteria applicable to those waters must be sufficient to protect those designated uses. In order to calculate such water quality criteria for the protection of human health it is necessary to first derive a dose of the chemical of concern which, based on available information, is estimated to present an acceptable health risk to exposed individuals. This dose level is then used together with estimates of consumption (this may vary with the particular designated uses of the waters in question), expected bioconcentration of the chemical in fish (assuming the water is designated for fishing uses), and size of the exposed individual, to calculate a concentration of the chemical in surface waters that is not expected to cause an exceedance of the acceptable dose to exposed individuals. Criteria for the protection of aquatic life are developed to prevent acute and chronic toxicity. EPA has calculated human health criteria for over 100 priority toxic pollutants and aquatic life criteria for more than 30 priority toxic pollutants, and has published the EPA recommended criteria together with extensive summaries of the scientific information reviewed in calculating the criteria. See U.S. EPA, Quality Criteria for Water 1986, EPA 440/5-86-001.

In the statement of proposed action accompanying Maryland's November 3, 1989, proposed numeric criteria for toxic pollutants, the State indicated that, with three exceptions, "the criteria proposed for adoption are based on existing EPA [recommended] criteria." 16 Maryland Register 2420 (November 3, 1989). As to those criteria with values corresponding to values recommended by EPA, the Agency finds that they are consistent with the Clean Water Act, based on the rationale provided in the EPA criteria documents together with other information in the administrative record. Maryland's use of a 10^{-5} risk level for carcinogens is consistent with a number of state and federal regulatory actions, and provides a level of protection against cancer effects that is within the range EPA considers acceptably protective of human health.

With respect to Maryland's estuarine and marine criteria for acute copper toxicity, Maryland used EPA procedures to recalculate the criteria based on resident species, rather than adopting EPA's recommended criteria. EPA finds that the scientific methods and site-specific approach used by Maryland to derive these criteria were adequately documented and justified, and that the resulting criteria are adequately protective of designated uses consistent with the requirements of the Clean Water Act.

EPA's acute aquatic life criterion for copper for salt water is 2.9 parts per billion (ppb). EPA does not have distinct criteria for estuarine waters and generally recommends use of its salt water criteria for this purpose. In its proposed action, Maryland included acute aquatic life criteria for copper for estuarine waters of 6.3 ppb and for salt water (marine waters) of 3.0 ppb. 16 Maryland Register 2420, 2427 (November 3, 1989). Based on a review of the data used to derive the acute aquatic life criterion for copper for salt water, Maryland revised its proposed criterion to 2.9 ppb. These proposed regulations were adopted on March 21, 1990. 17 Maryland Register 854, 855 (April 6, 1990). EPA notes that, although Maryland's subsequently revised criterion for salt water is identical to EPA's recommended criterion, it is the result of Maryland's own scientific, site-specific analysis.

The Maryland criterion for 2,3,7,8-Tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) is less stringent than that which would be recommended by EPA. See Ambient Water Quality Criteria for 2,3,7,8-Tetrachlorodibenzo-p-dioxin, February, 1984; Memorandum from LaJuana S. Wilcher to Water Management Division Directors entitled "State Policies, Water Quality Standards, and Permit Limitations Related to 2,3,7,8-TCDD in Surface Water", January 5, 1990. Because of Maryland's departure from recommended levels, and because of the substantial recent controversy regarding health hazards posed by 2,3,7,8-TCDD, the Maryland criterion, together with each of the factors used to derive it, is described in detail in Part III of this document.

III. CRITERION FOR 2,3,7,8-TCDD

State human health criteria for potential human carcinogens are based on at least three inter-related considerations: the cancer risk factor, exposure, and acceptable risk level. The cancer risk factor is an estimate of the human cancer risk per unit of dose, based on animal laboratory data. EPA's methodology for estimating the upper limit of the cancer risk of 2,3,7,8-TCDD has involved making a number of specific scientific assumptions in the absence of a clear scientific understanding. Exposure assessment requires consideration of a number of factors ranging from the bioconcentration factor (BCF), which is used to account for the concentration of toxic pollutants in fish tissue at levels higher than the ambient water, to the amount and frequency of fish consumed and the body weight of the individual eating the fish. The level of acceptable risk is expressed as a statement of the upper bound statistical risk of one person out of a specific population size developing an excess cancer (e.g. one excess cancer for each 1,000,000 in population). The upper bound concept means that the true risk, which we cannot accurately define, is not likely to be higher and may be lower than the stated risk. Probable human carcinogens are assumed to pose some risk at any level of exposure; the level of acceptable risk represents a risk manager's decision as to the amount of risk that is acceptable to the exposed population.

In deriving EPA's recommended water quality criteria for 2,3,7,8-TCDD the Agency used the following assumptions: a cancer risk factor of 1.56×10^5 per milligram per kilogram per day $(mg/kg/day)^{-1}$, a BCF of 5000, 6.5 grams per day (g/day) fish consumption, drinking water ingestion of 2 liters/day and a 70 kilogram exposed individual. See, Ambient Water Quality Criteria for 2,3,7,8-Tetrachloro-dibenzo-p-dioxin, U.S. EPA Office of Regulations and Standards, EPA 440/5-84-007, February 1984 (Water Quality Criteria Document). Although EPA recommended a criterion of zero for 2,3,7,8-TCDD, as it does for all potential/probable human carcinogens, EPA also calculated for information purposes, criteria values corresponding to upper bound risk levels of 10^{-5} to 10^{-7} (i.e. a range of one excess incidence of cancer in 100,000 to one in 10,000,000). These criteria values ranged from 0.14 to 0.0014 parts per quadrillion (ppq) if the only exposure route were through fish consumption, or 0.13 to 0.0013 ppq if it was assumed that exposed individuals were also drinking 2 liters per day of contaminated water.

In deriving a human health criterion for 2,3,7,8-TCDD, Maryland used many of the same assumptions used by EPA, but substituted a cancer risk factor, derived by the Food and Drug Administration (FDA) of 1.75×10^4 $(mg/kg/day)^{-1}$ compared to EPA's value of 1.56×10^5 $(pg/kg/day)^{-1}$. The resulting 1.2 ppq Maryland standard was established to protect to the 10^{-5} risk level.

Cancer Risk Factor

EPA's estimate of upper limit cancer risk is a higher number than that of other federal agencies. It is higher than FDA's estimate by a factor of approximately 9, higher than the Center for Disease Control's (CDC) estimate by a factor of 4, and higher than the Consumer Product Safety Commission's (CPSC) by a factor of 2.5. However, the CPSC cancer risk factor is not an upper limit value but a best estimate. If an upper limit had been used, the EPA and CPSC estimates would be nearly identical.

Although all four agencies based their risk estimates on the same scientific studies (Kociba et al., 1978), the agencies differed in their use of the data from these studies. EPA and FDA differed in their selection of tumor types in female rats. EPA combined all tumor types of significantly increased incidence, whereas FDA considered only liver tumor incidence. EPA made two adjustments in the data not made by FDA. EPA adjusted for high early mortality in high-dose animals by excluding all animals dying during the first year. EPA also incorporated two pathologists' reviews of the liver slides by using the geometric mean of the slope factors derived from each pathologist's analysis, while FDA considered only the original pathologist's review of the slides. While these differences in data selection account for some small proportion of the difference in the FDA and EPA risk estimates, the major contributing factor was choice of interspecies dose scaling factor. EPA used the surface area correction, whereas FDA used dose per body weight. When extrapolating from rat to man, the use of dose per surface area versus dose per body weight increases the risk estimate by a factor of 5.4. Background Document to the Integrated Risk Assessment for Dioxins and Furans from Chlorine Bleaching in Pulp and Paper Mills, U.S. EPA Office of Pesticides and Toxic Substances, Draft Report, July 1990, p. 3-7.

In 1988, EPA convened a Workgroup to reexamine the scientific basis and methods used by EPA for estimating the cancer risk for 2,3,7,8-TCDD. The Workgroup reviewed the cancer risk factors used by EPA, FDA and CDC and observed that there was no obvious scientific basis for excluding any of these values from the acceptable range. A Cancer Risk-Specific Dose Estimate for 2,3,7,8-TCDD, June 1988, p. 49. The Workgroup went on to recommend an increase in the risk specific dose associated with an upper limit 10^{-6} cancer risk level from the .006 pg/kg/day level presented in EPA's 1984 Water Quality Criteria Document to 0.1 pg/kg/day.[3] (Id. p. 50). EPA's Science Advisory Board (SAB) reviewed the Workgroup's report and concluded that there was no scientific basis for a change in the current assessment of the cancer risk factor at this time, and, therefore, no reason to raise the risk specific dose for 2,3,7,3-TCDD (i.e. reduce the risk factor).

There has also been considerable recent additional research and debate regarding 2,3,7,8-TCDD's carcinogenic properties. For example, in March of 1990, a panel of seven pathologists reexamined the slides of the female rats from the 1978 study that was used as the basis for EPA's 1984 risk factor calculations. (Kociba et al., 1978.) These pathologists classified tumors in the rat livers using a criteria for tumor classification reported by the National Toxicology Program. <u>See</u> Maronpot, R.R. et al. <u>National Toxicology Program Nomenclature for Hepatoproliferative Lesions of Rats</u>. Toxicol. Path. 14:263-273, 1986. These pathologic criteria are different from the earlier National Cancer Institute criteria used in the review of the Kociba study that formed the basis for EPA's 1984 risk factor estimate. <u>See</u> Squire, R.A. and Levitt, M.H. <u>Report of A Workshop on Classification of Specific Hepatocellular Lesions in Rats</u>. Cancer Res. 35: 3214-3223, 1975; <u>See</u> <u>Ambient Water Quality Criteria for 2,3,7,8-TCDD</u>, February 1984, at pp. C-165 <u>et seq</u>. Use of the new pathologic criteria, which are

---

[3] A "risk specific dose" is derived from a chemical's potency factor to yield a dose that is associated with a given risk level.

somewhat more discriminatory than past pathological practices with regard to identifying carcinogenic lesions, resulted in a reduced overall number of tumors counted in slides from the Kociba study. Use of this reevaluation would reduce EPA's cancer risk estimate by a factor of 3 to 4.[4]

EPA is currently reviewing the results of the re-reading of the Kociba slides, along with other factors, while discussing (both internally and with other federal agencies, the public and other countries) the cancer risk for 2,3,7,8-TCDD. In the meantime, EPA continues to recommend use of the risk factor used in EPA's 1984 criteria document. However, the basis for EPA approval of a State water quality criterion is not whether the State used EPA's recommended criterion, but whether the State's decision is scientifically defensible and protective of designated uses. Recognizing that legitimate differences of opinion regarding the cancer risk of 2,3,7,8-TCDD exist among substantial segments of the scientific community, EPA believes that Maryland is not necessarily required to adopt EPA's particular view. EPA believes that the FDA estimate of the cancer risk is within the bounds of uncertainty of

---

[4] Certain individual scientists have also recently expressed opinions that, because there is more research knowledge about 2,3,7,8-TCDD's behavior as a toxicant than for other compounds, the use of default assumptions in risk factor calculation procedures may significantly overstate the 2,3,7,8-TCDD risk. <u>See</u>, e.g., Letter from Vernon N. Houk, M.D., Assistant Surgeon General, Director, Center for Environmental Health and Injury Control, Center for Disease Control, to J. Leonard Ledbetter, Commissioner, Georgia Department of Natural Resources, dated November 27, 1989.

EPA's approach.[5] Since EPA believes, based on the above and other information in the administrative record, that the FDA cancer risk estimate is within the range of scientific defensibility, EPA finds that Maryland's use of this factor in calculating a 2,3,7,8-TCDD water quality criterion is acceptable for purposes of Section 303 of the Clean Water Act. However, as noted earlier, the FDA estimate of cancer risk is the lowest of four federal agencies and EPA would encourage Maryland to consider this in terms of its public health policy.

Bioconcentration Factor

The bioconcentration factor is the measure of a chemical's tendency to concentrate in the tissues of an organism at levels above ambient water concentrations. Although EPA used a bioconcentration factor (BCF) of 5000 in its water quality criteria document based on studies which yielded a range of measured values from 390 to 13,000[6] to derive the recommended criteria for 2,3,7,8-TCDD, as did Maryland, recent studies and reevaluation of the methods used in earlier studies suggest a much higher BCF.[7]

---

[5] Although FDA, in its estimate, did not account for higher early mortality among the high dose rats and did not include significant tumor types other than the liver, which EPA would prefer to account for, the risk factor is within the bounds of uncertainty of EPA's approach.

[6] The studies included in the Water Quality Criteria Document included Isensee and Jones (1975), Isensee (1978), U.S. EPA (1983) and Thomas (1983), and Branson et al. (1983). WQCD at p. B-5.

[7] The calculated criteria values are inversely proportional to the BCF; doubling the BCF would halve the criteria values.

The most recent peer-reviewed study (Mehrle, et al., Environmental Toxicology and Chemistry, 1988) gave measured BCF values ranging from 25,000 to 29,000. However, a steady-state was not reached, and the authors of the study estimated steady-state BCF values ranging from 36,000 to 86,000. In addition, this study used larval lake trout, which are very small and have low fat content. The BCF for larger, more fatty fish would be expected to be significantly greater. The most recent study performed by EPA's Duluth research laboratory estimated steady-state BCFs from 66,000 to 150,000, depending on the species and fat content. It is currently anticipated that this work will be submitted for peer-reviewed publication this fall.[8]

Despite the availability of recent studies on the BCF, EPA is not yet prepared to say that the BCF of 5000 is no longer within the range of scientific defensibility. A BCF of 5000 has been generally accepted for use in developing water quality criteria for 2,3,7,8-TCDD. When EPA developed its water quality criteria for 2,3,7,8-TCDD, it performed a full review of the existing studies on BCF in order to arrive at the estimated value of 5000. As indicated above, recent studies, including the Mehrle study and the

[8] In deriving recommended water quality criteria, EPA will typically utilize those studies and data it considers to be scientifically valid, whether or not they have had widespread review in the scientific community. With respect to the Mehrle study, which has been peer-reviewed, EPA has no reason to doubt the validity of the study and therefore believes that the data support a steady-state BCF of 39,000 for the low fat test species used.

work performed by EPA's Duluth research laboratory, indicate that a change in the estimated value of the BCF may be necessary. However, EPA has not yet made a definitive decision respecting a change in the calculation of the BCF for 2,3,7,8-TCDD.

Section 303(c) of the Clean Water Act gives to the states the authority to review and modify existing water quality standards and adopt new standards as appropriate for the protection of the public health or welfare and the enhancement of water quality. It is the express policy of the Act to recognize, preserve, and protect the primary responsibilities and rights of states to prevent, reduce, and eliminate pollution. Section 101(b) of the CWA. In consideration of the role of the states as described by the statute, the importance of an orderly administrative process in this case, and because EPA has not made a definitive determination regarding changes in the recommended calculation of the 2,3,7,8-TCDD BCF, EPA accepts at this time Maryland's decision to use the BCF used by EPA in the development of EPA's earlier recommended criteria and published in the existing EPA guidance document. However, EPA may require Maryland and other states to revise their criteria for 2,3,7,8-TCDD on a timely basis after EPA has completed a full review of the 2,3,7,8-TCDD BCF.

Fish Consumption[9]

Maryland used the same fish consumption estimate (6.5 g/day) in deriving its criterion for 2,3,7,8-TCDD that EPA used in deriving its recommended criterion for 2,3,7,8-TCDD. This value is based on the nationwide average consumption of commercially and recreationally harvested freshwater and estuarine finfish and shellfish as determined through analysis of a 1973-74 seafood consumption survey performed by the National Purchase Diary in conjunction with the National Marine Fisheries Service. (U.S. EPA, 1980; Stephan, C.E., memorandum dated July 3, 1980.)

As part of its overall review of risk assessment processes, EPA is focusing on the question of whether and when risk assessment should address special populations as opposed to national averages. Various research has indicated that the use of an average rate of fish consumption may not be adequate to protect particular subgroups of the population, such as sport fishermen and, particularly, subsistence fishermen.[10] These studies have shown that the average consumption levels in some areas for these segments of the population are 30 g/day for the average sport fishermen, and 140 g/day for the 90th percentile of sport

---

[9] The analysis of the average fish consumption value used by EPA to derive the recommended water quality criteria values for dioxin presented in its criteria document, and used by Maryland to derive its dioxin criterion, applies to all other toxic criteria for which this average fish consumption value was used by Maryland.

[10] See, Puffer, 1981, and Pierce, 1981, as discussed in the Exposure Factors Handbook, U.S. EPA, Office of Health and Environmental Assessment, March 1990, p. 1-15.

fishermen. See, Exposure Factors Handbook, U.S. EPA Office of Health and Environmental Assessment, March 1990, p. 1-15. However, EPA has also stated, with reference to the same data, that although these figures are recommended for use in estimating finfish/shellfish ingestion by recreational fishermen in any areas with large water bodies, no specific consumption rate values for these subgroups are recommended for small water body areas. Id. The studies which formed the basis for this recommendation were performed in Los Angeles, a marine fishing area, (Puffer, 1981) and Commencement Bay, Washington, along waterways in Tacoma, (Pierce, 1981). Review of the data supports the proposition that any state-specific survey of consumption patterns within the state should be designed to focus on these subgroups as well, especially where water bodies of a size comparable to those used in the studies are involved.

EPA is not aware of any Maryland-specific surveys of consumption of fish drawn from the types of waters to be covered by the Maryland 2,3,7,8-TCDD criterion. EPA encourages Maryland, as it encourages every state, to undertake such a state-specific survey in order to more accurately gauge consumption levels within the State. In the absence of State-specific data, EPA approves at the present time Maryland's use of the 6.5 g/day fish consumption estimate in deriving its 2,3,7,8-TCDD criterion.

Body Weight

The equation used to derive a water quality criterion includes an estimate of the body weight of the exposed individual. EPA used a body weight of 70 kg in deriving its recommended criterion. Ambient Water Quality Criteria for 2,3,7,8-TCDD, at p. C-243. This value approximates the average adult body weight, including both males and females. Exposure Factors Handbook, at p. 1-16. Maryland also used the 70 kg body weight in calculating its criterion for 2,3,7,8-TCDD. EPA approves of Maryland's use of this estimate.

Risk Level

The equation used to derive the water quality criterion for 2,3,7,8-TCDD based on cancer effects requires the choice of an acceptable risk level. As noted above, EPA set forth a range of criteria values corresponding to risk levels of 10^{-5} to 10^{-7} in its 1984 criteria document. The Maryland criterion is based on a 10^{-5} risk level. This risk level is frequently used in state and federal regulatory actions, and is considered by EPA to be within an adequately protective range.

Holistic Approach to Risk Assessment

Several commenters have argued that, although it is typically acceptable for a state developing regulatory criteria to rely on EPA's recommended criteria, including each factor used in deriving the criteria, if a state uses one less stringent factor than was used by EPA, the state must reevaluate all of the factors involved. This position acknowledges that EPA will typically not revise its criteria documents if it believes that the recommended "bottom-line" criteria values are valid, even if current information suggests that certain factors should be modified. It is possible, for example, that new information suggesting that a chemical is a less potent probable human carcinogen than originally expected will be counterbalanced by new information that the BCF is greater than originally expected. In such instances it is possible that EPA's "bottom line" recommended criterion should not change notwithstanding the new information. In such cases it would be inappropriate for a state to modify just the one factor (cancer risk), which may have been found to be overly protective, without also reviewing recent information on the other factors (including BCF), which may have been found to be insufficiently protective.

Where a state departs in a non-conservative direction with respect to one of the factors used by EPA in a criteria document, it is appropriate for EPA and/or the state to closely scrutinize all of the elements used in the state's risk assessment. This document has presented an evaluation of all of the factors involved in the Maryland assessment, and has concluded that the use of each factor is independently justifiable at this time.

For comparison purposes, EPA notes that, based on the assumptions used in deriving EPA's recommended criteria for

2,3,7,8-TCDD, the Maryland criterion yields a lifetime risk to an average exposed individual of no greater than 10^{-6}.[11] Thus, even using EPA's assumptions, the risk level is of a magnitude that is, depending on the circumstances, sometimes found acceptable to federal and state risk managers, including EPA.

In light of the above, and other information in the administrative record, EPA finds Maryland's water quality criterion for 2,3,7,8-TCDD to be protective of designated uses, and to otherwise meet the requirements of the Clean Water Act, as regards protection against cancer effects.

Non-cancer Effects

Water quality criteria to protect human health should, given sufficient reliable data, safeguard against both cancer and non-cancer endpoints. With respect to non-cancer endpoints, 2,3,7,8-TCDD has been shown in animal studies to be a reproductive developmental and hepatic toxicant. See U.S. EPA, Health Assessment Document for Polychlorinated Dibenzo-p-Dioxins, September, 1985. EPA scientists have used the data from these

[11] As described above, EPA is currently evaluating data which suggests a higher BCF than used in EPA's 1984 criteria document, and which would render Maryland's 1.2 ppq criterion protective only to the 10^{-5} risk level. EPA is also reevaluating the 6.5 g/day fish consumption value in light of data suggesting that certain subpopulations in some areas of the country consume greater quantities of fish. However, any such changes may be at least partially offset by changes with respect to other factors, such as cancer risk factor. After EPA has reevaluated all of these factors, Maryland may be required to adjust its criteria accordingly.

studies to calculate a reference dose (RfD) and health advisories (HAs) for 2,3,7,8-TCDD.[12]

An RfD is an estimate of the lifetime daily dose to the human population likely to be without any appreciable risk of deleterious effect. RfDs are generally based on studies involving lifetime exposures of animals. Usually doses that are less than the RfD are not likely to be associated with any health risks, and are therefore less likely to be of regulatory concern. However, as the frequency of exposures exceeding the RfD increases, and as the size of the excess increases, the probability increases that adverse effects may be observed in a human population. Nonetheless, a clear conclusion cannot be categorically drawn that all doses below the RfD are "acceptable" and that all doses in excess of the RfD are "unacceptable." The endpoints of concern in RfDs developed for 2,3,7,8-TCDD are reproductive and developmental effects. EPA scientists have calculated an RfD for 2,3,7,8-TCDD based on reproductive toxicity (the most sensitive endpoint for effects due to long-term exposures) of 1 X 10^{-6} micrograms per kilogram per day (ug/kg/day). Ambient Water Quality Criteria for 2,3,7,8-TCDD, p. C-179.

---

[12] The RfD for dioxin has not been subjected to the internal agency-wide peer review that EPA policies require prior to formalizing an RfD. The HAs have been developed by individual EPA Offices and, in accordance with Agency procedures for HAs, have not received Agency-wide review.

HAs are developed for less-than-lifetime exposures to chemicals of concern. HA dose levels are appropriate for comparison with single doses or short-term exposures. HAs for 2,3,7,8-TCDD have been calculated for hepatic effects: 1 day - 100 pg/kg/day and 10 day - 10pg/kg/day. See Background Document to the Integrated Risk Assessment for Dioxins and Furans from Chlorine Bleaching in Pulp and Paper Mills, (1990). These HA levels are also estimated to be protective against developmental toxicity. As for RfDs, HA levels do not necessarily represent levels to be used as a basis for regulatory action.

The RfD and HA values can be used to calculate ambient water concentrations of 2,3,7,8-TCDD that will not cause an exceedance of the dose values as a result of estimated fish consumption. Assuming a bioconcentration factor in fish of 5000, fish consumption of 6.5 grams/day, and a 70 kg individual, in-stream concentrations that would lead to exposures at the RfD level would be 2.15 parts per quadrillion.[13] Ambient Water Quality Criteria for 2,3,7,8-TCDD, p. C-179. The assumptions for body weight, bioconcentration factor and fish consumption used in this calculation are the same as those used in calculating criteria based on the 2,3,7,8-TCDD cancer risk, and their use is justified for the same reasons described above in the cancer risk section.

[13] This value would be somewhat greater if a correction were made to reflect studies indicating that humans do not absorb 100 percent of 2,3,7,8-TCDD ingested. See Boyer, I.J., Bioavailability of Ingested 2,3,7,8-TCDD and Related Substances (DRAFT), 1989.

Maryland's 1.2 ppq criterion for 2,3,7,8-TCDD is less than the 2.15 ppq level which is estimated to yield doses at the RfD level. However, EPA notes that the Maryland criterion is to be applied in permitting actions based on mean annual flow. COMAR § 26.08.02.06(a) (iii). The mean annual flow is simply the long-term arithmetic mean (or average) flow. Recently, EPA has circulated draft guidance for public comment recommending that harmonic mean flow be used rather than mean annual flow when implementing criteria designed to protect against toxic effects caused by long-term exposures to carcinogens. Draft Technical Support Document for Water Quality-Based Toxics Control, April 23, 1990, at pp.171-172. The same design flow would be appropriate when implementing criteria designed to protect against non-cancer effects caused by long-term exposures. The harmonic mean flow is that flow at which the in-stream concentration would be equal to the long-term arithmetic mean concentration. Mean annual flow is typically around three-fold greater than the harmonic mean flow.[14] Because mean annual flow is typically greater than harmonic mean flow, use of mean annual flow in dilution calculations allows

---

[14] For example, mean annual flow on the Potomac River in Maryland for the period 1939-1987 has been calculated at 3,298 cubic feet per second, while the harmonic mean flow for the same period was 1,043 cubic feet per second. Rossman, L.A., "Design Stream Flows Based on Harmonic Means," Journal of Hydraulic Engineering, Vol. 116, No. 7, p. 948, July, 1990. However, mean annual flow has been calculated to be as much as 33 times greater than harmonic mean flow in certain streams. Id. If such cases exist in Maryland, it may be appropriate for Maryland to develop site-specific criteria that are more stringent than the 1.2 ppq criterion.

greater quantities of pollutants to be discharged than would be allowed if harmonic mean flow were used.

Although EPA is still reviewing comments received on its draft guidance recommending use of harmonic mean flow, the final analysis of whether the Maryland criterion is adequately protective against long-term non-cancer effects would not change even if EPA were to conclude that harmonic mean flow <u>must</u> be used when implementing criteria for protection of human health against effects due to long-term exposures. Since mean annual flow is typically three times greater than harmonic mean flow, compliance with the Maryland 1.2 ppq 2,3,7,8-TCDD criterion based on mean annual flow would typically result in an in-stream concentration of 3.6 ppq at the harmonic mean flow. This value is just slightly greater than the 2.15 ppq level that corresponds to the RfD level for 2,3,7,8-TCDD. Given the facts that the RfD includes a safety factor of 1000, and that the RfD level does not necessarily represent a level of regulatory concern, and that derivation of the 2.15 ppq value assumes 100 percent absorption of ingested dioxin[15], this estimation of the increased concentration of 2,3,7,8-TCDD expected at harmonic mean flows, would not lead EPA to disapprove the Maryland criterion.[16]

---

[15] See footnote 14 above.

[16] In streams where the difference between mean annual flow and harmonic mean flow is greater than the typical difference, it may be appropriate for Maryland to develop site-specific criteria that are more stringent than the general 1.2 ppq criterion.

In light of the above, and other information in the administrative record, EPA finds that Maryland's water quality criterion for 2,3,7,8-TCDD is protective of designated uses, and otherwise meets the requirements of the Clean Water Act, as regards protection against long-term non-cancer effects.

With respect to protection against short-term effects, assuming a bioconcentration factor of 5000, daily consumption of 6.5 grams of fish, and a 70 kg person, the in-stream concentrations that would lead to exposures at 1 day and 10 day HA levels would be 215 ppq and 21.5 ppq, respectively. However, It may be inappropriate to use the 6.5 g/day long-term average fish consumption estimate in these calculations, since short-term fish consumption rates may be expected to exceed long-term average consumption rates. If a consumption estimate of 115 g/day (approximately 1/4 lb. of fish)[17] is substituted in the equation for the 1 day HA, the corresponding criterion would be 12.2 ppq. For the 10-day HA, substitution of a consumption value of 30 grams/day[18] would result in a water quality criterion of 4.66 ppq. In each of these calculations, lower criteria values would be derived if it

[17] While any single estimate of 1 day fish consumption values may be somewhat arbitrary, it appears reasonable to use 115 grams, or a typical fish meal, for purposes of this calculation.

[18] This value represents average fish consumption of recreational fishers on large water bodies. Exposure Factors Handbook, March 1990, p. 1-15.

were assumed that the same quantities of fish were being consumed by individuals smaller than 70 kg, that larger quantities of fish are consumed, or that fish bioconcentrate 2,3,7,8-TCDD to a greater degree.

The Maryland 1.2 ppq criterion is below the levels calculated to yield doses at the HA levels using the above assumptions, even taking into consideration the estimated 3.6 ppq concentration expected at the harmonic mean flow.[19]

In light of the above, and other information in the administrative record, EPA finds that Maryland's water quality criterion for 2,3,7,8-TCDD is protective of designated uses, and otherwise meets the requirements of the Clean Water Act, as regards protection against short-term human health effects.

---

[19] For some pollutants it may be appropriate to use low flow periods, rather than the harmonic mean flow, in calculating criteria to protect human health against short-term effects. See Draft Technical Support Document for Water Quality-based Toxics Control, p. 172, April 23, 1990. However, because it takes a long period of time for fish to achieve a steady-state with the surrounding 2,3,7,8-TCDD water concentration, (see Draft Lake Ontario TCDD Bioaccumulation Study, Chapter 9), it is not expected that the quantity of 2,3,7,8-TCDD in fish tissue will be significantly higher during low flow periods than it will be during periods corresponding to harmonic mean flow. And, because the preponderance of 2,3,7,8-TCDD exposure is expected to occur through fish consumption as opposed to drinking water consumption, it is not expected that there will be significantly greater risks during low flow periods than during flow periods that correspond to harmonic mean flow.

Aquatic Toxicity

The Maryland criterion for 2,3,7,8-TCDD is designed to protect human health. Accordingly, EPA's review is limited to assessing the adequacy of the numeric criterion for that purpose. In the absence of a numeric criterion for 2,3,7,8-TCDD to protect aquatic life, Maryland's narrative criteria must be interpreted in individual permitting actions to prevent harm to aquatic life. See COMAR § 26.10.01.03.B.(5)(b). Depending on the circumstances, greater protection than is afforded by Maryland's 1.2 ppq criterion may be required for this purpose.[20]

CONCLUSION

EPA approves Maryland's revisions to its water quality standards, with the exception of the Mixing Zone Policy, for the reasons stated above. The Antidegradation Policy is conditionally approved contingent on specific actions on the part of Maryland as outlined above. With regard to 2,3,7,8-TCDD, and other toxics as applicable, EPA is continuing to examine the various factors which are considered in the calculation of water quality criteria. As updated studies on these factors are made available to the public,

[20] Dioxin is highly toxic to aquatic organisms. The lowest test concentration among all known dioxin studies (38 ppq) produced 45 percent mortality in rainbow trout exposed to dioxin for 28 days. None of the dioxin studies to date have found a non-toxic exposure level for aquatic life. In interpreting its narrative criterion to protect aquatic life, Maryland should be advised to use an appropriate estimation factor to extrapolate from this value to a level that can reasonably be expected to protect aquatic life from chronic toxicity.

states may be advised by EPA to adjust water quality criteria accordingly.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
Region III
841 Chestnut Building
Philadelphia, Pennsylvania 19107

FEB 25 1991

Mr. Richard N. Burton
Executive Director
State Water Control Board
2111 North Hamilton Street
P.O. Box 11143
Richmond, Virginia 23230-1143

Dear Mr. Burton:

The Environmental Protection Agency (EPA) has completed its review of the revisions to Virginia's Water Quality Standards and supporting documentation from the Virginia administrative record which you submitted with your letter to Dr. Alvin Morris dated September 27, 1990. In addition, upon your invitation in response to EPA's request for additional information, EPA reviewed select documents from the State's administrative record during and subsequent to a visit to the Board's office in Richmond, Virginia on November 28, 1990. EPA also reviewed a petition from the Environmental Defense Fund (EDF) to disapprove Virginia's criterion for 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin), and other materials in the administrative record for this action.

The subject revisions were adopted by the Virginia State Water Control Board (Board) on May 14, 1990 and consist of the following: 1) a water quality criterion for dioxin of 1.2 parts per quadrillion for the protection of human health from the consumption of contaminated water and aquatic organisms, 2) the stream flow (i.e., mean annual) on which effluent limitations for dioxin will be based, and 3) a provision for site-specific modifications to the numeric criterion for dioxin.

EPA has conducted its review pursuant to Section 303(c) of the Clean Water Act and EPA's Water Quality Standards Regulation (40 CFR Part 131), and at this time, EPA is approving the revisions to Section VR 680-21-01.15 of Virginia's Water Quality Standards and disapproving EDF's petition. However, this approval does not affirm that Virginia has met the requirements of Section 303(c)(2)(B) of the Clean Water Act because Virginia has not yet adopted criteria for all Section 307(a)(1) pollutants for which criteria have been published by EPA under Section 304(a) and where the discharge or presence of such pollutants could reasonably be expected to interfere with designated uses. Therefore, at the present time, Virginia will be included in EPA's proposed national rule to promulgate toxics criteria for those States which have failed to meet the requirements of Section 303(c)(2)(B). EPA anticipates that the proposed national toxics rule will be published in the Federal Register during 1991. If Virginia achieves full compliance with Section 303(c)(2)(B) prior to publication of the final rule, Virginia will not be included in the final rule.

As you are aware, the scientific knowledge and data concerning toxic pollutants, including dioxin, are rapidly expanding. As new information becomes available, EPA will be advising States concerning any adjustments to the water quality criteria which may be necessary, based on EPA's review of bioconcentration factors, cancer potency factors, fish consumption rates, and stream design flows.

If you have any questions, please call me at (215) 597-9814, or have your staff contact Ms. Linda Holst at (215) 597-0133.

Sincerely,

Edwin B. Erickson
Regional Administrator

TECHNICAL SUPPORT DOCUMENT FOR EPA'S FEBRUARY 25, 1991 APPROVAL OF VIRGINIA'S WATER QUALITY STANDARDS REVISIONS

TABLE OF CONTENTS

TECHNICAL SUPPORT DOCUMENT FOR EPA'S FEBRUARY 25, 1991
APPROVAL OF
VIRGINIA'S WATER QUALITY STANDARDS REVISIONS

This document summarizes certain Environmental Protection Agency (EPA) considerations and conclusions in approving the revisions to Virginia's water quality standards adopted May 14, 1990, and effective July 18, 1990, specifically, the addition of an ambient water quality criterion for 2,3,7,8-tetrachlorodibenzo-p-dioxin ("2,3,7,8-TCDD" or "dioxin") of 1.2 parts per quadrillion (ppq).[1] EPA's decision is based on a review of all documents in the administrative record on this decision, including, but not limited to, the submission of the revisions and supporting documentation from Virginia[2], EPA's criteria document for 2,3,7,8-TCDD issued pursuant to Section 304(a) of the Clean Water Act (CWA), and a number of comments and a petition from the public.

Section 303(c) of the CWA requires the states to adopt water

[1] The regulations adopted by Virginia are found at VR680-21-01.15 Dioxin in Surface Waters.

[2] On September 27, 1990, in addition to the revisions to its water quality standards, Virginia submitted the State Attorney General's certification as required by 40 C.F.R. § 131.6(e), the Governor's review package (including a statement of purpose and impact), transcripts from public hearings held by the State Water Control Board (SWCB) on February 12 and 26, 1990, a March 19, 1990 summary of comments received, the staff presentation to the Board of the SWCB on the dioxin water quality standard (including technical considerations), and transcripts from SWCB meetings on December 11, 1989, March 19-20, 1990 and May 14, 1990. On November 7, 1990, EPA sent a letter to the SWCB requesting clarification of several issues of concern which arose during EPA's review of Virginia's submittal. By letter dated November 15, 1990, Richard N. Burton, Executive Director of the SWCB, invited EPA to review the remainder of the record in the SWCB offices in Richmond. On November 28, 1990, EPA staff visited the SWCB offices and reviewed select documents from the record.

quality standards, and review and update the standards at least once every three years. Water quality standards include the designated uses for the navigable waters and water quality criteria based upon such uses. The standards are to protect the public health or welfare, enhance the quality of the water and serve the purposes of the Act. Section 303(c)(2)(B) specifically requires states reviewing water quality standards to adopt numeric criteria for all toxic pollutants listed pursuant to Section 307(a)(1) of the CWA for which criteria have been published under Section 304(a), the discharge or presence of which in the affected waters could reasonably be expected to interfere with designated uses of the states' waters.

The states must submit the revised or newly adopted standards to the Regional Administrator of EPA for review and approval. See 40 C.F.R. § 131.20(c). EPA's review includes, among other things, a determination of whether the State has adopted water uses which are consistent with the requirements of the CWA, whether the State has adopted criteria that protect the designated water uses, and whether the State has followed its legal procedures for revising and adopting standards. See 40 C.F.R. §§ 131.5 and 131.6.

This document summarizes certain EPA considerations and conclusions in approving the water quality standards revisions submitted by Virginia.

I. ADOPTION OF STATE STANDARD PURSUANT TO STATE LAW

EPA's review of water quality standards adopted by a State includes a determination of whether the State has followed its legal procedures for revising or adopting standards. See 40 C.F.R. § 131.5. To enable EPA to make this determination, the State is required to submit a certification by the State Attorney General or other appropriate legal authority within the State that the water quality standards were duly adopted pursuant to State law. See 40 C.F.R. § 131.6(e).

Several commenters have argued that the SWCB's decision process in the adoption of the 1.2 ppq standard for 2,3,7,8-TCDD was tainted by undue consideration of economic impacts, technological feasibility, and analytical detection methods. These commenters contend that Virginia State law and the CWA do not allow consideration of these factors in developing criteria and that, consequently, EPA should disapprove the criterion.

EPA is aware of the suit filed by the Environmental Defense Fund (EDF) against the SWCB in the Circuit Court of the City of Richmond, which raises the issue of whether the SWCB adhered to the requirements of State law in its adoption of the 2,3,7,8-TCDD standard. However, the Office of the Attorney General of the Commonwealth of Virginia has certified that the criterion was duly adopted pursuant to State law, and EPA considers it appropriate at this time to rely on the Attorney General's certification regarding

State law issues pending the outcome of EDF's suit.

EPA does not view state consideration of economic impact, technological feasibility and analytical detection levels in establishing state water quality criteria as necessarily inconsistent with the CWA. Such matters may appropriately be considered in selecting among criteria levels that are protective of designated uses. With respect to the Virginia dioxin criterion, EPA's review of the transcript of proceedings of the SWCB indicates that some members of the Board took these matters into consideration in the course of deliberations on an appropriate criterion level; however, it is not clear from the record that any final determination was based on an inappropriate consideration of such matters. In any event, EPA believes, as described below, that the adopted criterion is within a range that is scientifically defensible and protective of designated uses.

II. NUMERIC WATER QUALITY CRITERIA

Where waters are designated for use by humans for such purposes as swimming, boating, fishing, and/or public water supply, or for use by aquatic organisms, the water quality criteria applicable to those waters must be sufficient to protect those designated uses. In order to calculate such water quality criteria for the protection of human health it is necessary to first derive a dose of the chemical of concern which, based on available information, is estimated to present an acceptable health risk to exposed individuals. This dose level is then used together with estimates of consumption (this may vary with the particular designated uses of the waters in question), expected bioconcentration of the chemical in fish (assuming the water is designated for fishing uses), and size of the exposed individual, to calculate a concentration of the chemical in surface waters that is not expected to cause an exceedance of the acceptable dose to exposed individuals. Criteria for the protection of aquatic life are developed to prevent acute and chronic toxicity. EPA has calculated human health criteria for over 100 priority toxic pollutants and aquatic life criteria for more than 30 priority toxic pollutants, and has published the EPA recommended criteria together with extensive summaries of the scientific information reviewed in calculating the criteria. See U.S. EPA, Quality Criteria for Water, 1986, EPA 440/5-86-001.

The Virginia human health criterion for 2,3,7,8-TCDD is less stringent than that which has been recommended by EPA. See Ambient Water Quality Criteria for 2,3,7,8-Tetrachlorodibenzo-p-dioxin, February, 1984; Memorandum from LaJuana S. Wilcher to Water Management Division Directors entitled "State Policies, Water Quality Standards, and Permit Limitations Related to 2,3,7,8-TCDD in Surface Water", January 5, 1990. Because of Virginia's departure from recommended levels, and because of the substantial recent controversy regarding health hazards posed by 2,3,7,8-TCDD, the Virginia criterion, together with each of the factors used to derive it, is described in detail in Part III of this document.

III. HUMAN HEALTH CRITERION FOR 2,3,7,8-TCDD

State human health criteria for human carcinogens are based on at least three inter-related considerations: the cancer risk factor, exposure, and acceptable risk level. The cancer risk factor is an estimate of the human cancer risk per unit of dose, based on animal laboratory data. EPA's methodology for estimating the upper limit of the cancer risk of 2,3,7,8-TCDD has involved making a number of specific scientific assumptions in the absence of a clear scientific understanding. Exposure assessment requires consideration of a number of factors ranging from the bioconcentration factor (BCF), which is used to account for the concentration of toxic pollutants in fish tissue at levels higher than the ambient water, to the amount and frequency of fish consumed and the body weight of the individual eating the fish. The level of acceptable risk is expressed as a statement of the upper bound statistical risk of one person out of a specific population size developing an excess cancer (e.g., one excess cancer for each 1,000,000 in population). The upper bound concept means that the true risk, which we cannot accurately define, is not likely to be higher and may be lower than the stated risk. Probable human carcinogens are assumed to pose <u>some</u> risk at any level of exposure; the level of acceptable risk represents a risk manager's decision as to the amount of risk that is acceptable to the exposed population.

In deriving EPA's recommended water quality criteria for 2,3,7,8-TCDD the Agency used the following assumptions: a cancer risk factor of 1.56×10^5 per milligram per kilogram per day $(mg/kg/day)^{-1}$, a BCF of 5000, 6.5 grams per day (g/day) fish consumption, drinking water ingestion of 2 liters/day and a 70 kilogram exposed individual. See, Ambient Water Quality Criteria for 2,3,7,8-Tetrachloro-dibenzo-p-dioxin, U.S. EPA Office of Regulations and Standards, EPA 440/5-84-007, February 1984 (Water Quality Criteria Document). Although EPA recommended a criterion of zero for 2,3,7,8-TCDD, as it does for all potential/probable human carcinogens, EPA also calculated, for information purposes, criteria values corresponding to upper bound risk levels of 10^{-5} to 10^{-7} (i.e., a range of one excess incidence of cancer in 100,000 to one in 10,000,000). These criteria values ranged from 0.14 to 0.0014 parts per quadrillion (ppq) if the only exposure route were through fish consumption, or 0.13 to 0.0013 ppq if it was assumed that exposed individuals were also drinking 2 liters per day of contaminated water.

In deriving a human health criterion for 2,3,7,8-TCDD, Virginia used many of the same assumptions used by EPA in its 1984 water quality criteria document for dioxin, but substituted a cancer risk factor, derived by the Food and Drug Administration (FDA) of 1.75×10^4 $(mg/kg/day)^{-1}$ compared to EPA's value of 1.56×10^5 $(mg/kg/day)^{-1}$. The resulting 1.2 ppq Virginia criterion was established to protect to the 10^{-5} risk level.

Cancer Risk Factor

EPA's estimate of upper limit cancer risk is a higher number than that of other federal agencies. It is higher than FDA's estimate by a factor of approximately 9, higher than the Center for Disease Control's (CDC's) estimate by a factor of 4, and higher than the Consumer Product Safety Commission's (CPSC's) estimate by a factor of 2.5. However, the CPSC cancer risk factor is not an upper limit value but a best estimate. If an upper limit had been used, the EPA and CPSC estimates would be nearly identical.

Although all four agencies based their risk estimates on the same scientific studies (Kociba et al., 1978), the agencies differed in their use of the data from these studies. EPA and FDA differed in their selection of tumor types in female rats. EPA combined all tumor types of significantly increased incidence, whereas FDA considered only liver tumor incidence. EPA made two adjustments in the data not made by FDA. EPA adjusted for high early mortality in high-dose animals by excluding all animals dying during the first year. EPA also incorporated two pathologists' reviews of the liver slides by using the geometric mean of the slope factors derived from each pathologist's analysis, while FDA considered only the original pathologist's review of the slides. While these differences in data selection account for some small proportion of the difference in the FDA and EPA risk estimates, the major contributing factor was choice of interspecies dose scaling factor. EPA used the surface area correction, whereas FDA used dose per body weight. When extrapolating from rat to man, the use of dose per surface area versus dose per body weight increases the risk estimate by a factor of 5.4. Background Document to the Integrated Risk Assessment for Dioxins and Furans from Chlorine Bleaching in Pulp and Paper Mills, U.S. EPA Office of Pesticides and Toxic Substances, July 1990, p. 3-7.

In 1988, EPA convened a Workgroup to reexamine the scientific basis and methods used by EPA for estimating the cancer risk for 2,3,7,8-TCDD. The Workgroup reviewed the cancer risk factors used by EPA, FDA and CDC and observed that there was no obvious scientific basis for excluding any of these values from the acceptable range. A Cancer Risk-Specific Dose Estimate for 2,3,7,8-TCDD, June 1988, p. 49. The Workgroup went on to recommend an increase in the risk specific dose associated with an upper limit 10^{-6} cancer risk level from the 0.006 picogram per kilogram per day (pg/kg/day) level presented in EPA's 1984 Water Quality Criteria Document to 0.1 pg/kg/day.[3] (Id. p. 50). EPA's Science Advisory Board (SAB) reviewed the Workgroup's report and concluded that there was no scientific basis for a change in the current assessment of the cancer risk factor at this time, and, therefore, no reason to raise the risk specific dose for 2,3,7,8-TCDD (i.e.,

---

[3] A "risk specific dose" is derived from a chemical's potency factor to yield a dose that is associated with a given risk level.

reduce the risk factor).

There has also been considerable recent additional research and debate regarding 2,3,7,8-TCDD's carcinogenic properties. For example, in March of 1990, a panel of seven pathologists reexamined the slides of the female rats from the 1978 study that was used as the basis for EPA's 1984 risk factor calculations. (Kociba et al., 1978.) These pathologists classified tumors in the rat livers using criteria for tumor classification reported by the National Toxicology Program. See Maronpot, R.R. et al. National Toxicology Program Nomenclature for Hepatoproliferative Lesions of Rats. Toxicol. Path. 14:263-273, 1986. These pathologic criteria are different from the earlier National Cancer Institute criteria used in the review of the Kociba study that formed the basis for EPA's 1984 risk factor estimate. See Squire, R.A. and Levitt, M.H. Report of A Workshop on Classification of Specific Hepatocellular Lesions in Rats. Cancer Res. 35: 3214-3223, 1975; See Ambient Water Quality Criteria for 2,3,7,8-TCDD, February 1984, at pp. C-165 et seq. Use of the new pathologic criteria, which are somewhat more discriminatory than past pathological practices with regard to identifying carcinogenic lesions, resulted in a reduced overall number of tumors counted in slides from the Kociba study. Use of this reevaluation would reduce FDA's and EPA's cancer risk estimate by a factor of approximately 3.

In addition, there are scientists who are of the opinion that, because there is more research knowledge about 2,3,7,8-TCDD's behavior as a toxicant than for other compounds, the use of default assumptions in risk factor calculation procedures may significantly overstate the 2,3,7,8-TCDD risk. See, e.g., Letter from Vernon N. Houk, M.D., Assistant Surgeon General, Director, Center for Environmental Health and Injury Control, Center for Disease Control, to J. Leonard Ledbetter, Commissioner, Georgia Department of Natural Resources, dated November 27, 1989.

EPA is currently reviewing the results of the re-reading of the Kociba slides and recent epidemiological and other studies[4], and continues to discuss, both internally and with other federal agencies, the public and other countries, the cancer risk for 2,3,7,8-TCDD. Pending resolution of the dioxin cancer risk controversy, EPA continues to recommend use of the risk factor used in EPA's 1984 criteria document. However, the basis for EPA approval of a State water quality criterion is not whether the State used EPA's recommended criterion, but whether the State's decision is scientifically defensible and protective of designated uses. Recognizing that legitimate differences of opinion regarding the cancer risk of 2,3,7,8-TCDD exist among substantial segments of the scientific community, EPA believes that Virginia is not necessarily required to adopt EPA's particular view. EPA believes that the FDA estimate of the cancer risk is within the bounds of

---

[4] See, e.g., Fingerhut, M.A. et al., 1991. "Cancer Mortality in Workers Exposed to 2,3,7,8-Tetrachlorodibenzo-p-dioxin," New England Journal of Medicine, 324:212-218.

uncertainty of EPA's approach.[5] Since EPA believes, based on the above and other information in the administrative record, that the FDA cancer risk estimate is within the range of scientific defensibility, EPA finds that Virginia's use of this factor in calculating a 2,3,7,8-TCDD water quality criterion is acceptable for purposes of Section 303 of the CWA.[6]

__Bioconcentration Factor__

The bioconcentration factor is the measure of a chemical's tendency to concentrate in the tissues of an organism at levels above ambient water concentrations. EPA used a bioconcentration factor (BCF) for dioxin in fish of 5000, as described in its water quality criteria document, based on studies which yielded a range of measured values from 390 to 13,000[7] to derive the recommended criteria for 2,3,7,8-TCDD, as did Virginia. However, recent studies and reevaluation of the methods used in earlier studies

---

[5] Although FDA, in its estimate, did not account for higher early mortality among the high dose rats and did not include significant tumor types other than the liver, which EPA would prefer to account for, the risk factor is within the bounds of uncertainty of EPA's approach.

[6] EPA notes from its review of Virginia's administrative record that the Virginia Department of Health (VDH) recommended the use of the CDC's cancer potency factor. However, the VDH concluded that it had no objection to the SWCB's choice to use the FDA cancer potency factor, and EPA is not prepared to determine that such use is scientifically indefensible or insufficiently protective of human health.

[7] The studies included in the Water Quality Criteria Document included Isensee and Jones (1975), Isensee (1978), U.S. EPA (1983) and Thomas (1983), and Branson et al. (1983). Water Quality Criteria Document at p. B-5.

suggest a much higher BCF.

The most recent published study (Mehrle, et al., Environmental Toxicology and Chemistry, 1988) gave measured BCF values ranging from about 26,000 to 29,000. However, a steady-state was not reached, and the authors of the study estimated steady-state BCF values ranging from about 37,000 to 86,000. In addition, this study used larval rainbow trout, which are very small and have low fat content.[8] The BCF for larger, more fatty fish would be expected to be significantly greater. The most recent study performed by EPA's Duluth research laboratory estimated steady-state BCFs from 66,000 to 150,000, depending on the species and fat content. This work has been accepted for publication.[9]

Despite the availability of recent studies on the BCF, EPA is not yet prepared to say that the BCF of 5000 is no longer within the range of scientific defensibility. A BCF of 5000 has been

---

[8] With respect to the Mehrle study, EPA has no reason to doubt the validity of the study and therefore believes that the data could support a steady-state BCF of 39,000 under laboratory conditions for the low-fat, unfilleted test species used. Of course, laboratory conditions may not necessarily reflect conditions existing in nature.

[9] The manuscript, by Philip M. Cook, Mary K. Walker, Douglas W. Kuehl, and Richard E. Peterson, entitled "Bioaccumulation and Toxicity of 2,3,7,8-Tetrachlorodibenzo-p-dioxin and Related Compounds in Aquatic Ecosystems," will appear in the Banbury Report on the Biological Basis for Risk Assessment of Dioxins and Related Compounds, published by the Cold Spring Harbor Laboratory in Long Island, N.Y.

generally accepted for use in developing water quality criteria for 2,3,7,8-TCDD. When EPA developed its water quality criteria for 2,3,7,8-TCDD, it performed a full review of the previously reported studies on BCF in order to arrive at the estimated value of 5000. As indicated above, recent studies, including the Mehrle study and the work performed by EPA's Duluth research laboratory, indicate that a change in the estimated value of the BCF may be necessary. However, EPA has not yet made a definitive decision respecting a change in the calculation of the BCF for 2,3,7,8-TCDD.

The staff of the SWCB calculated a State-specific BCF of 11,000 which was presented to the SWCB for their consideration and which was included in the administrative record reviewed by EPA.[10] While use of a state-specific BCF based on resident fish species is a scientifically defensible approach, EPA will not require the use of this or any other legitimate approach where another scientifically defensible approach to the derivation of a BCF is used. The SWCB ultimately chose to use the BCF of 5000 recommended by EPA in its Water Quality Criteria Document for 2,3,7,8-TCDD; as described above, EPA is not prepared to say at this time that the BCF is not scientifically defensible.

---

[10] The BCF of 11,000 was based on a measured, non-steady-state BCF of 28,664 for larval rainbow trout which was normalized for the lipid content in muscle tissue (i.e., 3% lipids) and converted to a BCF for resident fish species of Virginia (assuming an average 2.25 % lipids). EPA believes that the State should have used the predicted steady-state BCF of 39,000 and an estimated percent lipid of 2% for larval rainbow trout. With these corrections, the State-specific BCF using the approach contained in the Virginia administrative record would be 22,000.

Section 303(c) of the CWA gives to the states the authority to review and modify existing water quality standards and adopt new standards as appropriate for the protection of the public health or welfare and the enhancement of water quality. It is the express policy of the Act to recognize, preserve, and protect the primary responsibilities and rights of states to prevent, reduce, and eliminate pollution. See Section 101(b) of the CWA, 33 U.S.C. § 1251(b). In consideration of the role of the states as described by the statute, the importance of an orderly administrative process in this case, and because EPA has not made a definitive determination regarding changes in the recommended calculation of the 2,3,7,8-TCDD BCF, EPA accepts at this time Virginia's decision to use the BCF used by EPA in the development of EPA's earlier recommended criteria and published in the existing EPA guidance document. However, EPA may require Virginia and other states to revise their criteria for 2,3,7,8-TCDD on a timely basis after EPA has completed a full review of the BCF for 2,3,7,8-TCDD.

Fish Consumption

Virginia used the same fish consumption estimate (6.5 g/day) in deriving its criterion for 2,3,7,8-TCDD that EPA used in deriving its recommended criterion for 2,3,7,8-TCDD. This value is based on the nationwide average consumption of commercially and recreationally harvested freshwater and estuarine finfish and shellfish as determined through analysis of a 1973-74 seafood consumption survey performed by the National Purchase Diary in conjunction with the National Marine Fisheries Service. (U.S. EPA, 1980; Stephan, C.E., memorandum dated July 3, 1980.)

As part of its overall review of risk assessment processes, EPA is focusing on the question of whether and when risk assessment should address special populations as opposed to national averages. Various research has indicated that the use of an average rate of fish consumption may not be adequate to protect particular subgroups of the population, such as sport anglers and, particularly, subsistence fishers.[11] These studies have shown that the average consumption levels in some areas are 30 g/day for the average sport angler, and 140 g/day for the 90th percentile of sport anglers. See, Exposure Factors Handbook, U.S. EPA Office of Health and Environmental Assessment, March 1990, p. 1-15. However, EPA has also stated, with reference to the same data, that although these figures are recommended for use in estimating finfish/shellfish ingestion by sport anglers in any areas with large water bodies, no specific consumption rate values for this subgroup is recommended for small water body areas. Id. The studies which formed the basis for this recommendation were performed in Los Angeles, a marine fishing area (Puffer, 1981), and Commencement Bay, Washington, along waterways in Tacoma (Pierce, 1981). Review of the data supports the proposition that any state-

[11] See, Puffer, 1981, and Pierce, 1981, as discussed in the Exposure Factors Handbook, U.S. EPA, Office of Health and Environmental Assessment, March 1990, p. 1-15.

specific survey of consumption patterns within the state should be designed to focus on sport anglers and subsistence fishers as well, especially where water bodies of a size comparable to those used in the studies are involved.

EPA is not aware of any Virginia-specific surveys of consumption of fish drawn from the types of waters to be covered by the Virginia 2,3,7,8-TCDD criterion.[12] Information in the administrative record for Virginia's decision indicates that fishing practices and fish consumption by two Native American populations, the Mattaponi and Pamunkey Indian tribes, on the Mattaponi and Pamunkey Rivers may exceed the national average used by Virginia in the development of its water quality criterion for 2,3,7,8-TCDD. The Mattaponi and Pamunkey Rivers join to form the York River. Chesapeake Corporation's pulp and paper mill is located approximately one mile upstream from the confluence of the Mattaponi and Pamunkey Rivers and discharges to the Pamunkey River. EPA has made a preliminary investigation to determine fishing practices and fish consumption by these groups. Although no data are available on tribal fish consumption, tribal representatives indicated that they believe that members of their tribes may consume more than the 6.5 g/day average used by Virginia,

---

[12] A memorandum from the Virginia Seafood Council dated March 12, 1990 in Virginia's administrative record suggested that State-specific data on fish consumption were available from the Virginia Marine Products Board. EPA pursued this lead and was unable to locate any existing compilation of State-specific data on fish consumption.

especially during the spring when the shad run. However, their beliefs were not based on fish consumption studies.

EPA encourages Virginia, as it encourages every state, to undertake a State-specific survey in order to more accurately gauge consumption levels within the State. Such a survey, in the case of Virginia, should focus on subgroups which may consume significantly more fish than the 6.5 g/day average, such as the two Native American tribes. In the absence of State-specific data, EPA approves at the present time Virginia's use of the 6.5 g/day fish consumption estimate in deriving its 2,3,7,8-TCDD criterion. If data generated in the future suggest higher local fish consumption rates, it may be appropriate for Virginia to modify the criterion, or adopt adequately protective site-specific criteria.

Body Weight

The equation used to derive a water quality criterion includes an estimate of the body weight of the exposed individual. EPA used a body weight of 70 kg in deriving its recommended criterion. Ambient Water Quality Criteria for 2,3,7,8-TCDD, at p. C-243. This value approximates the average adult body weight, including both males and females. Exposure Factors Handbook, at p. 1-16. Virginia also used the 70 kg body weight in calculating its criterion for 2,3,7,8-TCDD. EPA approves of Virginia's use of this estimate.

Risk Level

The equation used to derive the water quality criterion for 2,3,7,8-TCDD based on cancer effects requires the choice of an acceptable risk level. As noted above, EPA set forth a range of criteria values corresponding to risk levels of 10^{-5} to 10^{-7} in its 1984 criteria document. The Virginia criterion is based on a 10^{-5} risk level.[13] This risk level is frequently used in state and federal regulatory actions, and is considered by EPA to be within an adequately protective range.

Effect of Harmonic Mean Flow Calculation

The 1.2 ppq criterion adopted by Virginia is to be applied in permitting actions based on mean annual flow in the affected streams. See, VR680-21-01.15(B). The mean annual flow is simply the long-term arithmetic mean (or average) flow. Recently, EPA has circulated draft guidance for public comment recommending that harmonic mean flow be used rather than mean annual flow when implementing criteria designed to protect against toxic effects caused by long-term exposures to carcinogens. Draft Technical Support Document for Water Quality-Based Toxics Control, April 23, 1990, at pp. 171-172. The harmonic mean flow is that flow at which

---

[13] EPA notes that the VDH recommended the use of the 10^{-6} risk level, and, furthermore, that Virginia has used the 10^{-6} risk level in the development of proposed water quality criteria for all other carcinogens. Despite this apparent inconsistency, EPA will not require Virginia to use the 10^{-6} risk level for 2,3,7,8-TCDD, since the choice of a risk level, within the range which EPA has determined to be acceptable, is a risk management decision and is the domain of the State.

the in-stream concentration would be equal to the long-term arithmetic mean concentration. Mean annual flow is typically around three-fold greater than the harmonic mean flow because of the influence of storm events.[14] Because mean annual flow is typically greater than harmonic mean flow, use of mean annual flow in dilution calculations allows greater quantities of pollutants to be discharged than would be allowed if harmonic mean flow were used.

To assess the significance of Virginia's decision to implement its criterion based on mean annual flow, EPA has reviewed the ratios between mean annual flow and harmonic mean flow for the three rivers which are the receiving streams for the discharges from the three pulp and paper mills located in Virginia which are known sources of dioxin discharge. The ratios for the Pamunkey River and the Jackson River, the receiving streams for the Chesapeake Corporation and Westvaco facilities, were 3.4 to 1 and 1.9 to 1, respectively.

The discharge from the Union Camp mill into the Blackwater River is a seasonal discharge from November through March. Therefore, the seasonal arithmetic mean flow (SAMF) and seasonal harmonic mean flow (SHMF) from November through March were used for these calculations. The SAMF for the Blackwater River was

---

[14] See, e.g., Rossman, L.A., "Design Stream Flows Based on Harmonic Means," Journal of Hydraulic Engineering, Vol. 116, No. 7, p. 949, July, 1990.

calculated to be thirty-nine (39) times greater than the SHMF. However, this variation would not have a linear effect on the calculated in-stream concentration of dioxin at the SHMF because dilution of an effluent includes the volume of the effluent (if the water source of the effluent is other than the receiving stream) in addition to the upstream flow. In the case of Union Camp, the effluent flow from the facility, which is derived from water sources other than the Blackwater River, is 159 cubic feet per second (cfs); the SAMF, measured upstream of the discharge, is 710 cfs; and the SHMF, measured upstream of the discharge, is 18 cfs. The dilution factor for Union Camp's effluent at the SAMF is 869 cfs divided by 159 cfs, or a factor of 5.46; the dilution factor for Union Camp's effluent at the SHMF is 177 cfs divided by 159 cfs, or a factor of 1.11. Therefore, the dilution of Union Camp's effluent at the SHMF is 4.9 (i.e., 5.46 divided by 1.11) times less than at the SAMF. When the 1.2 ppq concentration at SAMF is multiplied by 4.9 to get the actual in-stream concentration at SHMF, the resulting concentration is 5.9 ppq. The 4.9 to 1 ratio between the dilution factors at mean annual flow and harmonic mean flow for the Blackwater River is the largest such ratio for the three waters receiving pulp mill discharges in Virginia.

Using the assumptions used by Virginia, this increase in the in-stream concentration would represent a risk to the average individual of 5 x 10^{-5}.[15] EPA does not believe this slight variation from the risk level public-noticed by Virginia warrants a disapproval on the basis that Virginia did not properly inform its citizens of the risk level chosen.[16] Furthermore, EPA believes this risk level is within an adequately protective range. Moreover, the permit limit for the Union Camp mill, which is close to the border with North Carolina, must be calculated to ensure that the water quality standards downstream in North Carolina are maintained. See 40 C.F.R. § 122.44(d)(4). North Carolina has adopted a 2,3,7,8-TCDD criterion of 0.014 ppq; consequently, the 1.2 ppq criterion in Virginia will not be controlling in the case of the Union Camp discharge, and the projected 5.9 ppq concentration of dioxin at SHMF will not be likely to occur.[17]

---

[15] When this adjustment for the variation in stream flow is taken into consideration in combination with the risk analysis using EPA's assumptions presented below under the Holistic Approach to Risk Assessment (which yield a lifetime risk to the average exposed individual of 10^{-4}), the risk to the average exposed individual is only increased to 4.5 x 10^{-4}.

[16] Although in this analysis EPA has targeted the receiving streams for the three pulp and paper mills due to the mills' discharges of 2,3,7,8-TCDD, it may be appropriate for Virginia to develop site-specific criteria that are more stringent than the 1.2 ppq criterion for other stream segments where the mean annual flow greatly exceeds the harmonic mean flow. Alternatively, the State could, on a site-specific basis, apply the 1.2 ppq criterion at a design flow which more accurately represents the long-term average flow.

[17] The permit limit for the Union Camp mill must be more stringent in order to meet North Carolina's 0.014 ppq criterion than it would have to be to meet the 1.2 ppq criterion at SAMF in Virginia. EPA has recommended that Virginia propose a permit limit for 2,3,7,8-TCDD of 0.076 ppq, calculated to comply with the North Carolina criterion, as part of Union Camp's individual control strategy necessary to comply with the requirements of Section 304(l) of the CWA.

<u>Holistic Approach to Risk Assessment</u>

Several commenters have argued that, although it is typically acceptable for a state developing regulatory criteria to rely on EPA's recommended criteria, including each factor used in deriving the criteria, if a state uses one less stringent factor than was used by EPA, the state must reevaluate all of the factors involved. This position acknowledges that EPA will typically not revise its criteria documents if it believes that the recommended "bottom-line" criteria values are valid, even if current information suggests that certain factors should be modified. It is possible, for example, that new information suggesting that a chemical is a less potent probable human carcinogen than originally expected will be counterbalanced by new information that the BCF is greater than originally expected. In such instances it is possible that EPA's "bottom line" recommended criterion would not change notwithstanding the new information. In such cases it would be inappropriate for a state to modify just the one factor (cancer risk), which may have been found to be overly protective, without also reviewing recent information on the other factors (including BCF), which may have been found to be insufficiently protective.

Where a state departs in a non-conservative direction with respect to one of the factors used by EPA in a criteria document, it is appropriate for EPA and/or the state to closely scrutinize all of the elements used in the state's risk assessment. This document has presented an evaluation of all of the factors involved in the Virginia assessment, and has concluded that the use of each factor is independently justifiable at this time. Since each factor underlying the risk assessment is independently justifiable, EPA finds the 1.2 ppq criterion protective of designated uses and otherwise consistent with the requirements of the CWA as regards protection against cancer effects.

As described above, EPA is currently reevaluating the BCF, the 6.5 g/day fish consumption value and the dioxin cancer risk factor. It appears at this time that changes to the BCF and fish consumption factors that would be supported by recent research could tend to support more stringent dioxin criteria and that changes with respect to the cancer risk factor may support less stringent criteria. After EPA has reevaluated all of these factors, Virginia may be required to adjust its criterion accordingly.

For comparison purposes, EPA notes that, based on the assumptions used in deriving EPA's recommended criteria for 2,3,7,8-TCDD, the Virginia criterion yields a lifetime risk to an average exposed individual of 10^{-4}. Thus, even using EPA's assumptions (which EPA continues to support), the risk level is of a magnitude that is, depending on the circumstances, sometimes found acceptable to federal and state risk managers, including EPA.

In light of the above, and other information in the administrative record, EPA finds Virginia's water quality criterion of 1.2 ppq for 2,3,7,8-TCDD to be protective of designated uses and to otherwise meet the requirements of the CWA, as regards protection against cancer effects.

Non-cancer Effects

Water quality criteria to protect human health should safeguard against both cancer and non-cancer endpoints. With respect to non-cancer endpoints, 2,3,7,8-TCDD has been shown in animal studies to be a reproductive, developmental and hepatic toxicant. See U.S. EPA, Health Assessment Document for Polychlorinated Dibenzo-p-Dioxins, September, 1985. EPA scientists have used the data from these studies to calculate a reference dose (RfD) and health advisories (HAs) for 2,3,7,8-TCDD.[18]

An RfD is an estimate of the lifetime daily dose to the human population likely to be without any appreciable risk of deleterious effect. RfDs are generally based on studies involving lifetime exposures of animals. Usually doses that are less than the RfD are not likely to be associated with any health risks, and are therefore less likely to be of regulatory concern. However, as the frequency of exposures exceeding the RfD increases, and as the

[18] The RfD for 2,3,7,8-TCDD has not been subjected to the internal agency-wide peer review that EPA policies require prior to formalizing an RfD. The HAs have been developed by individual EPA Offices and, in accordance with Agency procedures for HAs, have not received Agency-wide review.

size of the excess increases, the probability increases that adverse effects may be observed in a human population. Nonetheless, a clear conclusion cannot be categorically drawn that all doses below the RfD are "acceptable" and that all doses in excess of the RfD are "unacceptable." The endpoints of concern in RfDs developed for 2,3,7,8-TCDD are reproductive and developmental effects. EPA scientists have calculated an RfD for 2,3,7,8-TCDD based on reproductive toxicity (the most sensitive endpoint for effects due to long-term exposures) of 1 X 10^{-6} micrograms per kilogram per day (ug/kg/day). Ambient Water Quality Criteria for 2,3,7,8-TCDD, p. C-179.

HAs are developed for less-than-lifetime exposures to chemicals of concern. HA dose levels are appropriate for comparison with single doses or short-term exposures. HAs for 2,3,7,8-TCDD have been calculated for hepatic effects: 1 day - 100 pg/kg/day and 10 day - 10pg/kg/day. See Background Document to the Integrated Risk Assessment for Dioxins and Furans from Chlorine Bleaching in Pulp and Paper Mills, (1990). These HA levels are also estimated to be protective against developmental toxicity. As for RfDs, HA levels do not necessarily represent levels to be used as a basis for regulatory action.

The RfD and HA values can be used to calculate ambient water concentrations of 2,3,7,8-TCDD that will not cause an exceedance of the dose values as a result of estimated fish consumption.

Assuming a bioconcentration factor in fish of 5000, fish consumption of 6.5 g/day, and a 70 kg individual, in-stream concentrations that would lead to exposures at the RfD level would be 2.15 parts per quadrillion.[19] Ambient Water Quality Criteria for 2,3,7,8-TCDD, p. C-179. The assumptions for body weight, bioconcentration factor and fish consumption used in this calculation are the same as those used in calculating criteria based on the 2,3,7,8-TCDD cancer risk, and their use is justified for the same reasons described above in the cancer risk section.

Virginia's 1.2 ppq criterion for 2,3,7,8-TCDD is less than the 2.15 ppq level which is estimated to yield doses at the RfD level. However, as noted above, the Virginia criterion is to be applied in permitting actions based on mean annual flow rather than harmonic mean flow.

Although EPA is still reviewing comments received on its draft guidance recommending use of harmonic mean flow, the final analysis of whether the Virginia criterion is adequately protective against long-term non-cancer effects would not change even if EPA were to conclude that harmonic mean flow must be used when implementing criteria for protection of human health against effects due to long-term exposures. Since mean annual flow is typically three

---

[19] This value would be somewhat greater if a correction were made to reflect studies indicating that humans do not absorb 100 percent of 2,3,7,8-TCDD ingested. See, Boyer, I.J., "Bioavailability of Ingested 2,3,7,8-TCDD and Related Substances" (DRAFT), 1989.

times greater than harmonic mean flow, compliance with the Virginia 1.2 ppq 2,3,7,8-TCDD criterion based on mean annual flow would typically result in an in-stream concentration of no more than 3.6 ppq at the harmonic mean flow.[20] This value is just slightly greater than the 2.15 ppq level that corresponds to the RfD level for 2,3,7,8-TCDD. Given the facts that the RfD includes a safety factor of 1000, and that the RfD level does not necessarily represent a level of regulatory concern, and that derivation of the 2.15 ppq value assumes 100 percent absorption of ingested dioxin[21], this estimation of the increased concentration of 2,3,7,8-TCDD expected at harmonic mean flows, would not lead EPA to disapprove the Virginia criterion as a Statewide criterion.[22] Compliance with the 1.2 ppq criterion at the seasonal arithmetic mean flow (SAMF) on the Blackwater River would result in an in-stream concentration of 5.9 ppq at the seasonal harmonic mean flow (SHMF). This value exceeds the 2.15 ppq level that corresponds to the RfD for 2,3,7,8-TCDD by only 3.75 ppq or a factor of 2.7. EPA believes that this variation is within the range of uncertainty inherent in these calculations and does not present a sufficient basis for

---

[20] Depending on the volume of the effluent flow, the resulting in-stream concentration could be much less than 3.6 ppq, or close to 1.2 ppq. (See pp. 20-21 for a discussion regarding the effect of the addition of the effluent flow to the stream flow on the in-stream concentration of dioxin.)

[21] See footnote 19 above.

[22] In streams where the difference between mean annual flow and harmonic mean flow is greater than the typical difference, it may be appropriate for Virginia to develop site-specific criteria that are more stringent than the general 1.2 ppq criterion.

disapproval of the 1.2 ppq criterion for this River. Furthermore, as noted above, the permit limit for the Union Camp discharge to the Blackwater River will be controlled by the North Carolina 0.014 ppq dioxin criterion, and the resulting in-stream concentration will not be likely to reach 5.9 ppq at the SHMF.

In light of the above, and other information in the administrative record, EPA finds that Virginia's water quality criterion for 2,3,7,8-TCDD is protective of designated uses, and otherwise meets the requirements of the CWA, as regards protection against long-term non-cancer effects.

With respect to protection against short-term effects, assuming a bioconcentration factor of 5000, consumption of 6.5 g/day of fish, and a 70 kg person, the in-stream concentrations that would lead to exposures at 1 day and 10 day HA levels would be 215 ppq and 21.5 ppq, respectively. However, it may be inappropriate to use the 6.5 g/day long-term average fish consumption estimate in these calculations, since short-term fish consumption rates may be expected to exceed long-term average consumption rates. If a consumption estimate of 115 g/day (approximately 1/4 lb. of fish)[23] is substituted in the equation for the 1 day HA, the corresponding criterion would be 12.2 ppq.

---

[23] While there may be competing views on selection of a single estimate of 1 day fish consumption values, it appears reasonable to use 115 grams, or a typical fish meal, for purposes of this calculation.

For the 10-day HA, substitution of a consumption value of 30 grams/day[24] would result in a water quality criterion of 4.66 ppq. In each of these calculations, lower criteria values would be derived if it were assumed that the same quantities of fish were being consumed by individuals smaller than 70 kg, that larger quantities of fish are consumed, or that fish bioconcentrate 2,3,7,8-TCDD to a greater degree.

The Virginia 1.2 ppq criterion is below the levels calculated to yield doses at the HA levels using the above assumptions for the typical flow regime, even taking into consideration the estimated 3.6 ppq concentration expected at the harmonic mean flow.[25] The concentration of 5.9 ppq that would result in the Blackwater River at the SHMF, applying the Virginia 2,3,7,8-TCDD standard as adopted, would exceed the level deemed to be protective against

---

[24] This value represents average fish consumption of recreational fishers on large water bodies. Exposure Factors Handbook, March 1990, p. 1-15.

[25] For some pollutants it may be appropriate to use low flow periods, rather than the harmonic mean flow, in calculating criteria to protect human health against short-term effects. See Draft Technical Support Document for Water Quality-based Toxics Control, p. 172, April 23, 1990. However, because it takes a long period of time for fish to achieve a steady-state with the surrounding 2,3,7,8-TCDD water concentration, (see Draft Lake Ontario TCDD Bioaccumulation Study, Chapter 9), it is not expected that the quantity of 2,3,7,8-TCDD in fish tissue will be significantly higher during low flow periods than it will be during periods corresponding to harmonic mean flow. And, because the preponderance of 2,3,7,8-TCDD exposure is expected to occur through fish consumption as opposed to drinking water consumption, it is not expected that there will be significantly greater risks during low flow periods than during flow periods that correspond to harmonic mean flow.

short-term health effects for the 10-day HA assuming 30 g/day fish consumption by 1.24 ppq or a factor of 1.27. However, due to the uncertainties inherent in these calculations, and the fact that HA levels are not necessarily levels of regulatory concern, EPA does not believe that this difference renders the Virginia 1.2 ppq unacceptable.[26]

In light of the above, and other information in the administrative record, EPA finds that Virginia's water quality criterion for 2,3,7,8-TCDD is protective of designated uses, and otherwise meets the requirements of the CWA, as regards protection against short-term human health effects.

IV. AQUATIC TOXICITY

The Virginia criterion for 2,3,7,8-TCDD is designed to protect human health. Accordingly, EPA has limited its review to assessing the adequacy of the numeric criterion for that purpose. Virginia did not submit a criterion for 2,3,7,8-TCDD for the protection of aquatic life. Depending on the circumstances, greater protection than is afforded by Virginia's 1.2 ppq criterion may be required for this purpose.[27] In the absence of a numeric criterion for

---

[26] Furthermore, the in-stream dioxin concentration in the Blackwater River is not expected to be as high as 5.9 ppq at the SHMF. *See* pp. 22 and 29 above.

[27] Dioxin is highly toxic to aquatic organisms. The lowest test concentration among all known dioxin studies (38 ppq) produced 45 percent mortality in rainbow trout exposed to dioxin for 28 days. None of the dioxin studies to date have found a non-toxic exposure level for aquatic life.

2,3,7,8-TCDD to protect aquatic life, Virginia's narrative criterion must, consistent with 40 C.F.R. § 122.44(d), be interpreted in individual permitting actions to prevent harm to aquatic life.

CONCLUSION

EPA approves Virginia's water quality standard for 2,3,7,8-TCDD as a statewide human health standard for the reasons stated above. EPA is continuing to examine the various factors which are considered in the calculation of water quality criteria, including 2,3,7,8-TCDD. As updated studies on these factors are made available to the public, states may be expected by EPA to adjust water quality criteria accordingly.

State of Oregon
DEPARTMENT OF ENVIRONMENTAL QUALITY
RECEIVED
JUN 10 1991
OFFICE OF THE DIRECTOR

VICTOR M. SHER (WSB# 16853)
TODD D. TRUE (WSB# 12864)
REBECCA E. TODD (WSB# pending)
Sierra Club Legal Defense Fund
216 First Avenue S., Suite 330
Seattle, Washington 98104
(206) 343-7340

BEFORE THE ENVIRONMENTAL QUALITY COMMISSION
OF THE STATE OF OREGON

In the Matter of the Petition of James River II, Inc. and Boise Cascade Corporation to Amend Subparagraph (2)(p)(B) of Oregon Administrative Rules Chapter 340, Division 41, Sections 205, 245, 285, 325, 365, 445, 485, 525, 565, 605, 645, 685, 725, 765, 805, 845, 885, 925, and 965.	MEMORANDUM IN OPPOSITION TO THE PETITION FOR RULE AMENDMENT

I. Introduction

This Memorandum in Opposition to the Petition for Rule Amendment is submitted by the Sierra Club Legal Defense Fund, Inc. on behalf of the American Oceans Campaign, the Campaign for Puget Sound, the Dioxin/Organochlorine Center, Friends of the Earth, National Audubon Society, Puget Sound Alliance, the Washington Environmental Council, and the Washington Toxics Coalition.[1] These organizations are non-profit environmental groups dedicated to and actively working toward the preservation and protection of water resources and all life dependent on them.

[1] American Oceans Campaign, 4007 Latona Avenue NE Seattle, WA 98105; Campaign for Puget Sound, P.O. Box 2807 Seattle, WA 98111-2807; Dioxin/Organochlorine Center, 1247 Willamette Street Eugene OR 97401; Friends of the Earth, 4512 University Way NE Seattle WA 98105; National Audubon Society, P.O. Box 462 Olympia, WA 98502; Puget Sound Alliance, 4516 University Way NE Seattle WA 98105; Washington Environmental Council, 5200 University Way NE Seattle WA 98105; and the Washington Toxics Coalition, 4516 University Way NE Seattle WA 98105.

In specific, the organizations seek to reduce and eliminate entirely the discharge of toxic organochlorines to the waters of the Pacific Northwest, including 2,3,7,8 tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD), commonly known as dioxin.[2]

We strongly oppose the Petition for Rule Amendment and urge the Environmental Quality Commission to deny the Petition. We are a group of national, regional, and Washington State environmental groups concerned about the water quality of the Pacific Northwest, Oregon, and the water resources shared by Oregon, Washington, and Idaho. The Columbia River receives much of the region's pulp and paper mill organochlorine discharge and for many hundreds of miles is a shared resource and border for Oregon and Washington.[3] The ambient water quality standard for 2,3,7,8-TCDD in Oregon necessarily affects these shared ecosystems and the livelihood and recreation of those living in both states. We are also concerned with the precedential implications that the Petition for Rule Amendment may have nationwide and for the Pacific Northwest.

---

[2] "Dioxin" as it refers to 2,3,7,8-TCDD is actually a misnomer. Dioxins are a family of approximately 75 separate chlorinated organic compounds, each of which is characterized by the existence of two oxygen atoms connecting two chlorinated benzene rings.

[3] The interdependence of the Pacific Northwest states with regard to the Columbia River has been recognized by the formation by Oregon and Washington of the Bistate Commission for the Columbia River, and the basin-wide protection strategies for the River established by the Environmental Protection Agency [EPA], including the establishment of Total Maximum Daily Loadings and Individual Control Strategies pursuant to the Federal Water Pollution Control Act, 33 U.S.C. §§ 1313(d) and 1314(l), respectively.

2,3,7,8-TCDD is a known human carcinogen, teratogen, and immunosuppressant.[4] Other types of damage caused by 2,3,7,8-TCDD include skin disorders, reproductive disorders, hormonal and metabolic effects, developmental defects, damage to the liver, kidney and thymus, wasting syndrome, neurobehavioural effects, and learning disabilities.[5] Furthermore, 2,3,7,8-TCDD is

---

[4] Some pertinent papers regarding this include:

Fingerhut, Marilyn A., William E. Halperin, David A. Marlow, Laurie A. Piacitelli, Patricia A. Honchar, Marie H. Sweeney, Alice L. Greife, Patricia A. Dill, Kyle Steenland, and Anthony J. Suruda, Cancer Mortality in Workers Exposed to 2,3,7,8 Tetrachlorodibenzo-p-dioxin, The New England Journal of Medicine 324: 212-218 (1991).

Schwartz, E., A Proportionate Mortality Ratio Analysis of Pulp and Paper Mill Workers in New Hampshire, British Journal of Industrial Medicine 45:234-238 (1988).

Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 (1989).

Skene, S.A., I.C. Dewhurst, and M. Greenberg, Polychlorinated Dibenzo-p-dioxins and Polychlorinated Dibenzofurans: The Risks to Human Health: A Review, Human Toxicology 8:173-203 (1989).

[5] Some pertinent papers regarding this include:

Bowman, R.E., S.L. Schantz, M.L. Gross, and S.A. Ferguson, Behavioral Effects in Monkeys Exposed to 2,3,7,8-TCDD Transmitted Maternally During Gestation and for Four Months of Nursing, Chemosphere 18:235-242 (1989).

Fish and Wildlife Service, Dioxin Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review, Biological Report 85, May 1986.

Jacobson, Joseph L., Sandra W. Jacobson, and Harold E.B. Humphrey, Effects of In Utero Exposure to Polychlorinated Biphenyls and Related Contaminants on Cognitive Functioning in Young Children, Journal of Pediatrics 116:38-45 (1990).

Larsson, Ake, T. Andersson, L. Forlin, and J. Hardig, Physiological Disturbances in Fish Exposed to Bleached Kraft Mill Effluents, Wat. Sci. Tech. 20:67-76, 1988.

McCormack, Craig and David Cleverly, United States Environmental Protection Agency, Analysis of the Potential Populations at Risk From the Consumption of Freshwater Fish Caught Near Paper Mills, Draft Report, April 23, 1990.

Schantz, Susan L., and Robert E. Bowman, Learning in Monkeys Exposed Perinatally to 2,3,7,8 Tetrachlorodibenzo-p-dioxin (TCDD), Neurotoxicology and Teratology 11:13-19, 1989.

bioaccumulative, bioconcentrative, and persistent.[6]

Moreover, while 2,3,7,8-TCDD is the most toxic substance ever identified, and hence the most toxic of the organochlorines, chlorine bleaching pulp and paper production generates tons of chlorinated organics which are toxicologically equivalent to 2,3,7,8-TCDD. In other words, these other organochlorines act within the body and the environment in virtually the same toxicological manner as 2,3,7,8-TCDD. For example, in issuing a recent Fish Consumption Advisory for Lake Roosevelt, the Washington State Department of Health recognized that 90% of the dioxin toxicity is due to 2,3,7,8 tetrachlorodibenzofuran.[7] As one of the leading scientific experts has written,

---

Svensson, Bengt-Goran, Anita Nilsson, Marianne Hansson, Christopher Rappe, Bjorn Akesson, and Staffan Skerving, Exposure to Dioxins and Dibenzofurans Through the Consumption of Fish, The New England Journal of Medicine 116:8-12 (1991).

Swain, Wayland R., Human Health Consequences of Consumption of Fish Contaminated with Organochlorine Compounds, Aquatic Toxicology 11:357-377 (1988).

Tanabe, S., N. Kannan, An. Subramanian, S. Watanabe, and R. Tatsukawa, Highly Toxic Coplanar PCBs: Occurrence, Source, Persistency and Toxic Implications to Wildlife and Humans, Environmental Pollution 47:147-163 (1987).

[6] The toxicokinetic half-life of 2,3,7,8-TCDD in human tissue has been predicted to be approximately 5 to 8 years and the half-life in sediments is even longer. See, Bowman, R.E., S.L. Schantz, N.C.A. Weerasinghe, M.L. Gross, and D.A. Barsotti, Chronic Dietary Intake of 2,3,7,8 Tetrachlorodibenzo-p-dioxin (TCDD) at 5 or 25 Parts Per Trillion in the Monkey: TCDD Kinetics and Dose-Effect Estimate of Reproductive Toxicity, Chemosphere 18:243-252 at 250 (1989), and Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 at 458 (1989).

[7] Washington Department of Ecology, First Progress Report on Ecology's Dioxin/Furan Survey in Lake Roosevelt, Memorandum from Art Johnson, Dave Serdar, and Stuart Magoon to Carl Nuechterlein, August 8, 1990.

> it is misleading to consider dioxin as a single entity, and the potential health risks are properly evaluated by taking into account exposures to mixtures of the hundreds of isomers and related compounds in this group.[8]

An approach, therefore, which focuses on the cancer risks from 2,3,7,8-TCDD necessarily underestimates cancer risks from pulp and paper mill effluent[9] and also ignores other arguably more important organismic and ecosystem level impacts from 2,3,7,8-TCDD such as adverse reproductive, developmental, and wildlife effects.

//

//

//

//

//

---

[8] Silbergeld, Ellen K. and Thomas A. Gasiewicz, Dioxins and the Ah Receptor, American Journal of Industrial Medicine 16:455-474 at 456 (1989).

[9] EPA itself recognizes that its cancer risk and attendant water quality standard of .013 ppq vastly underestimate the actual cancer risk suffered by certain sensitive populations. EPA estimates that a Native American adult consuming Columbia River Basin fish in an amount average for Native Americans per day contaminated with 6.5 parts per trillion (ppt) 2,3,7,8-TCDD equivalents exceeds the EPA threshold of concern for reproductive effects by over nine times. See, McCormack, Craig and David Cleverly, United States Environmental Protection Agency, Analysis of the Potential Populations at Risk From the Consumption of Freshwater Fish Caught Near Paper Mills, Draft Report, April 23, 1990.

Furthermore, in calculating the cancer risk and water quality standard for 2,3,7,8-TCDD, EPA assumed a fish consumption rate of only 6.5 grams per day, while actual fish consumption rates are approximately five times higher than this, and Native American fish consumption rates are approximately fifteen times higher. More realistic fish consumption rates, therefore, would make the cancer risk standards five to fifteen times higher, respectively. Id.

II. The Environmental Quality Commission Should Deny the Petition for Rule Amendment.

We strongly urge the Commission to deny the Petition for Rule Amendment filed by James River II and the Boise Cascade Corporation on May 23, 1991. A new rulemaking effort makes little sense in light of the limited resources of the State of Oregon. Indeed, Oregon initially adopted the .013 ppq standard established by EPA's Quality Criteria for Water 1986 with the express realization that the State had insufficient resources to undertake adequately a separate analysis of the health risks of 2,3,7,8-TCDD. As the State continues to suffer from limited resources, it continues to be ill-advisable for the State to undertake the complex analysis of human and environmental health risks from 2,3,7,8-TCDD necessary in deciding the water quality standard.

The adoption of a water quality criterion or standard is a significant task. EPA regulations mandate that every water quality criteria

> must be based on sound scientific rational and must contain sufficient parameters or constituents to protect the designated use. For waters with multiple use designations, the criteria shall support the most sensitive use.

40 C.F.R. § 131.11(b)(1)(1990). To adopt a new water quality standard requires that the rulemaking body employ "scientifically defensible methods" in assuring that the most sensitive uses are protected. 40 C.F.R. § 1313.11(b)(1)(1990) Establishing a new water quality standard for 2,3,7,8-TCDD would be extremely resource intensive, consuming the kind of time and energy that the State of Oregon has already recognized that it lacks.

Furthermore, the issue of the proper water quality standard for 2,3,7,8-TCDD will be debated shortly in another forum. EPA established the Total Maximum Daily Loadings [TMDL] for the Columbia River on February 25, 1991, regarding the total allowable discharge of 2,3,7,8-TCDD into the Basin. We anticipate legal challenges to the TMDL asserting that the .013 ppq standard is inadequate to protect human health and wildlife. In this connection, we believe that the appropriate water quality standard for 2,3,7,8-TCDD is zero, as detailed in Section III below.

Furthermore, from an ecosystem perspective it is nonsensical to allow mills in Oregon to discharge bioaccumulative and persistent organochlorines into the Columbia River Basin at 2.3 ppq, while Idaho and Washington mills comply with the applicable .013 ppq state standards, a difference of orders of magnitude. Fish, endangered Bald Eagles feeding on them, mink, otter, other wildlife, as well as sensitive human populations such as Native Americans, Asian Americans, and subsistence and sport fishers cannot differentiate among the 2,3,7,8-TCDD contamination from Oregon and that from other states. With regard to these especially sensitive groups, the State of Oregon has a duty to protect all of the people that compose the population of the State. While the .013 ppq standard is not adequately protective of either humans and wildlife, the suggested 2.3 ppq standard is even less so.

//

//

At this time and given the limited resources of the State, the most logical and protective course of action for the Commission is to deny the Petition for Rule Amendment.

III. Alternatively, If the Environmental Quality Commission Revisits the Rulemaking Procedure, the Proper Water Quality Standard for 2,3,7,8-TCDD is Zero.

The chlorine bleaching pulp and paper mills insist that new data indicate that the ambient water quality standard for 2,3,7,8-TCDD should be loosened. It is our position, and the position of the best scientific experts in the field, that available data militate for a <u>more stringent and protective</u> standard. These data include human reproductive and developmental effects, the effects on wildlife reliant on contaminated ecosystems, and the bioaccumulation, bioconcentration, and persistence of 2,3,7,8-TCDD in animal tissue and sediments. If the Petition for Rule Amendment is granted, we expect that the Commission will find itself in the midst of an extremely involved and complex dispute, with both sides presenting evidence and expert opinion regarding the proper water quality standard for 2,3,7,8-TCDD.

If the Commission does indeed elect to reopen rulemaking, we anticipate arguing that the standard for 2,3,7,8-TCDD is properly zero, that is, that the Commission should allow no discharges of 2,3,7,8-TCDD at all.

//

//

//

We are not the first to suggest to the State of Oregon that the water quality standard for 2,3,7,8-TCDD should be zero. Over the past several years, the United States Fish and Wildlife Service has consistently advised that because of the long-term health effects on wildlife that 2,3,7,8-TCDD discharges be reduced and eliminated:

> We recommend that the DEQ consider limiting the [pulp and paper mills' National Discharge Elimination System, or NPDES] permit[s] to a discharge of no dioxins...

Letter from the United States Fish and Wildlife Service to the Oregon Department of Environmental Quality dated July 10, 1989. Six months later the Fish and Wildlife reiterated that

> we believe it is appropriate for DEQ to develop a long-term goal that decreases and eventually eliminates the production of dioxin and other chlorinated byproducts.

Letter from the United States Fish and Wildlife Service to the Oregon Department of Environmental Quality dated January 19, 1990.

In recognition of the severity of the organochlorine contamination in the Columbia River Basin, the Fish and Wildlife Service most recently explained that

> considering the longevity of organochlorine compounds and the potential impact of small quantities of dioxins on fish, waterfowl, and endangered species, we recommend that the EPA strive towards limiting NPDES permits to zero discharge of dioxins to the Columbia River Basin.

Letter from the United States Fish and Wildlife Service to Region 10 EPA dated November 21, 1990. The zero discharge standard is the only standard for 2,3,7,8-TCDD that will adequately protect human, wildlife, and environmental health.

There are many technologies available and in use worldwide that reduce and eliminate the use of chlorine or chlorine compounds that are the necessary precursors for all chlorinated organic compounds. Without chlorine or chlorine compounds present in the production process, organochlorines cannot be formed and discharged to the environment. Many European mills and some North American mills currently employ chlorine-free technology in their pulp and paper production. Many if not all the mills in the United States are at the very least exploring ways in which they can reduce their use of chlorine and the subsequent discharge of toxic organochlorines.

Furthermore, the public is becoming increasingly aware of the human and environmental health risks associated with chlorine bleaching and is demanding chlorine-free pulp and paper products. The mill in Lyons Falls, New York is one example of a mill that has converted to a chlorine-free technology and has subsequently experienced an increase in its market share. As consumers increasingly demand chlorine-free paper products, those mills that can supply them are enjoying competitive success in the marketplace.

As has been long recognized elsewhere, there are no functional uses of pulp and paper products that demand the super bright whiteness normally achievable with chlorine bleaching processes. Non-chlorine bleaching renders pulp and paper products that are nearly as bright white as chlorine bleached products. These chlorine-free products are suitable for every use to which pulp and paper products are put today.

Because of the availability of chlorine-free technologies, the complete lack of need for chlorine bleached pulp and paper, and the serious and persistent risks to human and environmental health, if the Commission grants the Petition for Rule Amendment, we anticipate returning to urge the Commission to promulgate an ambient water quality standard of zero for 2,3,7,8-TCDD.

IV. Conclusion

On behalf of the organizations listed above, we offer this Memorandum in Opposition to the Petition for Rule Amendment. We will gladly provide the Commission with any of the data discussed above. As we have not had the opportunity to view all the information submitted by the mills, we are unable to respond directly to their particular scientific or other assertions. Should the Commission like us to provide a more detailed response to their specific claims, we will arrange to procure the mills' lengthy submission and provide a detailed scientific analysis for the Commission's review. That being said, however, we believe that the wisest, most protective, and most efficient course of

//

//

//

//

//

//

//

//

action for the Commission is to deny the Petition for Rule Amendment and we urge the Commission to do so.

Dated this 10th day of June, 1991.

Respectfully submitted,

Victor M. Sher /RET

VICTOR M. SHER

Todd D. True /RET

TODD D. TRUE

Rebecca E. Todd

REBECCA E. TODD

Sierra Club Legal Defense Fund, Inc.
216 First Avenue S. Suite 330
Seattle, WA 98014
(206) 343-7340

Attorneys for American Oceans Campaign, Campaign for Puget Sound, Dioxin/Organochlorine Center, Friends of the Earth, National Audubon Society, Puget Sound Alliance, Washington Environmental Council, and Washington Toxics Coalition.

Sent by telecopy to:

Chair William P. Hutchison, Jr.	(503) 223-5550
Vice Chair Emery N. Castle	(503) 737-1574
Commissioner Henry Lorenzen	(503) 276-3148
Commissioner Carol A. Whipple	(503) 584-2129
Commissioner William W. Wessinger	(503) 229-4689
Director Fred Hansen	(503) 229-6124

cc: Mr. Larry Edelman
Ms. Dana Rasmussen
Mr. Rick Albright
Ms. Adrianne Allen

Oregon

DEPARTMENT OF ENVIRONMENTAL QUALITY

February, 1991

Attached is the Department of Environmental Quality's report to the Legislature on the Status of Recycling in Oregon as required by ORS 459.168. In addition to providing information on implementation of the Opportunity to Recycle Act, this report also includes information on local government waste reduction programs, the Metropolitan Service District's Waste Reduction Program, and the status of lead-acid battery recycling in Oregon.

The information in this report is based solely on data collected under the Opportunity to Recycle Act and, therefore, includes information related primarily to residential curbside recycling and waste recycled through the recycling depots at solid waste disposal sites. The report also provides information on compliance status with the current Oregon recycling law.

The report stresses the need to collect more complete information about recycling and waste reduction on a statewide basis. This information is needed not only to monitor Oregon's progress in recycling and waste reduction, but also to develop better markets for recyclable materials and establish recycling goals to reduce the amount of solid waste disposed. Information is needed on the composition of the solid waste stream statewide, as well as information about the amount and types of materials collected and processed through such things as buy-back centers, volunteer collection projects, industries like Goodwill, and recycling through the bottle bill and lead-acid battery programs.

The Department is seeking to improve data collection and information management through its proposed amendments to the Opportunity to Recycle Act in SB183.

Respectfully submitted,

William P. Hutchison Jr.
Chair, Environmental Quality Commission

Fred Hansen
Director, Department of Environmental Quality

JW:b
G:\YB10271
Attachment

811 SW Sixth Avenue
Portland, OR 97204-1390
(503) 229-5696

Status of Recycling in Oregon

Environmental Quality Commission Biennial Report
to the Oregon Legislature

prepared by the
Oregon Department of Environmental Quality

January 1991

TABLE OF CONTENTS

REPORT TO OREGON LEGISLATURE
January, 1991

I. STATUS OF RECYCLING IN OREGON[1]

Under the Recycling Opportunity Act of 1983, Oregonians have doubled the amount of waste recycled through on-route collection and disposal site depot collection. In 1989, 80 pounds of municipal solid waste per capita was recycled. This compares to an estimated 40 pounds per capita in 1987. Of a total of 115,540 tons of recycled material collected, 24% came from curbside collection programs, 25% came from disposal site collection centers and 51% came from other types of collection. The increase in materials collected between 1987 and 1989 has come largely from communities that have implemented recycling programs that go beyond the basic requirements of the Recycling Opportunity Act. Despite the materials collected for recycling, 2,200,000 tons of municipal solid waste was disposed in Oregon in 1989. That equals 1,580 pounds per capita per year of municipal solid waste disposed in Oregon landfills.

Under the Recycling Opportunity Act, newspapers, ferrous and non-ferrous metals, used oil, container glass, office paper, cardboard, aluminum, tin cans, and yard debris are considered to be principal recyclable materials in Oregon in 1989. Plastics, mixed waste paper, and magazines are also recycled to a limited extent in some areas, although they are not considered principal recyclable materials. Today the Oregon recycling program is at a significant crossroad which will determine how much recycling can be increased. Earth Day 1990, along with an increased awareness of environmental problems by the general public, commercial businesses and state and local government, has increased the desire of Oregonians to recycle and the amount of material available for recycling within the state. The major weakness in the system is one of economics. Viable markets do not always exist to accept and process materials that are technically recyclable. In order to further increase recycling, it is important that strong markets are nurtured and developed. Oregonians have the interest and the materials to recycle. What is needed now to make recycling successful is improved collection systems and development of markets and capabilities to process the material for return to the economic mainstream.

---

[1]Information based on 1989 data from Wasteshed Reports; does not include other recycling efforts or materials collected under the "Bottle Bill".

II. LEGISLATIVE HISTORY

Prior to 1971, Oregon had no recycling legislation. However, recycling was an established part of industrial production. For many years, Oregon industry worked closely with scrap dealers who collected and delivered recyclable scrap metal and paper from commercial and industrial sources back to primary manufacturers. In addition, newspapers, scrap metal and rags were collected from commercial and residential sources and sold to industry for recycling. This recycling activity was motivated by the economic value of the recovered material. In the early 1970s, spurred by the environmental movement, community and environmental groups also started local recycling depots.

In response, the 1971 Legislature passed the Oregon Bottle Bill. This legislation mandated the return of recyclable material to the original manufacturer for recycling, stimulating more interest and activities in recycling which resulted in more recyclable material available for industrial users. In turn, new mills were constructed that used recycled feed stock.

Finally in the 1980s, as Oregonians became concerned about landfill capacity, recycling took its place as a solid waste management tool. The trend was a shift from community recycling to government regulated recycling.

Major changes to the state's solid waste laws occurred in 1983 with the passage of the Recycling Opportunity Act and the establishment of the Solid Waste Management Hierarchy. The hierarchy set a clear public policy that waste reduction, reuse, and recycling should be considered as waste management options over and above incineration and disposal. The Recycling Opportunity Act also required that minimum opportunities must be provided to the citizens of Oregon for recycling collection, education, and promotion. Wastesheds were identified to help provide these opportunities.

For the past twenty years, Oregon's recycling laws have been successful, voluntary programs because there is a strong environmental ethic, proper education, and convenient recycling collection systems.

III. ROLES AND RESPONSIBILITIES IN RECYCLING

As recycling has developed and matured in Oregon, a cooperative spirit has developed among government, business and citizens that has helped Oregon continue to slowly expand its recycling efforts. Each player has an important role and cooperatively all players take responsibility for recycling in Oregon.

A. State Government

DEQ is responsible for developing legislation and administrative rules relating to waste reduction and recycling. The agency also oversees (provides compliance oversight for) the waste reduction activities of Metro and wastesheds throughout the state. It monitors the "Opportunity to Recycle Act" by reviewing wasteshed reports prepared by cities and counties to determine the effectiveness of municipal solid waste recycling programs. Finally, DEQ provides grants and technical assistance to local governments and administers the Pollution Control Tax Credit program, which provides monetary incentives for recycling and resource recovery facilities and processes.

The General Services Department is responsible for coordination of recycling programs in state agencies and implementation of procurement practices to stimulate the use of recycled material.

B. Local Government

Cities and counties have responsibility for solid waste collection. Collection service is provided by private haulers, who are regulated by the city or county, or by the local government directly. In some areas of the state, haulers are franchised and in other areas they are not.

For the purpose of implementing the "Opportunity to Recycle Act", cities and counties are organized into designated "wastesheds". A wasteshed, although not an official governmental body with any real authority, is directed by statute to carry out the following responsibilities:

- Ensure that on-route collection of recyclables is provided, where required. At a minimum, each community of 4,000 or more people must have on-route collection of recyclable material at least once a month.

- Provide a promotion and education program which notifies individuals about the importance of recycling, recycling opportunities that are available, the materials that can be recycled, and how to prepare those materials for recycling.

- o Prepare annual recycling reports (wasteshed reports) for DEQ. These reports must include the materials that are recyclable, the manner in which these materials are collected, information on public education and promotion activities, the number of collection customers who set out recyclables for collection by each on-route collection program, and the amount of materials recycled in the previous year for each on-route and depot collection program.

- o Where yard debris has been identified as a recyclable material, wastesheds are responsible for planning and implementing yard debris recycling programs through on-route collection, depot collection or another alternative approved by DEQ.

C. Portland Metropolitan Service District (Metro)

This is a regional government for the Portland metropolitan area, including Multnomah, Clackamas and Washington Counties.

Metro is responsible for waste reduction in the tri-county region through: 1) solid waste management planning authority for Clackamas, Multnomah and Washington Counties, 2) responsibility for implementing the region's Waste Reduction Program, 3) responsibility for waste disposal within the Metropolitan Service District boundary, and 4) functional planning authority for areas and activities which impact the orderly and responsible development of the metropolitan area.

Executive Order 78-16 gave Metro responsibility for solid waste planning in the tri-county area. This requires developing programs and facilities that reduce the amount of waste going to landfills in a manner consistent with the state hierarchy. In addition, Chapter 679, Oregon Laws, 1985 required that Metro develop and implement a comprehensive Waste Reduction Program for the region.

D. Business Sector

- o Garbage Haulers

  Through contracts and ordinances, cities and counties designate garbage hauling companies to be responsible for providing the on-route recycling collection programs required under the "Opportunity to Recycle Act". In franchised areas, the recycling requirement is contained in the garbage hauling franchise. In areas where no franchise exists, the haulers are required by ordinance to provide recycling collection. Many haulers also offer commercial recycling programs. However, commercial and multi-family on-route collection is not presently required under franchise or ordinance although it is considered a part of the requirements under the Opportunity to Recycle Act.

- Private Recyclers

  In an effort not to restrict trade or activity, the Opportunity to Recycle Act, and state law in general, places no specific requirements on private companies that collect or process recyclable materials. The Act specifically excludes materials "purchased or exchanged for fair market value" and materials collected at recycling depots (other than disposal site recycling depots) from regulation or franchise requirements.

  However, some local governments do regulate private recyclers. For example, Clackamas County requires all private recyclers to register with the county and purchase a recycling license.

- Manufacturers, Wholesale and Retail Businesses

  For beverage containers and lead acid batteries, Oregon law, other than the Recycling Opportunity Act, requires that businesses take back the used or spent item and recycle or reuse it. The law also bans lead-acid batteries from being landfilled or incinerated.

E. Individual Citizens and Citizen Groups

It is the desire and will of the people and their voluntary participation in recycling programs that guide and direct the development and success of recycling in Oregon. Citizens participate in special interest organizations, government advisory groups, collection programs, and education and promotion programs.

IV. COMPLIANCE STATUS

- Wasteshed Reports

  For 1989, all but one of the thirty-eight wastesheds submitted the required annual report and the quarterly data on participation rates in a timely manner. DEQ staff review of the reports found that 95% of the wastesheds are in compliance with the "Opportunity to

Recycle Act" minimum requirements. Currently there is no mandatory participation for recycling required in Oregon. Statewide, on-route participation increased from 14% in 1987 to 21% in 1989. The areas with the greatest increase in participation are those which went to weekly on-route collection and provided containers for source separation of recyclable material (See Attachment A for statistics and examples). Even though on-route participation rates increased between 1987 and 1989, there is still room for improvement with 12 of the 38 wastesheds having less than 10% participation.

Based on the information reported by the wastesheds, only 24% of the principal recyclable materials collected under the "Opportunity to Recycle Act" were collected through the residential on-route collection program. 25% of the materials were collected through disposal site collection centers and 51% by other programs such as buy-back recycling centers. Thirty-six of the thirty-eight wastesheds have met the minimum requirement for a recycling depot located at the disposal site or an alternatively more convenient location. The two wastesheds not meeting the requirement are on a compliance schedule that requires a depot to be in place by July 1, 1991. (See Attachment B for the status of wasteshed recycling depots in Oregon.) Based on the data reported to the Department, 115,554 tons of principal recyclable material was recycled under the Opportunity to Recycle Act in Oregon in 1989; compared to 66,201 tons in 1987. (This does not include material recycled through the Bottle Bill or material collected by programs such as Goodwill or Boy Scouts.)

o Lead-Acid Battery Recycling and Disposal Ban[2]

A Department survey on the implementation of the lead-acid battery recycling requirements enacted by the 1989 Oregon legislative assembly focused primarily on automotive lead-acid batteries, since they comprise 90% of the lead-acid batteries in the United States. Results indicate at least a 90% recycling rate for lead-acid batteries in Oregon statewide. The majority of spent lead-acid batteries from Oregon are collected by the manufacturers and shipped for processing and reclamation to two large smelters in California, GNB in Los Angeles and RSR in the City of Industry.

---

[2]Information based on Background Report on the Status of Lead Acid Battery Recycling in Oregon, December 1, 1990.

Information gathered during the survey indicates that the disposal ban is working in Oregon. There appear to be no new illicit disposal problems as a result of the ban. Land disposal facilities have reported no major problems.

- o Metro's Waste Reduction Program

The Portland Metropolitan Service District is required by law to prepare and implement a solid waste reduction program plan. Metro originally adopted a Waste Reduction Program in 1986, but failed to implement the program. In 1989, the Environmental Quality Commission ordered Metro to implement the original 1986 Waste Reduction Program or to carry out an alternative set of activities set forth in the Administrative Order. Metro chose to implement the activities outlined in the Order.

Metro has complied with the activities required for 1989 and 1990. Some of the activities implemented include:

1. Set up 5 pilot programs for recycling collection at multi-family dwellings.

2. Awarded $252,000 in grants to local governments for multi-family dwelling recycling programs.

3. Provided waste audit services for commercial establishments.

4. Conducted detailed waste characterization study of commercial sector wastestream.

5. Distributed recycling containers to 60,000 households in Clackamas County.

6. Evaluated selected sites and added collection capability for yard debris to those sites.

7. Held a series of workshops for local governments, haulers, and chippers of yard debris to encourage and enhance yard debris recycling.

8. Developed a model procurement policy for local governments.

9. Carried out a recycled products survey and produced a recycled products index.

10. Conducted waste composition studies.

11. Conducted annual recycling market surveys.

12. Distributed over $700,000 in grants for recycling development and demonstration projects.

Key actions remaining to be taken by Metro under the Order include:

1. Provide assurance of development and construction of material recovery facilities by January 1, 1991. (Metro has requested an extension.)

2. Construction of all facilities called for under Metro's plan by January 1, 1993 or another date agreeable to Metro and the Department. (Metro has requested a 1994 date.)

3. Material recovery on-line at Metro South or another designated facility by July 1, 1992.

- Education and Promotion of Recycling

All wastesheds met the minimum requirements for education and promotion in 1989, however, some wastesheds have gone beyond the minimum by hiring a person specifically assigned to education and promotion, establishing school and community group programs, and setting up a recycling advisory committee, and by maintaining high recycling visibility through effective media campaigns.

Activity	Wastesheds
o School/Community Group Programs	53%
o Identified Education and Promotion Person	32%
o Recycling Advisory Committee	18%

Wastesheds that use these techniques have proven to be more successful in terms of awareness and participation with their recycling programs.

V. RECYCLING DATA AND INFORMATION

Accurate and complete data about recycling and solid waste generation statewide is essential for policy development, decision making and monitoring progress in solid waste management, recycling, and waste reduction. This information is needed on a local level as well as on a statewide basis. Currently, the monitoring and collection of this information is fragmented at best. The following information is currently collected and available on a consistent statewide basis:

1) Annual/quarterly volume/weight of waste disposed in permitted landfills/incinerators. (Beginning in FY91)

2) Monthly data on the type and weight of material recovered on-route by residential haulers.

3) Monthly data on the type and weight of material recovered at permitted disposal site recycling depots.

The following additional data are needed in order to have a complete picture of recycling activity locally and statewide:

1) Weight/volume and type of material recovered at buy-back/drop-off centers.

2) Weight/volume and type of material recycled by commercial generators who ship material directly to market.

3) Weight/volume and type of material recovered from commercial generators by haulers/recyclers who do not do residential collection.

4) Weight/volume of lead-acid batteries returned.

5) Weight/volume of used oil recycled (other than residential on-route).

6) Weight/volume of yard debris recycled.

7) Weight/volume of material recovered from the "Bottle Bill".

The following key problems have been identified related to data collection and availability:

1) No statewide tracking system of waste movement, therefore, difficult to know county-specific data.

2) Data sources are both public and private sector, therefore, confidentiality is an issue.

3) Lack of authority to collect data from all sources.

4) Reporting lines not clear, therefore, double counting is problem.

5) Material collected by industries like Goodwill for reuse and recycling can be significant in weight and volume, but lack a reliable mechanism for data collection.

6) Demolition and industrial waste is difficult to define and measure.

7) A definition for municipal solid waste versus industrial solid waste is needed.

VI. REPORT QUALIFICATIONS

The information provided in this report is based on the data that are currently collected and available through the quarterly and annual wasteshed reports. These data represent a relatively small portion of the information needed to assess the true status of recycling activity in Oregon. This report covers only the statutory recycling requirements in Oregon and does not provide information on other activities occurring in Oregon. This report provides no information related to "Bottle Bill" collection and recycling activities.

This report is intended to satisfy the following statutory reporting requirements:

1. Opportunity to Recycle Act status report, required by ORS 459.168.

2. Local government waste reduction programs (required for using certain permitted landfills), required by ORS 459.055(5).

3. Metro Solid Waste Disposal Activities and Waste Reduction Program Status Report, required by ORS 459.355.

4. Status of lead acid battery recycling, required by HB 3305 laws of 1989.

The Oregon Recycling Opportunity Act 1989 Data Report prepared by the Department of Environmental Quality is a companion report to this report to the Legislature.

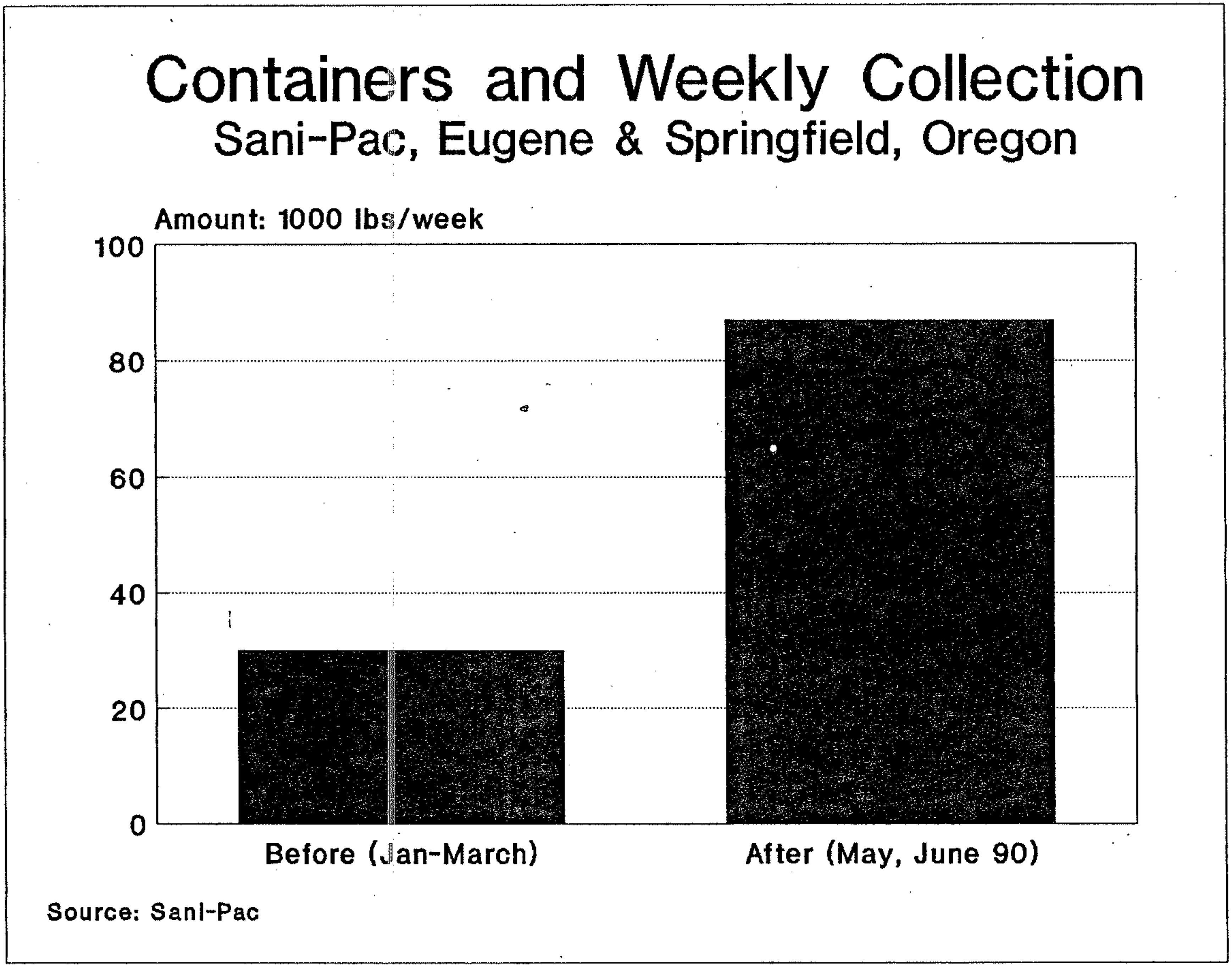
Estimated On-route Recycling Participation 1987-1989

The results below are Department estimates based on setout data provided by on-route recycling collectors one month each quarter from April 1987 through 1989. Population is based on 1986 data (except West Linn).

WASTESHED	1986 population	population in full-line collection area	estimated households participating 1987	1988	1989	estimated participation rate 1987	1988	1989
Baker	15500	9405	258	237	145	8.2	7.6	4.6
Benton-Linn	150503	111870	6588	6923	8431	17.7	18.6	22.6
Clackamas	233895	233895	8082	9352	13665	10.4	12.0	17.5
Clatsop	32900	16460	1178	1331	1206	21.5	24.3	22.0
Columbia	36100	9215	74	88	107	2.4	2.9	3.5
Coos	57500	27245	83	101	143	0.9	1.1	1.6
Crook	13500	10400	272	208	220	7.8	6.0	6.3
Curry**	16900	6300	17	20	47	0.8	1.0	2.2
Deschutes	65400	39880	992	973	1473	7.5	7.3	11.1
Douglas	92700	46350	776	760	760	5.0	4.9	4.9
Gilliam	1800	0						
Grant	8350	0						
Harney	7100	0						
Hood River	16200	6470	185	187	258	8.6	8.7	12.0
Jackson	138400	100750	3263	3367	5197	9.7	10.0	15.5
Jefferson	12000	0						
Josephine	61450	21800	753	732	641	10.4	10.1	8.8
Klamath	56700	33000	188	188	265	1.7	1.7	2.4
Lake	7300	0						
Lane	261650	217100	7228	8925	12953	10.0	12.3	17.9
Lincoln	36900	18590	589	641	789	9.5	10.3	12.7
Malheur	26200	10822	79	98	140	2.2	2.7	3.9
Marion	222876	177780	11090	11296	15049	18.7	19.1	25.4
Milton-Freewater	5850	5850	173	142	86	8.9	7.3	4.4
Morrow	7800	0						
Multnomah	86059	75700	3161	5010	5716	12.5	19.9	22.7
Polk	32691	19790	694	703	1077	10.5	10.7	16.3
Portland	480130	480130	30692	46036	46968	19.2	28.8	29.4
Sherman	2100	0						
Tillamook**	21300	4430	24	31	40	1.6	2.1	2.7
Umatilla	52850	14900	124	151	171	2.5	3.0	3.4
Union	23000	0						
Wallowa	7200	0						
Wasco	21600	13600	623	798	897	13.7	17.6	19.8
Washington	272615	236650	9768	12456	17385	12.4	15.8	22.0
West Linn* 1989	15000	15000	2381	3372	4366	47.6	67.4	87.3
Wheeler	1500	0						
Yamhill	57680	37125	1036	1092	1405	8.4	8.8	11.4
	2659199	2000507	92358	117206	141607	13.9	17.6	21.2

* Formula for determining participation rate is less accurate at high participation levels.

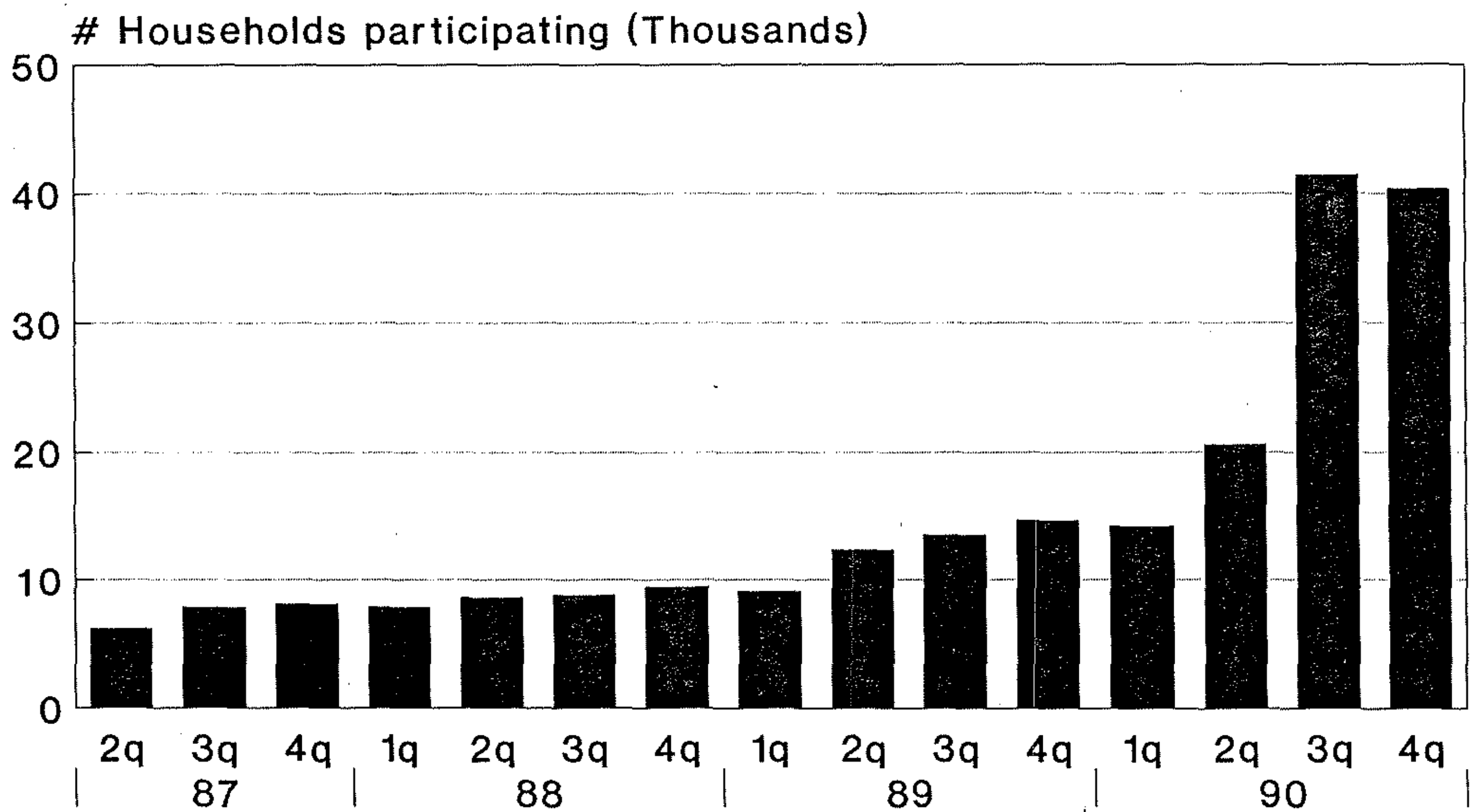
** Collection not required in Tillamook, and was not required in Curry in 1987 or 1988.



Containers and Weekly Collection
Sani-Pac, Eugene & Springfield, Oregon
Amount: 1000 lbs/week
100
80
60
40
20
0
Before (Jan-March)
After (May, June 90)
Source: Sani-Pac

Effect of Containers

Clackamas County Collectors



Containers introduced 2nd quarter 1990

Source: Oregon DEQ

Attachment B

WASTESHED DISPOSAL SITES IN OREGON
(Compiled 12/10/90, based primarily on 1989 Recycling Report Forms)

Wasteshed	Total # Disposal Sites	# Meeting Required Recycling	# Refer Alter. Sites	# Rural Exempt	Private or Comm. Sites	Recyclers with Permits
Baker	6	1	1	4	0	0
Benton-Linn	4	4	0	0	0	0
Clackamas	4	2	0	0	1	1
Clatsop	4	2	1	1	0	0
Columbia	2	1	1	0	0	0
Coos	4	2	0	0	2	0
Crook	1	1	0	0	0	0
Curry	4	3	0	1	0	0
Deschutes	6	5	0	0	1(A)	0
Douglas	14	9	0	5	0	0
Gilliam	2	2	0	0	0	0
Grant	6	0	1	5	0	0
Harney	9	1	0	8	0	0
Hood River	1	1	0	0	0	0
Jackson	4	4	0	0	0	0
Jefferson	2	2	0	0	0	0
Josephine	2	2	0	0	0	0
Klamath	14	14	0	0	0	0
Lake	8	(*)	0	7	0	0
Lane	17	16	1	0	0	0
Lincoln	4	4	0	0	0	0
Malheur	7	2	0	5	0	0
Marion	6	4	0	0	1	1
Milton Freewater	1	1	0	0	0	0
Morrow	1	1	0	0	0	0
Multnomah	0	0	0	0	0	0
Polk	0	0	0	0	0	0
Portland	4	1	0	0	0	3
Sherman	1	1	0	0	0	0
Tillamook	3	3	0	0	0	0
Umatilla	4	3	1	0	0	0
Union	4	1	0	3	0	0
Wallowa	6	(*)	0	5	0	0
Wasco	3	1	0	2	0	0
Washington	3	2	0	0	1(R)	0
West Linn	0	0	0	0	0	0
Wheeler	3	2	0	1	0	0
Yamhill	2	2	0	0	0	0
Totals	**166**	**100**	**6**	**47**	**6**	**5**

(*) One recycling site required to be in place by July 1, 1991
(A) Private facilities refering to alternate site for recycling
(R) Private facilities which have recycling

January, 1991

The 1987 Oregon Legislature enacted H.B. 3386 (ORS 448.405 to 448.470, 448.992 and 448.994) establishing a certification requirement for water and wastewater personnel. The statute requires a joint biennial report to the Legislative Assembly from the Department of Environmental Quality and the Health Division.

Attached is the report which is a summary and evaluation of actions taken under ORS 448. Appropriate recommendations are included.

Respectfully Submitted,

Michael R. Skeels, PhD, MPH
Division Administrator,
Health Division

Fred Hansen
Director, Department of
Environmental Quality

William P. Hutchison Jr.
Chair, Environmental
Quality Commission

Legislative Report
Water & Wastewater Certification Program
January 1988 through December 1990

The 1987 Oregon Legislature enacted H.B. 3386 (ORS 448.405 to 448.470, 448.992 and 448.994) requiring the certification of operators of public water systems and wastewater systems (Attachment A). A part of that statute (ORS 448.409) requires the Department of Environmental Quality and the Health Division to submit a biennial report to the Legislative Assembly. The report is to include:

1. A summary of actions taken under the statute;

2. An evaluation of the effectiveness of such actions; and

3. Any information and recommendations, including legislative recommendations, the Department or Division considers appropriate.

Herewith are the water and wastewater certification program reports which collectively make up this biennial report to the Legislature.

Attached:
1) Drinking Water Certification Program Report with attachments
2) Wastewater System Certification Program Report with attachment
3) ORS 448.405 et seq. (Attachment A)

Drinking Water Certification Program
Biennial Report to the Legislature

Actions Taken

ORS 448.407 required the appointment of a joint advisory committee to assist the Division and the Department in the development of the rules to carry out the intent of the statutes. Rules were developed and adopted in the previous biennium and with that accomplished the joint advisory committee was dissolved. The Division however, appointed another policy advisory committee on certification representing all areas of the State to continue to assist the Division in rule review and policy development. The members of this committee are listed in Attachment B. The 1989 Legislature amended the statute (S.B. 1099) to exempt water systems with fewer than 150 service connections and whose water source was groundwater from the requirement of having a certified operator although they are still subject to the continuing education (ceu) requirements. The advisory committee was most helpful with the amendments to the rules and the policy developments necessary to carry out these changes.

During this biennium a total of 581 examinations were administered on 6 different dates with a passing rate of 83%. Presently there are 1394 persons certified in water distribution or water treatment. The acceptance and response to this program has been very positive with many utilities now requiring certification as a prerequisite for employment rather than only having the person in direct responsible charge to be certified to meet the minimum of the law. This indicates that the program is accepted as providing a measure of training and competency by the water service industry and the public.

During this biennium the Division contracted for a study to assist in the development of examinations to replace the exams that have been in use for several years. The study developed a "need to know" matrix for each level of certification. From that matrix, exam questions can be categorized and a computer bank of questions will be developed.

Rules were amended to reflect changes in the law, feedback from the industry and to reduce the certification fee for those persons having more than one type of certification, such as being certified as both a water treatment plant operator and a distribution system operator. This action was indicated in the last legislative report as an action to be taken. A copy of the current rules is found in Attachment C.

The program also developed a method of auditing certification renewal applications for the required continuing education units that greatly reduced paperwork and staff time.

Effectiveness

A number of indicators clearly show the effectiveness of the program. Since the program began in 1987, systems with certified operators have improved compliance with monitoring and reporting requirements from 90% to 98% and compliance with water quality standards have increased from 92% to 97%.

The effects of the amendment of the law exempting systems with a groundwater source and less than 150 service connections only 18 months after the effective date of the law are as of yet unclear although current data shows lower compliance rates for both monitoring and reporting (98% vs 94%) and bacteriological standards (97% vs 92%) for those systems exempted from certification requirements vs those still subject to the rule. This despite the fact that the latter group represents primarily surface water systems which historically have higher levels of water quality violations than do groundwater systems.

Program effectiveness is further seen in the increased attendance in the training being offered and in the increased number of training courses available. Attendance at the "Small Water Systems Short Course" offered by the Division has doubled since the certification program took effect. Linn-Benton Community College reports that attendance at training workshops doubled last year from 700 to over 1400. The fact that more operators are obtaining training and the positive evaluations of training received from the participants gives assurance of the professionalization of the industry and that there is a better understanding of what is required to continue to provide safe drinking water.

The fiscal effect of the amendment exempting those systems with groundwater sources and fewer than 150 services connections will not be known (for sure) until after the renewal period ends this year although some impact will be felt. For example in 1989 we issued 167 variances to these systems. At $40.00 each this exclusion will result in a loss of revenue of $6,680.00. The statute requires that the program be totally supported by fees. Of the 979 community water systems in Oregon, 638 are now exempt from the requirements of having a certified system operator. However, the larger system practice of having several people certified offsets some of these losses and we would expect that many operators will continue to renew their certification for personal reasons. Attachments D and Da represent year end summaries of program elements.

Recommendations

The legislature may wish to consider if it wishes to continue receiving a biennial report on the program or rely on the Drinking Water Program's biennial report which captures much of this material on a fiscal biennium (June-July) basis.

The fiscal impact of exempting two thirds of the community water systems from the requirements of this program may necessitate a reevaluation of funding options. The excluded systems are the largest recipients of the training, provided statewide by the Division. S.B. 1099 also requires the small exempted systems to obtain continuing education, but without a designated operator accountable for this training, enforcement will be difficult. Further review of this requirement and the possible means to achieve it will be made after the operator reporting period.

It is recommended that the Division continue to coordinate with the Environmental Services Advisory Committee for the development and evaluation of training.

Consideration should be given to authorizing the Health Division to require that systems operating under a contract with a certified operator file an annual report with the Division setting out the time spent and services performed by the contractor during the previous year. We have received indications that some contractors are not being asked or authorized to perform the functions for which they have contracted.

ATTACHMENT B

Certification Review Committee
Water System Operators
1989

Mark F. Knudson	Senior Engineer with the City of Portland, Bureau of Water Works, 1120 SW 5th Ave., 6th Floor, Portland 97204, telephone 796-7499. Mark has been with the City for over 6 years where he is involved with the City's water treatment improvements (Bull Run Headworks Improvements, and Ozone/Filtration Pilot Studies). He is chairman of AWWA, Pacific Northwest Section, Certification Committee and holds two certificates (WT III and WD IV) and is a registered professional Civil Engineer in Oregon.
Ronald Gross	Director of Public Works, City of LaGrande, 800 "X" Ave., LaGrande 97850, telephone 962-1325. Ron had been active in the voluntary certification program and serves on the Drinking Water's Watershed Management Group. He is certified (WT I and WD I).
Noel N. Groshong	General Manager of the Umpqua Basin Water Association, 4972 Garden Valley Road, Roseburg 97470, telephone 672-5559. Noel is certified (WD II) and currently is president of the AWWA South Central Subsection and is on the Oregon Association of Water Utilities (OAWU) Board of Directors.
Harold Haight	System Superintendent, Kernville-Gleneden Beach-Lincoln Beach Water District, PO Box 96, Gleneden Beach 97388, phone 764-2475. Hal served on 1987-88 Rules Committee and is certified (WD III).
John Carnegie	Chair of Linn-Benton Community College's Water-Wastewater Department, 6500 SW Pacific Blvd., Albany 97321, phone 928-3620. John is a past president of the Alaska Water Management Assoc. and was instrumental in establishing Alaska's certification program. John served on the 1987-88 Rules Committee.

Robert MacRostie	Manager, Deschutes Valley Water District, 1141 SW Old Culver Highway, Madras 97741, phone 475-3849. Bob is past president of the Oregon Association of Water Utilities (OAWU), an organization that represents many smaller water systems in Oregon. Bob served on the 1987-88 Rules Committee and is also certified (WD II).
Daniel T. Bradley	Superintendent of Water/Wastewater correction, City of Salem, 1410 20th St. SE, Bldg. #2, Salem 97302, telephone 588-6487. Dan is certified in both classifications (WT IV and WD IV). Presently, he is president of the Northwest Subsection of AWWA.
Steven D. Sundseth	Supervisor of the Water Treatment Plant for the City of Albany, PO Box 490, Albany 97321, telephone 967-4319. Steve is certified as a WT IV operator. He has worked for both Cities of Albany and Redmond.
Brian R. Stahl	Water Quality Control Supervisor at the Water Treatment Facility for the City of The Dalles, 6780 Reservoir Rd., The Dalles 97058, telephone 298-1242. Brian is certified in both classifications (WD II and WT IV). Brian is president of the AWWA Subsection of the Mid-Columbia Deschutes Region.
King A. Phelps	Engineer with the Coos Bay-North Bend Water Board, PO Box 539, Coos Bay 97420, telephone 267-3128. King is a Professional Engineer and also certified as a Water Distribution III Operator. He will be representing the South Coast Section of AWWA.

ATTACHMENT C

STATE OF OREGON
WATER PERSONNEL
CERTIFICATION RULES

333-61-205 PURPOSE

(1) The purpose of the certification program is public health protection by providing a system whereby persons responsible for the production, treatment and distribution of drinking water for public consumption may be examined and rated by the Division to determine their ability to meet an established standard of proficiency in their respective areas of responsibility.

(2) The principal objectives of the program:

a. To insure the safe and proper operation of water supply systems for protection of the public health.
b. To establish classes and grades of operators and qualifications for certification.
c. To advise and assist applicants for certification, set forth conditions of reciprocity, make provisions for variances, and provide for examinations of candidates.
d. To award certificates and maintain a register of current certificate holders by class and grade.
e. To establish and maintain communications between the Division and the operators to insure a flow of information necessary to each party in order to carry out their respective responsibilities.
f. To improve the caliber of water system operation and thereby assure maximum protection of the public's health and the State's water resources and further maximize the returns from the public's investment in these systems.

333-61-210 SCOPE

These rules shall be applied to all potable water treatment plants and water distribution systems that have 15 or more service connections used by year-round residents or that regularly serve 25 or more year-round residents.

333-61-215 DEFINITIONS

(1) "Certificate" means a certificate of competency issued by the Division stating that the operator meets the requirements for a specific operator classification.

(2) "Contact Hours" shall mean classroom hours of lecture or the equivalent.

(3) "Continuing Education Unit (CEU)" - A nationally recognized unit of measurement similar to college credits. One CEU is awarded for every ten contact hours of participation in an organized continuing education experience, under responsible sponsorship, capable direction and qualified instruction.

(4) "Direct Responsible Charge (DRC)" means active, daily, on-site and on-call charge and performance of operations or active, on-going, on-site and on-call direction of employees.

(5) "Directly Supervised" means an active, on-site charge and performance of operations.

(6) "Distribution System" see "Water Distribution System".

(7) "Division" means Oregon State Health Division of the Department of Human Resources.

(8) "On Call" shall mean available to respond by radio or telephone.

(9) "Operational Decision Making" means having to choose among the alternatives in the performance of the Water Treatment Plant or the Water Distribution System.

(10) "Operator" shall mean, those individuals certified in fields of Water Treatment and Water Distribution. This term shall not normally apply to those individuals who do not have direct "hands on" responsibilities in the classifications described in these rules. It is not intended that this title shall include city or county managers, utility engineers, directors of public works or equivalent whose duties do not include the actual operation or direct on-site supervision of systems and operators. It shall not apply to welders, equipment operators, truck drivers and other employees whose work is limited to a single activity which does not include direct responsibility for safeguarding the public and the environment in the practice of disciplines described in these rules.

(11) "Operator in Training" - "OIT" this classification is not to be construed as a certification level, but rather as the entry level for persons new in the field.

(12) "Post High School Education" shall mean, that education acquired through programs such as short schools, bona fide correspondence courses, trade schools, colleges, or universities, formalized workshops, seminars, etc. that are acceptable to the Division.

(13) "Responsible Charge" see "Direct Responsible Charge".

(14) "Responsibly Employed" means working on a job under a specified time frame.

(15) "Subordinate Position" shall mean a position in which the operator is subject to direct administrative and technical supervision and must in turn carry out the policies and programs of the person in responsible charge.

(16) "Water Distribution System" means that portion of a potable water system in which water is stored and conveyed from the water treatment plant or other supply point to premises of the consumer.

(17) "Water Distribution System Operator (WD)" means any person who is engaged in the operation of a water distribution system either in part or in its entirety. This term shall not normally apply to an individual whose primary duty is not waterworks operation.

(18) "Water System" means the system that has 15 or more service connections used by year-round residents or that regularly serve 25 or more year-round residents.

(19) "Water Treatment Plant" shall mean that portion of the potable water system which in some way improves the physical, chemical or microbiological quality of the water being treated.

(20) "Water Treatment Plant Operator (WT)" means any person engaged in the on-site, day to day operation of a water treatment system that improves the physical, chemical or microbiological quality of water.

333-61-220 APPLICATION FOR CERTIFICATION

(1) Each applicant for certification must meet the minimum requirements of experience and training as listed under 333-61-260 "Operator Grade Requirements" in order to be eligible for admission to written examination.

Each applicant for initial certification must have been engaged in the "hands on" operation of the type of system for which the applicant is seeking certification for a period of at least one year, or its equivalent prior to the examination date for which they are making application.

(2) All applications for admission to the certification examinations must be submitted to the Division by the first of the month preceding the month of the scheduled examination.

a. All claims for education must be documented.

(3) Applicants denied admission to the certification examination or denied certification by reciprocity, have the right to appeal such a decision to the Division.

(4) Application forms for Operator certification may be obtained upon written request from the Division.

(5) Requests for examination to be held at times other than those mentioned in above, shall be made in writing to the Division. The Division will act upon these requests at its earliest opportunity. Each application

for an examination, requested to be taken other than at the regular time, must be accompanied by a fee that is twice the regular fee established for examination applications.

(6) No applicant will be allowed to take the same examination more than twice in a twelve month period.

333-61-225 GENERAL REQUIREMENTS

(1) No water supplier shall employ, contract with or otherwise utilize any person to be in direct responsible charge of a water treatment plant or water distribution system who does not possess an appropriate valid operators certificate as prescribed in these rules, except that this rule shall not apply to a water system that is directly supervised by a registered professional engineer who has a valid certificate to practice engineering issued under ORS 672.002 to 672.325.

(2) Not withstanding Section (1) above the requirements for a certified operator shall not apply to a water system for which the source of water is groundwater and that has less than 150 service connections. However, the operator of a water system exempt under this section shall not be exempt from any continuing educational requirements established by these rules.

(3) An operator in direct responsible charge of a water treatment plant or a water distribution system shall be certified at a grade equal to or greater than the classification of that plant or system.

(4) Certification grades for operators will be classified according to the size and complexity of the system/plant in which they are experienced and the level of their responsibilities. (See 333-61-250).

(5) Transcripts or proof of satisfactory completion of all post high school education claimed, must be submitted with the application.

(6) Operators may, be examined at one grade higher than the classification of the plant or system in which they are employed and upon passing the examination and meeting all other requirements (listed below) for the next higher grade, be awarded certificates in the grade requested.

a. Meet the time requirements for education, experience and operational decision making for the next higher grade, and
b. Are currently certified, and
c. Have been employed and certified for at least two (2) years in their currently highest rated position, and
d. Have been able to observe and learn the duties and the responsibilities of the higher grade, and all other experience requirements for certification in the requested higher grade.

(7) Maintaining CEU records shall be the responsibility of the applicant.

(8) Experience and education qualifications are based on years of experience and education, or their equivalence.

a. A year of experience is deemed to be each year of satisfactory experience that the operator has completed in association with the duties of the position for which application is made.

b. Experience not directly in the discipline for which application is being made but relative to it, shall be considered by the Division and credit allowed in accordance with the following formulation:

EXPERIENCE ALLOWABLE IN APPLYING FOR WATER SYSTEMS CERTIFICATION:

(1). Wastewater Collection Operator 0-50%
(2). Wastewater Treatment Plant Operator 0-50%
(3). Wastewater Collection Management 0-25%
(4). Wastewater Treatment Plant Laboratory 0-50%
(5). Wastewater Treatment Plant Maintenance 0-50%
(6). Water Treatment Plant Experience When Applying for a Water Distribution Certificate. . . 0-50%
(7). Water Distribution System Experience When Applying for a Water Treatment Certificate 0-50%

c. Maximum experience for every applicant for examination, when requesting substitute experience as outlined in the preceding section, shall be 6 (six) months equivalent as described in this section.

d. Education (post-high school): Each year of college education completed, (one year of college education is 30 semester hours or 45 quarter hours, or their equivalence) in the fields of engineering, chemistry, water/wastewater technology or allied sciences.

e. Courses must be either acceptable as college transfer or directly related to the field of water treatment/water distribution for education gained in programs such as short schools, bona fide correspondence courses, trade schools, community colleges, formalized workshops, seminars, etc. Credit will be allowed in accordance with the following schedule at the discretion of the Division:

10 classroom hours	=	1 CEU (Continuing Education Units)
1 college credit	=	1 CEU
45 CEU	=	1 year college
45 CEU	=	30 semester hours
45 credit hours	=	1 year college
30 semester hours	=	1 year college
45 credit hours	=	1 year experience
30 semester hours	=	1 year experience

f. The Division shall consider the relevance of the subject matter covered at seminars, workshops, conferences, etc., when determining the number of CEU's allowed for specialized operator training.

g. CEU to be acceptable must be approved by the Environmental Services Advisory Committee (ESAC) of the Oregon Department of Education; or from an accredited college or university. CEU's from other states having standards equal to or greater than these rules may be accepted by the Division.

h. The applicant has the responsibility for providing program information and attendance verification to the Division for credibility and evaluation.

333-61-230 EXAMINATIONS

(1) Examinations shall be given at least twice annually at locations and at times designated by the Division.

(2) The qualifications of each applicant will be reviewed by the Division for the purpose of determining that minimum requirements for experience, education and special training as listed in these rules, have been satisfied.

a. An examination fee shall be charged for all applications submitted to the Division. The examination fee shall entitle the passing applicant to be certified for the rest of the certification year.

b. The Division, at its discretion, may require or allow oral examination of any applicant seeking certification, as evidence of proficiency in a particular grade.

(3) Examinations shall be reviewed and graded by the Division and upon successfully passing the examination and meeting all other requirements, the Division shall issue a Certificate of Competency to the applicant.

(4) A minimum score of 70% is required to pass the examination.

333-61-235 CERTIFICATES

(1) Certificates will be granted to the applicants on the following basis:

a. The information submitted on the application form.

b. An evaluation of the applicants qualifications by the Division.

c. Successfully passing an examination endorsed and conducted by the Division.

d. By reciprocity with other states or provinces having recognized certification programs. Certification may be granted at the grade level where the examination, experience and training requirements are equivalent to those outlined in these Rules, and providing the applicant has a currently valid certificate from the state or province from which the applicant is seeking reciprocity.

(2) The names of successful applicants who receive certificates shall be filed in the official records of the Division.

(3) The terms for all certificates shall expire on December 31st each year. Every certificate shall be renewed annually upon the payment of a renewal fee and satisfactory evidence presented to the Division that the operator has demonstrated continued professional growth in the field. The accumulation of two college credits or Continuing Education Units every two years is considered satisfactory evidence of professional growth.

(4) An operator who has failed to renew the certificate pursuant to the provisions of this section by March 31st following the date of expiration must apply for reinstatement of certification by submitting an application accompanied by a reinstatement fee. If an operator fails to renew for a year following the date of expiration, they shall meet the requirement established for new applicants by passing an examination and paying a reinstatement fee.

(5) For those public water systems whose source of supply is groundwater and who have fewer than 150 service connections there shall be a person designated to obtain the required continuing education credits required by these rules. The water system shall be responsible to report on or before July 1, 1992, and biennially thereafter the name of that person and the 2.0 CEUs of approved training received.

333-61-240 VARIANCES

Variances can be granted in accordance with ORS 448.455 under the following criteria:

(1) When it is demonstrated to the satisfaction of the Division that strict compliance with the rule would be highly burdensome or impractical due to special conditions or causes; and

(2) When the public or private interest in the granting of the variance is found by the Division to clearly outweigh the interest of the application of uniform rules;

(3) When there is verification from the governing body or owner of the system that a person was satisfactorily fulfilling the duties of an operator prior to September 28, 1987, and that there are special conditions that warrant issuance of a certification without examination. A certificate can be issued and conditioned to be valid only for operating the existing plant or system. Major modification of the type of treatment shall result in the certification issued under this section to be invalid. Proof shall be submitted that the person has continued to satisfactorily perform the duties of an operator and that special conditions still warrant the issuance of a certification without examination.

(4) Application shall be made each year to continue the variance under the certification program.

(5) Continuing Education Units (CEU) per year are required as indicated by these rules.

333-61-245 FEES

(1) All fees collected shall be made payable to the Health Division.

(2) Once action is initiated by the Division upon any application, the fees are not refundable.

(3) Applications will be accepted for processing only when accompanied by a fee as indicated in Table 1.

Table 1

Certification Renewal	$40
Examinations	$35
Reciprocity Review	$30
Reinstatement	$50
Certification with Variance	$40
Combination Certification - each additional	$20

(4) Water system personnel having more than 1 (one) certification pertaining to water systems (water treatment and water distribution) may receive a combination certification. The fee shall be full certification renewal fee for one certification and a lesser fee for each additional certification.

333-61-250 Classification of Water Treatment Plants and Water Distribution Systems

(1) All water treatment plants and systems shall be classified as to size and complexity by the Division. The classification of these systems and treatment plants are as follows:

a. At water systems where there is no treatment, or where the only treatment is disinfection, slow sand filtration and/or fluoridation, the classification is based solely on the population served, as follows:

Classification of Distribution System	Population
Class I (WD I)	1,500 & less
Class II (WD II)	1,501 - 15,000
Class III (WD III)	15,001 - 50,000
Class IV (WD IV)	50,001 - >>>>>>

(2) Those water treatment facilities where treatment in addition to disinfection and/or fluoridation is provided or treatment is by slow sand filtration serving a population of 1,501 or over, the classification shall be based on a point system. Points shall be assigned as follows:

a. Water Treatment Plants;

Items For Classification

Item	Points
Treatment system size (use either population or flow)	
Population served	1/10,000 (max. 25)
Average daily flow	1/1 mgd (max. 25)
Treatment system water source	
Groundwater	3
Surface water	5
Treatment	
Aeration for CO_2	2
Air Stripping	4
Ozone	7
pH adjustment or Corrosion control	4
Taste and odor control	
Watershed algae control	2
Permanganate	3
Activated carbon	3
Color adjustment	4
Iron and manganese	
Ion exchange	2
Oxidation	2
Polyphosphates	2
pH Adj., Cl2, Filter	4
Softening	
Ion-exchange softening	10
Chemical precipitation (lime and soda ash)	20
Coagulation process	
Rapid mix	5
Flocculation	5
Sedimentation	5
Filtration	
Conventional rapid sand	10
Direct rapid sand	7
Diatomaceous earth	7
Slow sand filtration	5
Sludge treatment (dewatering)	
Dewatering lagoon	2
Pressure/belt filter	2
Coagulant recovery	2
Other treatment	as appropriate
Fluoridation	5
Chlorination or equal	5

Bacteriological or Chemical Laboratory	
MPN-Total coliform, Fecal coliform	2
MF-Total coliform, Fecal coliform, Fecal strep, Heterotrophic Plate Count/Standard Plate Count	2
Wet chemistry	2
Algae Enumeration	2
Spectrophotometric/Atomic Absorption	2

Classification of Water Treatment Plants

Class	Points
Class I - (WT I)	30 or less
Class II - (WT II)	31 to 55
Class III - (WT III)	56 to 75
Class IV - (WT IV)	76 >>>>>

333-61-255 OPERATOR IN TRAINING "OIT"

A person who does not meet the experience requirement under these rules and who is otherwise qualified may take the Grade I examination and if a passing score is achieved may be given an OIT classification.

1. Job Description: Employment in or the pursuit of employment in any class of plants or systems for the purpose of acquiring skill and knowledge in system operation.

2. Qualifications: High School education, or its equivalent, and passing the Grade I examination with a passing grade of 70%. Upon satisfactory completion of one year experience or 6 months experience with an associate degree in water technology, and upon application for Grade I Operator, the applicant will be granted the status of a certified Grade I Operator in the field in which the applicant has gained the one year experience.

333-61-260 OPERATOR GRADE REQUIREMENTS

Grades for operator certification shall be awarded at four (4) levels consistent with the plant or system classification schedule of these rules and subject to requirements as follows:

Classification	Grade
Water Treatment Operator	WT
Water Distribution Operator	WD

(1) Class I (Grade I), Operator Certification (entry level);
  a. Job Description:
    A. Those operators responsibly employed in operation and/or maintenance of Class I plants/systems.
    B. Those operators employed in subordinate positions in higher classed plants.
  b. Qualifications:
    A. Education; High School (12 years or equivalent).

B. Experience; 12 months (one year). Education cannot be substituted for this requirement except that an associate degree in water technology may be substituted for 6 months experience.
C. Successful completion of written examination.

(2) Class II (Grade II), Operator Certification.
a. Job Description:
A. Those operators responsibly employed in Class II plants or systems, or those persons employed in subordinate positions in a higher class plant.
b. Qualifications:
A. Education; High school (12 years or equivalent) plus 3 (three) years of experience and/or post high school education.
B. Admission to the Grade II examination may be gained with experience and post high school education combined as one of the following combinations:
i. 3 (three) years of experience, or
ii. 2 (two) years of experience and 1 year of post high school education.
C. Successful completion of the written examination.

(3) Class III (Grade III) Operator Certification.
a. Job Description:
A. Those operators or supervisors with experience in Class II or higher plants/systems. At least 50% or not less than 2 years, of the required experience must have been involved in operational decision making of a class II or higher plant/system.
b. Qualifications:
A. Education; High school (12 years or equivalent) and a minimum of one year post high school education.
B. Admission to Grade III examination may be gained with experience and post high school education combined as one of the following combinations:
i. One (1) year post high school education and 5 (five) years experience, of which 2.5 years must have been involved in operational decision making.
ii. Two (2) years of post high school education and four (4) years of experience, of which at least two (2) years must have been in involved in operational decision making.
iii. Three (3) years of post high school education and three (3) years of experience, of which at least 1.5 years must have been in involved in operational decision making.
C. Successful completion of the written examination.

(4) Class IV (Grade IV), Operator Certification.
a. Job Description:

A. Those operators or supervisors with experience in Class III or higher plant/systems. At least 50% but not less than two (2) years of the required experience must have been involved in operational decision making of a Class III or higher plant/system.

b. Qualifications:

A. Must be certified at the grade III level.

B. Education; High school (12 years or equivalent) plus a minimum of two (2) years of post high education.

C. Admission to the Grade IV examination may be gained with experience and post high school education combined as one of the following combinations:

i. Four (4) years of experience, of which two (2) years must have been involved in operational decision making, plus four (4) years post high school education, or

ii. Five (5) years experience, of which 2.5 years must have been involved in operational decision making, plus three (3) years of post high school education, or

ii. Six (6) years experience, of which three (3) must have been involved in operational decision making, plus two (2) years post high school education.

D. Successful completion of the written examination.

(5) Sequential advancement for grade I through III shall not be required providing the applicant meets all other requirements of education and experience in these rules.

(6) Experience can be granted up to 1 year where a person has Direct Responsible Charge for the design and construction of water distribution system or a water treatment plant.

333-61-265 CONTRACTING FOR SERVICES

(1) The person contracted with and responsible for the active daily technical operation of a public water system is required to be certified. Water systems that do not have a certified operator shall contract with a certified operator or a water system having certified operators to provide supervision. The contract operator shall be certified at the grade equal to or greater than the classification of the plant or system.

(2) The supervision required in section (1) of this rule shall be sufficient that the contracted certified operator shall:

a. Be available on 24 hour call and able to respond on-site upon request.

b. Recommend corrective action when the results of analyses or measurements indicate maximum contaminant levels have been exceeded or minimum treatment levels are not maintained and report the results of these analyses as prescribed by OAR 333-61-040.

c. Recommend that all elements of routine operation and maintenance of the water systems are completed in accordance with accepted public health practice.

(3) Proof of the contract shall be submitted to the Division.

333-61-270 REFUSAL OR REVOCATION OF CERTIFICATION

(1) The Division may refuse or revoke a certification of competency or refuse a variance application if it finds after opportunity for hearing under ORS 183 that:

a. The certificate was obtained by fraud or deceit, or
b. There is proven gross negligence, incompetence or misconduct in the performance of duties of an operator.
c. That the governing body or owner of the system has failed to provide proof that a variance issued under 333-61-240(3) is warranted for continuance.

(2) No person whose certificate has been revoked under this rule shall be eligible for a certificate for one year from the effective date of the final order of revocation. Any such person who reapplies for recertification shall meet all the requirements established for new applications and pay a reinstatement fee.

333-61-290 PENALTIES

(1) Violation of these rules shall be punishable as set forth in ORS 448.994, which states that any person who knowingly and willfully violates ORS 448.455 (2) and that any person who knowingly makes any false statement, representation, or certification in any application, record, report, plan or other document filed or required to be maintained under any of these rules shall upon conviction, be punished by a fine of not more than $500 or by imprisonment for not more than six months, or both.

(2) Pursuant to ORS 448.280, 448.285 and 448.290, any person who violates these rules shall be subject to a civil penalty. Each and every violation is a separate and distinct offense, and each day's violation is a separate and distinct violation.

(3) Under ORS 448.290, only the Administrator can impose penalties and the penalties shall not become effective until after the person is given an opportunity for a hearing.

(4) The civil penalty for the following violations shall not exceed $500 per day for each violation:

a. Failure to employ or otherwise utilize an operator to be in direct responsible charge who has an appropriate valid operators certificate as prescribed in these rules.
b. Failure to employ or otherwise utilize an operator to be in direct responsible charge who has maintained the required continuing education units.
c. Failure to comply with an order issued by the Administrator.

(5) Civil penalties shall be based on the population served by public water systems and shall be in accordance with Table 2 below:

Table 2

Daily Population Served	Maximum Civil Penalty
10 to 100	$ 50/day
101 to 300	$100/day
301 to 1,500	$250/day
over 1,500	$500/day

333-61-295 SEVERABILITY

These rules are severable, if any part thereof or the application of such rules to any person or circumstance is declared invalid, that invalidity shall not affect the validity of any remaining portion of these rules.

ATTACHMENT D

WATER CERTIFICATION PROGRAM
Current Program Status

1989 Report

1. <u>Water Treatment Plant Operators</u>

Renewal Certificates	342	
New Certificates (WT-I Exams)	11	
Reciprocity Certificates	8	
Exams given 1989 (includes 32 upgrades)	88	
**Variances granted operators	2	
Total Certified Plant Operators		424

2. <u>Water Distribution System Operators</u>

Renewal Certificates	851	
New Certificates (WD-I Exams)	104	
Reciprocity Certificates	2	
Exams given 1990 (includes 54 upgrades)	234	
Variances granted operators	39	
Variances to systems	167	
Total Certified Distribution Operators		1070

**Included in renewal certificates

Total Currently Certified Water Treatment/Distribution Operators 1494

3. Total Revenues received for 1989 (as of December 31, 1989) $97,000.00

ATTACHMENT Da

WATER CERTIFICATION PROGRAM
Current Program Status
1990 Report

1. Water Treatment Plant Operators

Renewal Certificates	350	
New Certificates (WT-I Exams)	45	
Reciprocity Certificates	8	
Exams given 1990 (includes 28 upgrades)	73	
**Variances granted operators	2	
Total Certified Plant Operators		403

2. Water Distribution System Operators

Renewal Certificates	896	
New Certificates (WD-I Exams)	90	
Reciprocity Certificates	5	
Exams given 1990 (includes 89 upgrades)	179	
**Variances granted operators	39	
Variance to systems	2	
Total Certified Distribution Operators		991

**Included in renewal certificates

Total Currently Certified Water Treatment/Distribution Operators 1,394

3. Total Revenues received for 1990 (as of December 31, 1990) $30,870.00

4. Total Revenues received for report period (1/1/89-12/31/90) $127,870.00

Wastewater System Operator Certification Program Report

1989 - 1990

The following is a report on the Wastewater System (sewage treatment works) Operator Certification Program (Program) as administered by the Department of Environmental Quality (Department) under Oregon Administrative Rules, Chapter 340, Division 49 (Rules). Pursuant to ORS 448.410, the Environmental Quality Commission adopted these rules on September 9, 1988. Generally, the statute (ORS 448.415) and the associated rules require that wastewater system owners have the technical operation of their systems (collection and/or treatment) supervised by a certified operator.

PROGRAM STATISTICS

Classified Wastewater Systems

System Class	Collection		Treatment	
IV	25		26	
III	28		29	
II	125		84	
I	157		306	
Total	335	+	445	= 780

Note: The Rules include a classification system so that more complex wastewater systems must be supervised by an operator with a higher level of experience and knowledge. Class IV wastewater systems are the most complex facilities, the operation of which must be supervised by a Grade Level IV operator. Also, the complexity of the collection system is independent of the treatment system consequently a given municipality may have a Class IV treatment system, but only a Class III collection system.

Operator Certificates

Certificate Grade Level	Collection		Treatment
IV	155		224
III	148		123
II	314		259
I	127		309
Provisional	9		43
Total	753	+	958 = 1711

> **Note:** A Provisional Certificate is a temporary (twelve month) certificate granted to persons who are working in collection and/or treatment systems under the supervision of a certified operator <u>and</u> enrolled in, or have completed, Department approved training. Generally, these people are "operators-in-training" who are gaining experience and knowledge to qualify for certification at Level I. This provisional certificate may be converted to a "standard" Level I certificate upon completion of the required experience and passing the Level I examination. The individual may take the Level I examination while provisionally certified.

As of December 31, 1990, there are 1405 individuals participating in the Program and a total of 1711 certificates have been issued. The number of certificates represents an 88% increase from December 1988. Three hundred and six (306) operators (about one out of five) hold both a treatment certificate and a collection certificate. The figures show that Oregon has significantly more certified operators than wastewater facilities. This ensures an adequate pool of certified operators to replace people who retire or otherwise leave service.

In accordance with ORS 448.420, the Rules provided for the issuance of certificates to those persons who were certified prior to May 1, 1989 under the voluntary Oregon wastewater certification program. Of those who were eligible, 95% converted their voluntary certificates.

Another provision of the Rules gave wastewater collection system personnel a temporary "window" in which to apply for certification without having to pass a written examination. Persons could certify at a specific grade level based on their meeting established minimum qualifications for education and experience. In the four month period prior to a May 1, 1989 deadline, 480 persons made application and were accorded new or upgraded certificates under that provision.

Examinations

With the exception of operators requesting certification by reciprocity, all applicants must take an examination and score at least 70% in order to pass.

During the two-year period 1989 - 1990, a total of 524 individual examinations were scheduled (1989: 290 and 1990: 234). The examinations were given on eight different dates (1989: 5 times and 1990: 3 times) and at various locations geographically located around the state.

A total of 459 persons (1989: 259 and 1990: 200) actually attended and completed the exams. This represents an average "no show" rate of approximately 12%. At this time, the Program does not charge a rescheduling fee. There is a fee of $35.00 for retaking a failed exam. Approximately 15% of the exams taken were re-examinations. Of those who failed the exam on the first attempt, better than 90% passed on the second attempt following a period of additional study.

Certificate Grade Level	Pass Rate Collection	Pass Rate Treatment
IV	100%	88%
III	100%	70%
II	90%	73%
I	97%	77%
Provisional	71%	83%

Pass Rate overall: 79%
Pass Rate by group: collection: 92% and treatment: 77%

Revenue and Expenses

As of November 30, 1990, the Department has collected in the 1989-91 biennium a total of $30,875 in operator certification fees. In carrying out the Program, the Department has expended, as of November 30, 1990, $77,389.24. Certificate renewal fees are collected biennially and are next due on July 1, 1991. The Department expects to receive about $60,000 of additional fee revenue before the end of the 1989-91 biennium.

The current fees schedule is as follows:

Application Type	Fee
New Certification (Includes examination)	$ 50.00
Renewal Certification (Two-year period)	$ 40.00
Certification to a Higher Grade (Includes examination)	$ 35.00
Certification through Reciprocity	$ 55.00
Reinstatement of Lapsed Certificate	$ 50.00

Note: Persons holding both collection and treatment certificates at grade level I and/or II may renew both certificates for a single fee of $40.00.

Based upon the current number of certificates, current fees, and two years of experience of conducting the operator certification program, the Department projects that $79,600 will be received in the 1991-93 biennium.

The Department has requested 1.33 FTE to operate the Program as part of one of the decision packages in its 1991-93 budget request. The cost of this component of the decision package is $85,477. Fees may have to be increased to cover the costs of conducting the Program.

SUMMARY OF SIGNIFICANT ACTIONS

The Department believes that the Program is providing better trained and more knowledgeable wastewater system operators. The Rules require a minimum of two Continuing Education Units (CEUs) of approved training as a condition of renewing an operator's certification. This requirement has resulted in substantially increased attendance at wastewater treatment plant operator short schools, workshops, and seminars.

Under the Rules, the Department has established a standing advisory committee for the Program (see Attachment 1). The committee's purpose is to assist in developing examinations, to evaluate Program effectiveness, and to recommend needs of the Program. The committee is required to meet at least two times per year, but, in fact, met quarterly in 1990.

The Department intends to use the wastewater discharge permit as the mechanism for enforcing the requirements of the Program. At this time, the Department has been including operator certification requirements in permits as they are renewed. Consequently, there are still many permits without operator certification requirements. The Department is considering modifying all permits in mass to include operator certification requirements.

In October of 1990, subsequent to a permit compliance investigation, the Department revoked the treatment certificate of an operator who falsified operational reports of the system that he supervised. The rules provide for suspension or revocations of a certificate based on misconduct, negligence or falsification of records or reports. In addition, the Department issued a Notice of Intent To Assess a Civil Penalty to the system owner for Waste Discharge Permit violations including falsification of records and failure to adequately operate, maintain and staff the treatment system.

RECOMMENDATIONS

The Department has no recommendations for any changes to the Program. The Department does recommend that the Legislature approve the Department's decision package to provide necessary staff to properly conduct the Program.

ATTACHMENT 1

DEPARTMENT OF ENVIRONMENTAL QUALITY
WASTEWATER SYSTEM OPERATOR CERTIFICATION PROGRAM
ADVISORY COMMITTEE

Gerald W. Breazeale
City of Madras
(League of Oregon Cities)
416 Sixth Street
Madras, OR 97741

Glen R. Hogue
City of La Grande,
Public Works Dept.
800 X Avenue
La Grande, OR 97850

Leo B. Lightle
City of Brookings
898 Elk Drive
Brookings, OR 97415

Holly Mason
ETC Inc.
P.O. Box 2097
Corvallis, OR 97339

Woodie Muirhead
Brown & Caldwell
P.O. Box 23158
Portland, OR 97223

Terry D. Penhollow
Sunriver Utilities
P.O. Box 3699
Sunriver, OR 97707

J. Michael Read
City of Portland
5001 N. Columbia Blvd.
Portland, OR 97203

Paul D. Rogers
Parks and Recreation Department
(State of Oregon)
525 Trade Street
Salem, OR 97310

Wayne Weaver
Bear Creek Valley
Sanitary Authority
3915 S. Pacific Hwy.
Medford, OR 97501

Stephen R. Yoder
City of Silverton
1453 Pine Street
Silverton, OR 97381

nity water supply system under state law or an ordinance of such city; or

(b) Any violation of any rule of the division or the authorities having control of the city water system for the protection of the purity of the domestic water supply source or the community water supply system.

(3) May take any person arrested for any violation under this section before any court having jurisdiction thereof to be proceeded with according to law.

(4) When on duty, shall wear in plain view a badge or shield bearing the words "Special Police" and the name of the city for which appointed. [Formerly 449.315]

448.320 Jurisdiction over violations of city ordinances. The municipal or recorder's court of any city passing an ordinance under authority of ORS 448.300 or 448.305 and the justice of the peace court or district court of the county wherein such city is located or in which the watershed area is located shall have concurrent jurisdiction to try and determine any prosecution brought under such ordinance. If prosecution is had in a justice of the peace court or a district court, the court shall remit to the city, after deducting court costs, the amount of any fine collected, except as otherwise provided by ORS 46.045 (2). If a jail term is imposed, the convicted person shall be confined in the city jail or in the county jail and if confined in the county jail the county shall be entitled to recover from the city the actual costs of such incarceration. [Formerly 449.328]

448.325 Injunction to enforce city ordinances. In cases of violation of any ordinance adopted under ORS 448.300 or 448.305 any city or any corporation owning a domestic water supply source or the community water supply system for the purpose of supplying any city or its inhabitants with water may have the nuisance enjoined by civil action in the circuit court of the proper county. The injunction may be perpetual. [Formerly 449.340]

(Water Pipes and Fittings)

448.330 Moratorium of pipe and fittings for potable water supply; acceptability criteria; exceptions. (1) The Assistant Director for Health may prohibit the sale of water pipe used to carry potable water and solders, fillers or brazing material used in making up joints and fittings in this state and the installation or use of water pipe used to carry potable water and solders, fillers or brazing material used in making up joints and fittings in any private or public potable water supply system or individual water user's lines until such time as the assistant director determines that adequate standards exist and are practiced in the manufacture of water pipe used to carry potable water and solders, fillers or brazing material used in making up joints and fittings to insure that the pipe and solder do not present a present or potential threat to the public health in this state.

(2) The Assistant Director for Health shall adopt, by rule, product acceptability criteria for water pipe used to carry potable water and solders, fillers or brazing material used in making up joints and fittings for water supply purposes which insure that the pipe and solder do not present a threat to the public health in this state. The Health Division shall be responsible for the monitoring of the sale and use of water pipe used to carry potable water and solders, fillers or brazing material used in making up joints and fittings for compliance with the product acceptability criteria. The Building Codes Agency shall cooperate with, and assist, the Health Division in its monitoring efforts.

(3) No water pipe used to carry potable water or solders, fillers or brazing material used in making up joints and fittings which does not conform to the product acceptability criteria adopted under subsection (2) of this section shall be sold in this state or installed in any part of any public or private potable water supply system or individual water user's lines.

(4) Notwithstanding subsection (1) or (3) of this section, the Assistant Director for Health may grant exemptions from any prohibition of the sale or use of water pipe used to carry potable water for the emergency repair or replacement of any existing part of a water supply system, or for the necessary use by a well driller in the installation of a well. The assistant director may require any person using water pipe used to carry potable water under this subsection to notify the Health Division of the date and location of that use. [1979 c.535 §1; 1987 c.414 §152]

OPERATOR CERTIFICATION FOR SEWAGE TREATMENT WORKS AND POTABLE WATER TREATMENT PLANTS

(Generally)

448.405 Definitions for ORS 448.405 to 448.470. As used in ORS 448.405 to 448.470:

(1) "Commission" means the Environmental Quality Commission.

(2) "Department" means the Department of Environmental Quality.

(3) "Director" means the Director of the Department of Environmental Quality.

(4) "Division" means the Health Division of the Department of Human Resources.

(5) "Operator" means a person responsible for the operation of a potable water treatment plant, water distribution system or sewage treatment works.

(6) "Person" means any individual, partnership, firm, association, joint venture, public or private corporation, trust, estate, commission, board, public or private institution, utility, cooperative, municipality or any other political subdivision of this state, any interstate body or any other legal entity.

(7) "Potable water treatment plant" means that portion of a water system that in some way alters the physical, chemical or bacteriological quality of the water being treated.

(8) "Sewage treatment works" means any structure, equipment or process required to collect, carry away and treat domestic waste and dispose of sewage as defined in ORS 454.010.

(9) "Supervise" means to operate or to be responsible for directing employees that are responsible for the operation of a water system.

(10) "Water distribution system" means that portion of the water system in which water is stored and conveyed from the potable water treatment plant or other supply point to the premises of a consumer.

(11) "Water system" includes sewage treatment works or potable water treatment plants and water distribution systems that have 15 or more service connections used by year-round residents or that regularly serve 25 or more year-round residents. [1987 c.635 §1]

Note: 448.405 to 448.470 and 448.992 and 448.994 were enacted into law by the Legislative Assembly but were not added to or made a part of ORS chapter 448 or any series therein by legislative action. See Preface to Oregon Revised Statutes for further explanation.

448.407 Advisory committee to commission and division. To aid and advise the Environmental Quality Commission and Health Division in the adoption of rules under ORS 448.410 and 448.450, the Director of the Department of Environmental Quality and the Assistant Director for Health shall appoint an advisory committee. The members of the committee shall include but need not be limited to representatives of all types of water systems. [1987 c.635 §16]

Note: See note under 448.405.

448.409 Biennial report. On or before January 1, 1989, and biennially thereafter, the Department of Environmental Quality and Health Division shall develop and submit a joint report to the Legislative Assembly. The report shall include, but need not be limited to:

(1) A summary of actions taken under ORS 448.405 to 448.470, 448.992 and 448.994;

(2) An evaluation of the effectiveness of such actions; and

(3) Any information and recommendations, including legislative recommendations the department or the division considers appropriate. [1987 c.635 §17]

Note: See note under 448.405.

(Sewage Treatment Works)

448.410 Authority and duties of Environmental Quality Commission. (1) The commission shall:

(a) Adopt rules necessary to carry out the provisions of ORS 448.410 to 448.430 and 448.992.

(b) Classify all sewage treatment works. In classifying the sewage treatment works, the commission shall take into consideration size and type, character of wastewater to be treated and other physical conditions affecting the sewage treatment works and the skill, knowledge and experience required of an operator.

(c) Certify persons qualified to supervise the operation of sewage treatment works.

(d) Subject to the approval of the Joint Ways and Means Committee of the Legislative Assembly, or the Emergency Board if the legislature is not in session, establish a schedule of fees for certification under paragraph (c) of this subsection. The fees established under the schedule shall be sufficient to pay the costs incurred by the department in carrying out the provisions of ORS 448.410 to 448.430 and 448.992.

(2) The commission may grant a variance from the requirements of ORS 448.415, according to criteria established by rule by the commission.

(3) In adopting rules under this section, the commission shall consult with the Health Division in order to coordinate rules adopted under this section with rules adopted by the Health Division under ORS 448.450. [1987 c.635 §2]

Note: See note under 448.405.

448.415 Certification required for operators. (1) Except as provided in ORS 448.430, any sewage treatment works, whether publicly or privately owned, used or intended for use by the public or private persons must be supervised by an operator certified pursuant to ORS 448.410. The operator's certification must correspond to the classification of the sewage treatment works supervised by the operator.

(2) Except as provided in ORS 448.430, a person may not:

(a) Allow any sewage treatment works to be operated unless the operator is certified or the sewage treatment works is supervised by an operator certified under the provisions of ORS 448.410 to 448.430 and 448.992.

(b) Perform the duties of an operator unless the person is certified under the provisions of ORS 448.410 to 448.430 and 448.992. [1987 c.635 §§3, 4]

Note: See note under 448.405.

448.420 Special certification provisions. On and after September 27, 1987, an operator holding a current Oregon sewage treatment certification issued under a voluntary certification program shall be considered certified under the program established under ORS 448.410 at the same classification and grade. Certification of operators by any state that, as determined by the director, accepts certifications made under ORS 448.410 to 448.430 and 448.992, shall be accorded reciprocal treatment and shall be recognized as valid and sufficient within the purview of ORS 448.410 to 448.430 and 448.992, if in the judgment of the director, the certification requirements of such state are substantially equivalent to the requirements of ORS 448.410 to 448.430 and 448.992 or any rule adopted under ORS 448.410 to 448.430 and 448.992. [1987 c.635 §5]

Note: See note under 448.405.

448.425 Deposit and use of fees. Any fees collected pursuant to the schedule adopted under ORS 448.410 shall be deposited in the General Fund of the State Treasury to the credit of the Department of Environmental Quality. Such fees are continuously appropriated to the department to pay the cost of administering the provisions of ORS 448.410 to 448.430 and 448.992. [1987 c.635 §6]

Note: See note under 448.405.

448.430 Certification exception. The requirements of ORS 448.415 shall not apply to:

(1) Any sewage treatment works with an approved design flow of less than 75,000 gallons a day, if the owner has contracted with a certified operator to provide part-time supervision as the commission by rule determines necessary; or

(2) A subsurface sewage disposal system as defined in ORS 454.605. [1987 c.635 §7]

Note: See note under 448.405.

(Potable Water Treatment Plants)

448.450 Authority and duties of Health Division. (1) The Health Division shall:

(a) Adopt rules necessary to carry out the provisions of ORS 448.450 to 448.470, 448.992 and 448.994.

(b) Classify all potable water treatment plants and water distribution systems actually used or intended for use by the public. In classifying the potable water treatment plants and water distribution systems, the division shall take into consideration size and type, character of water to be treated and other physical conditions affecting the treatment plants and distribution systems and the skill, knowledge and experience required of an operator.

(c) Certify persons qualified to supervise the operation of a potable water or a water distribution system.

(d) Subject to the approval of the Joint Ways and Means Committee of the Legislative Assembly, or the Emergency Board if the legislature is not in session, establish a schedule of fees for certification under paragraph (c) of this subsection. The fees established under the schedule shall be sufficient to pay the cost of the division in carrying out the provisions of ORS 448.450 to 448.470, 448.992 and 448.994.

(2) The division may grant a variance from the requirements of ORS 448.455 according to criteria established by rule by the division.

(3) In adopting rules under this section, the division shall consult with the Department of Environmental Quality in order to coordinate rules adopted under this section with rules adopted by the Environmental Quality Commission under ORS 448.410. [1987 c.635 §9]

Note: See note under 448.405.

448.455 Certification required for operators. Except as provided in ORS 448.470, any potable water treatment plant or water distribution system whether publicly or privately owned, used or intended for use by the public or private persons must be supervised by an operator certified pursuant to ORS 448.450. The operator's certification must correspond to the classification of the water treatment plant or distribution system supervised by the operator.

(2) Except as provided in ORS 448.470, a person may not:

(a) Allow any potable water treatment plant or water distribution system to be operated unless the operator is certified or the potable water treatment plant or water distribution system is supervised by an operator certified under the provisions of ORS 448.450 to 448.470, 448.992 and 448.994.

(b) Perform the duties of an operator unless the person is certified under the provisions of ORS 448.450 to 448.470, 448.992 and 448.994. [1987 c.635 §§10, 11]

Note: See note under 448.405.

448.460 Special certification provisions. On and after September 27, 1987, an operator holding a current Oregon water treatment certification issued under a voluntary certification program shall be considered certified under the program established under ORS 448.450 at the same classification and grade. Certification of operators by any state that, as determined by the division, accepts certifications made under ORS 448.450 to 448.470, 448.992 and 448.994, shall be accorded reciprocal treatment and shall be recognized as valid and sufficient within the purview of ORS 448.450 to 448.470, 448.992 and 448.994, if in the judgment of the Assistant Director for Health, the certification requirements of such state are substantially equivalent to the requirements of ORS 448.450 to 448.470, 448.992 and 448.994 or any rule adopted under ORS 448.450 to 448.470, 448.992 and 448.994. [1987 c.635 §12]

Note: See note under 448.405.

448.465 Deposit of fees. Any fees collected pursuant to the schedule adopted under ORS 448.450 shall be deposited in the General Fund of the State Treasury to the credit of the Health Division. Such fees are continuously appropriated to the department to pay the cost of administering the provisions of ORS 448.450 to 448.470, 448.992 and 448.994. [1987 c.635 §13]

Note: See note under 448.405.

448.470 Certification exception. (1) The requirements of ORS 448.455 shall not apply to a water system for which the source of water is ground water and that has less than 150 service connections. However, the operator of a water system exempt under this section shall not be exempt from any continuing educational requirements established by rule by the Health Division.

(2) The requirements of ORS 448.455 shall not apply to a water system that is directly supervised by a registered professional engineer who has a valid certificate to practice engineering issued under ORS 672.002 to 672.325. [1987 c.635 §14; 1989 c.1091 §1]

Note: See note under 448.405.

PENALTIES

448.990 Penalties for violation of swimming facility or water system requirements. (1) Violation of ORS 448.005 to 448.090 by any person, firm or corporation, whether acting as principal or agent, employer or employee, is punishable, upon conviction, by a fine of not less than $25 nor more than $500 or by imprisonment in the county jail not exceeding six months, or by both. Each day that the violation continues is a separate offense.

(2) Violation of any of the following is punishable as a Class A misdemeanor:

(a) Any rule of the Health Division adopted pursuant to ORS 448.115 to 448.330.

(b) Any order issued by the Health Division pursuant to ORS 448.175.

(c) ORS 448.265 or 448.315 (2)(a). [Amended by 1967 c.344 §8; subsections (2) to (5) enacted as 1973 c.835 §177; 1975 c.254 §18; part renumbered subsection (5) of 468.990; 1983 c.271 §4]

448.992 Sewage treatment works violation penalties. (1) Except as provided in subsection (2) of this section, any person who knowingly and wilfully violates ORS 448.415 (2) shall upon conviction be punished by a fine of not more than $500 per day of violation or imprisonment for not more than six months, or both.

(2) Any person who knowingly makes any false statement, representation, or certification in any application, record, report, plan or other document filed or required to be maintained under ORS 448.410 to 448.430, or by any rule adopted under ORS 448.410 to 448.430, shall upon conviction, be punished by a fine of not more than $500 or by imprisonment for not more than six months, or both. [1987 c.635 §8]

Note: See note under 448.405.

448.994 Potable water treatment plant violation penalty. (1) Except as provided in subsection (2) of this section, any person who knowingly and wilfully violates ORS 448.455 (2) shall upon conviction be punished by a fine of not more than $500 per day of violation or imprisonment for not more than six months, or both.

(2) Any person who knowingly makes any false statement, representation, or certification in any application, record, report, plan or other document filed or required to be maintained under ORS 448.450 to 448.470 and 448.992, or by any rule adopted under ORS 448.450 to 448.470 and 448.992, shall upon conviction, be punished by a fine of not more than $500 or by imprisonment for not more than six months, or both. [1987 c.635 §15]

Note: See note under 448.405.

Oregon

DEPARTMENT OF ENVIRONMENTAL QUALITY

January, 1991

Under the direction of the 1989 Legislature (Senate Bill 1079), the Department of Environmental Quality appointed a Task Force to study the impacts of regulating or eliminating phosphorus from detergents and other sources. Attached is the Task Force Report.

The Department recommends passage of legislation banning the sale, distribution and use of detergents containing phosphates in the State of Oregon, with some exceptions. The Department has reviewed the Task Force Report and concludes that the potential benefits of a detergent phosphate ban justify the action. The Environmental Quality Commission supports this recommendation.

The Department supports a phosphate detergent ban for two primary reasons. First, a ban would be a pollution prevention measure. Phosphorus, in low amounts, is a natural element of a healthy aquatic ecosystem. An over abundance of phosphorus, however, can become a pollutant causing excessive algae and plant growth. The resulting water quality problems impair beneficial uses of the waters of the state. A detergent phosphate ban is an action the State can take to minimize the discharge of phosphorus to our waterways.

Second, a ban would raise the public's awareness of the need to reduce nutrient discharges to our waterways. Because laundry detergents are the primary target of a ban, nearly every household would be a participant in this effort to minimize the pollution of our lakes and streams.

Thank you for your consideration of this recommendation.

Respectfully Submitted,

William P. Hutchison
Chair, Environmental
Quality Commission

Fred Hansen
Director, Department of
Environmental Quality

811 SW Sixth Avenue
Portland, OR 97204-1390
(503) 229-5696

PHOSPHORUS
AND
WATER QUALITY

February 1991

Prepared For:

The 66th Oregon Legislative Assembly

Prepared By:

A Task Force
For
Oregon Department of Environmental Quality
Water Quality Division
811 SW Sixth Avenue
Portland, Oregon 97204-1390

WH4432

TABLE OF CONTENTS

TABLE OF CONTENTS
(Continued)

APPENDICES

EXECUTIVE SUMMARY

A Task Force was appointed by the Director of the Department of Environmental Quality, as requested in Senate Bill 1079 (1989), to identify sources of phosphorus and other nutrients contributing to growth of algae, and to identify the potential impacts of regulating phosphorus in detergents and other sources. The Task Force used the specific knowledge of its members and available information, including knowledge of the general biology of algal growth in water, published reports from other regions on algal growth control strategies, and the limited Oregon data that were available.

Excessive growth of algae interferes with beneficial uses in several Oregon water bodies. Controlling algal growth requires controlling one or more of the factors necessary for growth. The concentration of the nutrient phosphorus is the growth factor that is most practical to control in fresh waters. Other nutrients have relatively larger natural and nonpoint sources, which makes them more difficult to control. The phosphorus concentration in surface water must be decreased to the level where it becomes the nutrient limiting the growth of algae. Concentrations of phosphorus that prevent unacceptable algal growth are estimated from general studies and field investigations conducted nationally and in Oregon, and from EPA criteria.

Sources of phosphorus to Oregon waterways include municipal wastewater treatment plants, septic system drainage, and the runoff of animal waste and fertilizers from agricultural, forestry and urban lands. The Task Force focused on the control of phosphorus in municipal wastewater. Laundry detergents contribute about one third of the phosphorus discharged from municipal wastewater treatment plants that do not remove phosphorus.

There will be economic benefits from decreased phosphorus levels entering those municipal treatment plants that remove phosphorus from their wastewater by the use of chemicals. These cost savings result from the need to purchase fewer chemicals and handle and dispose of less sludge. The savings are typically proportional to the decrease in the amount of phosphorus that must be removed.

The decrease in phosphorus resulting from a phosphorus laundry detergent ban alone, will not be sufficient to reach the low levels of phosphorus required by the Total Maximum Daily Loads (TMDL) established for three Oregon rivers to date. A phosphate detergent ban is one control strategy; others must also be used. Land application, removal through chemical or biological processes and decreased industrial discharge are other potential strategies to control point sources of phosphorus. The task force did not determine in which waterbodies a ban on phosphorus detergents would eliminate or delay the need for other phosphorus control strategies. This delay could also result in economic benefits.

Phosphate detergent bans are easily implemented and enforced at minimal cost to public agencies. The cost to consumers of an Oregon ban would be negligible. Companies currently manufacture many types of non-phosphate products and make these products available to Oregon residents. Over one-third of the population in the United States now resides in areas where phosphorus laundry detergents are banned. Some European countries also have such bans. METRO has recently adopted a ban for the Portland area. Current bans typically exempt those cleaning products containing phosphorus for which no substitutes are available.

The elimination of phosphorus laundry detergents is an economical way to decrease the amount of phosphorus in Oregon wastewaters. A reduction in phosphorus discharged to lakes and streams will help maintain algae at acceptable levels.

SUMMARY OF FINDINGS

NUTRIENTS, ALGAL GROWTH AND WATER QUALITY

1. Excessive algal growth produces widespread water quality problems in Oregon. Sixteen of Oregon's 18 river basins have some waterbody segments that do not support beneficial uses due to excessive algal growth.

2. Beneficial uses that may be impaired by excessive algal growth include: domestic drinking water supply, aesthetics, swimming, boating, salmonid fish spawning and rearing, resident fish and aquatic life, wildlife, fishing, and livestock watering.

3. The potential water quality impacts of excessive algal growth include: unpleasant taste and odor, dissolved oxygen depletion, the formation of unsightly algal mats, discoloration of the water, and high pH levels. The impacts on dissolved oxygen and pH in turn affect the health of aquatic ecosystems.

4. Algae need sunlight, nutrients and a favorable physical environment in order to grow. Phosphorus, nitrogen and carbon are the major nutrients that contribute to algal growth.

5. Studies of a large number of lakes in North America and worldwide show that high levels of phosphorus are more often found in lakes having excessive algae and aquatic plant growth.

6. Phosphorus generally restricts algal growth in fresh waters (streams and lakes), while nitrogen generally restricts algal growth in marine waters. Algal growth in fresh waters can be controlled by restricting the availability of phosphorus.

7. The U.S. Environmental Protection Agency has identified phosphorus concentrations above which excessive algal growth

generally occurs. EPA has recommended phosphorus criteria for streams and lakes based on these concentrations. The Oregon Environmental Quality Commission has adopted phosphorus standards for individual waterbodies based on their specific characteristics.

8. To date, the Department of Environmental Quality has established or identified a need for phosphorus TMDLs (total maximum daily loads) for 8 rivers and 3 lakes (see Appendix D, Table D-1 for list). Phosphorus TMDLs are established to eliminate excessive algal growth and resulting water quality standards violations.

9. There is limited experimental information for Oregon waterbodies relating phosphorus concentrations to the growth of algae.

10. Water quality managers do not typically attempt to limit nitrogen for controlling algal growth in fresh waters. Nitrogen deficient waterbodies can favor the growth of algal species capable of using atmospheric nitrogen, a source which can not be controlled.

SOURCES OF NUTRIENTS IN SURFACE WATER AND MUNICIPAL WASTEWATER

11. Sources of nutrients to water quality limited waterbodies in Oregon include:

    a. Point sources, such as municipal wastewater treatment plants, direct industrial discharges, and combined sewer overflows;

    b. Nonpoint sources, such as runoff from agricultural, forestry and urban lands, and on-site sewage disposal systems; and

    c. Natural sources.

12. The proportions of the phosphorus load originating from point versus nonpoint sources will vary by basin, depending on the sources, land uses and physical characteristics of a particular basin.

13. In the three river basins for which phosphorus TMDLs have been established (the Tualatin River, the Yamhill River and Bear Creek), the largest phosphorus contributors are the municipal wastewater treatment plants.

14. Residential, commercial and industrial sources contribute phosphorus to wastewater treatment plants (WWTPs). The proportion of the phosphorus load generated from each source varies according to the population size and industrial distribution in the service area. Typically, residential sources contribute more phosphorus to municipal WWTPs than commercial or industrial sources. The phosphorus from residential sources is primarily from human sewage and from detergents containing phosphate.

15. Laundry detergents typically account for one-third of the total phosphorus entering municipal wastewater treatment plants.

16. The primary source of nitrogen to WWTPs is residential wastewater. There are some industrial sources. The nitrogen in residential sources originates primarily from human waste.

CONTROL OF PHOSPHORUS IN WASTEWATER

17. The two primary methods to remove phosphorus in a wastewater treatment system are: a) chemical/physical removal, such as treatment with aluminum or iron compounds, where the phosphorus is precipitated out of the waste stream and a sludge is created and removed; and b) biological removal, where microorganisms are used to take up the phosphorus. Chemical removal is most commonly used.

18. There are approximately 275 wastewater treatment plants in Oregon that discharge to surface waters. Two of these currently remove phosphorus with chemicals (the Rock Creek and Durham plants in the Tualatin basin). Three additional plants (Lafayette, McMinnville, Ashland) are considering various phosphorus removal systems to achieve new permit limits. Port Orford must also find an alternative to its current effluent disposal as the result of a phosphorus TMDL. As more Total Maximum Daily Loads are established, phosphorus

limits will be included in the permits of additional plants (e.g., La Grande and Hermiston are anticipating phosphorus limits as they develop facility plans).

19. The 2 Oregon WWTPs (Rock Creek and Durham) that currently remove phosphorus with chemicals are subject to the phosphate detergent ban recently adopted by METRO.

20. Other potential methods for treatment plants to prevent the discharge of phosphorus to streams include applying effluent to land, reusing effluent for irrigation, and using constructed wetlands for treatment. These practices may become a preferred method where suitable land is available.

21. A reduction in the phosphorus load entering wastewater treatment plants that chemically remove phosphorus results in cost savings. The cost savings are from reduced chemical use and sludge handling. The estimated savings from a 30 percent reduction in influent phosphorus range from approximately $100,000 to $200,000 per year per 10 million gallons daily plant discharge.

22. Source reduction of phosphorus would aid in improving water quality if concentrations are reduced to the levels required to prevent excessive algal growth.

EFFECTS OF A PHOSPHATE DETERGENT BAN

23. Phosphate in detergents is a source of phosphorus identified as being easily reduced at the source through statewide regulation. Statewide regulation of industrial discharges and nonpoint sources were not analyzed in this report due to their complexity and study resource limitations.

24. Phosphate detergent bans significantly reduce effluent phosphorus loads from WWTPs that do not practice phosphorus removal. Data from eight states and one region that have imposed phosphate detergent bans show 24-51% phosphorus reductions in effluent from these types of plants.

25. For the 3 Oregon river basins that currently have TMDLs, eliminating detergent phosphates alone will not reduce instream phosphorus concentrations to the levels required by

the TMDLs. A phosphate detergent ban would be only one component of a complete strategy for the control of algal growth in these basins.

26. In areas where WWTPs remove phosphorus through chemical treatment, a detergent phosphate ban would produce an economic benefit because of lower amounts of chemicals used and less sludge generated.

27. A detergent phosphate ban is not expected to result in the elimination of detergent products or brands. All major detergent producers manufacture non-phosphate laundry detergents formulations. An estimated 37 percent of the U.S. population lives in areas (12 states and 5 regions) where phosphate laundry detergents are not sold. Products without substitutes, such as automatic dish-washing detergents, are exempted from current bans.

28. A statewide ban will minimize the possibility of consumers unintentionally bringing phosphate detergents into areas with local bans.

29. Detergent phosphate bans do not appear to increase costs of laundry detergents to the consumer.

30. A detergent phosphate ban is a pollution prevention measure, which reduces phosphorus from the source.

31. Despite the lack of experimental verification in Oregon, the best available information indicates that a statewide phosphate detergent ban could be a valuable component of an overall strategy for water quality management in Oregon lakes and rivers.

PHOSPHORUS AND WATER QUALITY

I. INTRODUCTION

Concern over the growth of algae in Oregon waters and the water quality impacts that may result led the 1989 Legislature to adopt Senate Bill 1079 (shown in Appendix B). The bill directs the Department of Environmental Quality (Department, DEQ) to appoint a task force to study potential sources and control of the problem. This report of the Task Force summarizes the impacts of controlling phosphorus and other nutrients for the purpose of reducing or preventing algal growth in Oregon waters. In particular, the Task Force evaluated the effects of regulating or eliminating phosphorus in detergents.

A glossary is provided in Appendix A to help the reader with terms used in this report.

SB 1079 asked the Task Force to conduct the following tasks:

1. Identify the sources of phosphorus and other nutrients contributing to the growth of algae in waters where algal growth is adversely affecting water quality.

2. Identify the sources of nutrients to wastewater treatment plant (WWTP) influent and the relative contribution of those sources to WWTP effluent.

3. Identify the potential impacts of regulating or eliminating phosphorus from detergents and other sources.

4. Report the findings to the 66th Legislature (1991).

The Task Force focused its efforts on the nutrient phosphorus and on phosphate detergents as a source for possible control. These topics were selected because they are specifically identified in Senate Bill 1079, because of time and resource limitations, and for the reasons explained in Sections II & III below.

TASK FORCE

The Phosphorus Task Force was appointed in July, 1990 as a working group. The members researched and summarized information on the control of algal growth in surface waters. The Task Force met four times between August, 1990 and January, 1991.

Dr. Benno Warkentin, Director of the Water Resources Research Institute at Oregon State University, chaired the Task Force. Representatives of the following agencies and organizations participated:

- The Association of Oregon Sewerage Agencies.
- The Oregon Department of Forestry.
- The Metropolitan Service District of Oregon (METRO).
- The Conference of Local Health Officials.
- Devils Lake Water Improvement District.
- Associated Oregon Industries.
- The Soap and Detergent Association.
- Oregonians for Food and Shelter (agriculture).
- The Oregon Environmental Council.
- River Watch.

A list of Task Force members is included in Appendix B.

METHODOLOGY

The Task Force relied on literature review, existing data, Task Force expertise, DEQ expertise, and the legislation and experiences of states and regions which have already imposed phosphate detergent bans, to develop this report. The Task Force did not conduct new water quality field studies.

Considerable literature is available on phosphate detergent bans and their results. Twelve states and 5 regions across the country have banned phosphate detergents since the early 1970's. The Portland metropolitan area and 2 other regions in the Northwest U.S. are among those which have recently adopted bans.

The major sources of existing Oregon data available at the Department include ambient water quality monitoring data, Biennial Water Quality Assessment reports, the 1988 Oregon Statewide Assessment of Nonpoint Sources of Water Pollution, and DEQ water quality studies such as those conducted to establish total maximum daily loads (TMDLs).

II. NUTRIENTS, ALGAL GROWTH AND WATER QUALITY

THE IMPACTS OF ALGAL GROWTH ON WATER QUALITY AND BENEFICIAL USES

Oregon's water quality program and standards are designed to protect the "beneficial uses" of our waters. Beneficial uses include domestic water supply, industrial water supply, irrigation, livestock watering, salmonid fish rearing and spawning, resident fish and aquatic life, wildlife and hunting, fishing, boating, water contact recreation, aesthetic quality, hydroelectric power, and commercial navigation and transportation (Oregon Administrative Rules, Chapter 340, Division 41).

Algae, like other plants, are a natural component of a healthy ecosystem. Algae are primary producers, the foundation of the food chain, which transform the energy of the sun, through photosynthesis, into matter which can be consumed by higher organisms. In low amounts, they do not interfere with beneficial uses of water.

An over-abundance of algae, however, harms water quality, aquatic ecosystems, and the ability of rivers and lakes to support beneficial uses. One beneficial use directly affected is aesthetics. Algae blooms may occur, causing domestic water supplies to have unpleasant taste and odor problems, decreasing water clarity, causing the water to turn a murky greenish-brown color, and forming unsightly floating mats on the water surface. An attached form of algae, called periphyton, may cover streambeds, and aquatic plants may overgrow lakes, interfering with boating and swimming.

In addition, excessive algal growth affects the dissolved oxygen and pH of streams and lakes, sometimes damaging the health of aquatic ecosystems and causing water quality standards violations. When this occurs, additional beneficial uses are not supported, potentially including: drinking water supply, salmonid fish rearing and spawning, resident fish and aquatic life, wildlife, fishing, and livestock watering.

NUTRIENTS AND ALGAL GROWTH

Algae need nutrients, light and a favorable physical environment in order to grow. Nitrogen, carbon and phosphorus are the nutrients required in relatively large amounts. Algae also need a variety of other nutrients in small or trace amounts. Given adequate nutrients and physical conditions, excessive or nuisance levels of algae can accumulate in lakes and streams if water flow is slow relative to the algal growth rate.

Any one of the required nutrients may be present in such low concentrations that growth is limited, regardless of the availability of light or other nutrients. This nutrient then controls the rate at which algae grow. This is called the "limiting nutrient" concept (Ryding, 1989). As nutrient concentrations in water increase from low values, growth of algae increases proportionally until some other factor becomes limiting. This is most clearly seen in experiments where one limiting nutrient is added in successive increments. Carbon seldom limits overall algal production. Phosphorus, nitrogen and sometimes nutrients needed in smaller amounts, such as silicon or iron, can limit growth. Additional information on the relationship between algal growth and nutrients is provided in Appendix C.

A considerable body of scientific literature has accumulated over the past 50 years on the growth of algae in surface waters. The overwhelming evidence from the literature allows a general conclusion. In those waterbodies where a nutrient limits growth, the limiting nutrient in marine environments is generally nitrogen, and the limiting nutrient in fresh water is generally phosphorus. Field studies attempting to quantify the relationship between phosphorus and algal mass have not shown consistent results, probably due to the large number of other variables in the natural environment.

Algae require larger amounts of nitrogen than phosphorus, but nitrogen is also more abundant in the natural environment. Some species of algae can use nitrogen from the atmosphere. These "nitrogen-fixing" algae are blue-green species and are less desirable. Nitrogen is also available from soils, and in the soluble form it moves readily through soils. Multiple sources and solubility make it difficult to control nitrogen additions to waterbodies.

Phosphorus is adsorbed readily on soil particles, so soluble phosphorus is found in only low concentrations in nature. It does not move readily through soil. Nonpoint sources, such as runoff, contain both soluble and adsorbed phosphorus. Additions of high concentrations of soluble phosphorus to waterbodies are largely from wastewater. Discharges from wastewater treatment plants (WWTPs) contain predominantly soluble phosphorus, which is readily available to algae for growth.

The phosphorus concentration in waterbodies is therefore more controllable or manageable than nitrogen. Phosphorus has been selected as the focus for control of algae in fresh waters.

The Environmental Protection Agency (EPA, 1986) recommends that for the prevention of nuisance algal growth, phosphorus concentrations should not exceed:

- 0.025 mg/l in lakes and reservoirs,
- 0.05 mg/l in streams entering lakes or reservoirs, and
- 0.10 mg/l in other flowing waters.

There are no nitrogen criteria recommended by EPA for this purpose.

In-stream phosphorus standards have been adopted by the Oregon Environmental Quality Commission for some rivers and lakes in Oregon. These standards were established following intensive water quality investigations of the following waterbodies:

- Tualatin River -- 0.07 mg/l Total Phosphorus.
- Yamhill River -- 0.07 mg/l Total Phosphorus.
- Bear Creek -- 0.08 mg/l Total Phosphorus.
- Clear Lake (near Florence) -- 0.009 mg/l Total Phosphorus.

ALGAL GROWTH PROBLEMS IN OREGON

Excessive algal growth is a widespread water quality problem in Oregon. Sixteen of Oregon's 18 river basins have some waterbodies that do not support beneficial uses due to excessive algae and aquatic plants (DEQ, 1990). According to DEQ's 1990 Water Quality Assessment Report, 745 river miles only partially support or do not support their designated beneficial uses due to excessive nutrients or plant growth. Many lakes across the state also have excessive algae or plant growth problems. Water quality data are shown below and in Appendix D.

The Task Force recognizes that we do not have sufficient data to know precisely how many waterbodies in Oregon have algal growth problems caused by excess nutrients. Nor do we know how many of Oregon's algal growth problems could be corrected through phosphorus reduction and how many could be corrected through nitrogen control.

To date, the Department of Environmental Quality has established phosphorus standards and TMDLs, and Oregon lake restoration projects have identified phosphorus control, as the means to solve algal growth problems. This strategy is consistent with EPA recommendations and with similar efforts and studies conducted around the country and around the world.

Statewide Data

Tables 1 and 2 list the Oregon waterbodies assessed as "water quality limited" due to dissolved oxygen, pH or aesthetic problems where these problems result at least in part from algal growth (DEQ, 1990). A waterbody is "water quality limited" (as defined by the Federal Clean Water Act) if it does not meet water quality standards even though all the point sources discharging to the waterbody are permitted and meet the current technology-based standards. A waterbody may also be designated water quality limited due to a lack of data or because the minimum technology based standards have not yet been fully implemented.

Table 1 shows the water quality limited waterbodies which DEQ has identified as priorities for receiving total maximum daily loads (TMDLs). Table 2 lists additional "water quality limited" streams which have a potential algal growth problem, and septic system drainage or municipal sewage treatment discharge as a suspected source. Table 3 lists Oregon lakes which do not fully support their designated beneficial uses due to algae or weed growth, and with septic drainage as a suspected source of nutrients.

Table 1

Water Quality Limited (303d1) Waterbodies in Oregon with Algal Growth or Related Problems

(Continued)

Waterbody	Basin	Parameters of Concern	Suspected or Known Sources	Status
Tualatin R. RM 0-39	Willamette	Bact, Nutrients, pH, DO, Algae	Municipal, Agric, Urban, Natural	TMDL Established
Tualatin R. RM 39-63	Willamette	Bacteria, Nutrients	Agric, Urban, Septic	TMDL Established
Lake Oswego	Willamette	DO, pH, Algae, Nutrients	Municipal, Agric, Urban, Natural	TMDL Established
Columbia Slough RM 0-15	Willamette	Bacteria, Nutrients, Algae, pH, Organics, Metals	Municipal, Urban, Industrial, Nat.	TMDL Proposed
Umatilla RM 0-79	Umatilla	pH, Solids, Nutrients, Bacteria	Municipal, Agric, Septic, Natural	TMDL Proposed, RM 35-79 (Est. TMDL Needed RM 0-35)
Grande Ronde RM 82-179	Grande Ronde	pH, Bacteria, Nutrients	Municipal, Agric, Septic, Natural	TMDL Proposed
Klamath River & Lake Ewauna RM 209-250	Klamath	pH, Algae, Nutrients, Metals	Municipal, Agric, Indust, Natural	TMDL Proposed
Link River RM 250-255	Klamath	pH, Algae, Nutrients	Agric, Natural	TMDL Proposed
J.C. Boyle Reservoir	Klamath	DO, pH, Algae, Nutrients	Municipal, Agric, Indust, Natural	TMDL Proposed

NOTE:

These waterbodies are "water quality limited" as defined by Section 303d1 of the Federal Clean Water Act.

SOURCE: Draft 1990 Water Quality Status Assessment Report (305b), DEQ, Portland, Oregon, Appendix A.

SA\WH4435

Table 1

Water Quality Limited (303d1) Waterbodies in Oregon with Algal Growth or Related Problems

Waterbody	Basin	Parameters of Concern	Suspected or Known Sources	Status
Garrison Lake	S. Coast	Weeds, Nutrients, Algae, pH	Municipal, Septic, Natural	TMDL Established
N.F. Coquille RM 0-10	S. Coast	DO	Municipal, Natural	TMDL Proposed
Coquille R./ Estuary, RM0-39	S. Coast	DO, Bacteria	Municipal, Agric, Forest, Natural	TMDL Proposed
South Umpqua RM 0-15	Umpqua	pH, DO, Ammonia, Bact, Nutrients	Municipal, Agric, Indust, Low Flow	TMDL Proposed
Bear Creek RM 0-27	Rogue	pH, Nutrients, Bact. Algae, pH	Municipal, Agric, Septic, Low Flow	TMDL Established
C.F. Willamette RM 0-29	Willamette	DO, pH	Municipal, Agric, Septic	TMDL Proposed
Rickreall Creek RM 0-20	Willamette	DO	Municipal	TMDL Needed
S. Yamhill RM 0-05	Willamette	Algae, Nutrients	Municipal, Agric, Septic	TMDL Established
Yamhill R RM 0-11	Willamette	Algae, Nutrients, pH	Municipal, Agric, Septic	TMDL Established
Pudding R. RM 0-30	Willamette	DO, Bacteria	Municipal, Agric, Septic, Natural, Industrial	TMDL Proposed

NOTE:

These waterbodies are "water quality limited" as defined by Section 303d1 of the Federal Clean Water Act.

SOURCE: Draft 1990 Water Quality Status Assessment Report (305b), DEQ, Portland, Oregon, Appendix A.

(Continued Below)

Table 2

Water Quality Limited Streams (303d3)
with Municipal or Septic Sources Contributing

Waterbody	Basin	Parameters of Concern	Suspected or Known Sources	Status
S.F. Coquille RM 0-62	S. Coast	DO, Bacteria	Municipal, Septic	TMDL Proposed (Part of Segment)
Cow Creek RM 0-27	Umpqua	pH	Municipal, Indust, Natural	--
Umpqua River RM 103-112	Umpqua	Bacteria	Municipal, Urban, Indust, Natural	Estimated TMDL Needed
Elk Creek RM 0-27	Umpqua	DO, Bacteria, pH, Nutrients	Municipal, Agric, Septic	Estimated TMDL Needed
Rogue River RM 95-132	Rogue	Bacteria, Nutrients	Municipal, Agric, Septic	Estimated TMDL Needed
Rogue River RM 29-95	Rogue (Wild & Scenic)	Nutrients	Municipal, Agric, Natural	Use Threatened
Willamette R. RM 0-26	Willamette	Bacteria, Organics, Metals, Pest.	Municipal, Urban, Agric, Septic	Estimated TMDL Needed
Willamette R. RM 26-80	Willamette	Bacteria, Organics	Municipal, Urban, Agric, Septic, Industrial	Estimated TMDL Needed
Salt Creek RM 0-35	Willamette	Bacteria, DO, Algae, Nutrients	Municipal, Agric, Septic, Natural	Estimated TMDL Needed
Crooked River RM 0-70	Deschutes	Bacteria, Nutrients, Solids	Municipal, Septic, Natural	Estimated TMDL Needed
John Day RM 185-212	John Day	pH, Bacteria, Solids	Agric, Septic, Municipal, Natural	Estimated TMDL Needed
Umatilla RM 0-35	Umatilla	Solids, Bacteria, Nutrients	Municipal, Agric, Septic, Natural	TMDL Proposed RM 35-57 (Est. TMDL Needed RM 0-35)

NOTE:

Waterbodies with bacteria problem only not included. These waterbodies are "water quality limited" as defined by section 303d3 of the Federal Clean Act.

SOURCE: Draft 1990 Water Quality Status Assessment Report (305b), DEQ, Appendix A.

Waterbodies affected by municipal and septic sources are shown in the affected by a phosphate detergent ban, the focus of this report. It should be recognized that there are also waterbodies experiencing algae-related water quality problems that do not have municipal or septic sources. The nutrient inputs in these cases are from nonpoint, natural or industrial point sources.

Table 3

Oregon Lakes with Algae or Weed Growth Problems and Septic Systems as a Suspected Source of Nutrients

Basin	Lake	
North Coast	• Cullaby Lake	• Sunset Lake
Mid Coast	• Devils Lake • Sutton Lake • Collard Lake • Tahkenitch Lake	• Eckman Lake • Mercer Lake • Siltcoos Lake
South Coast	• North Tenmile L.	• Tenmile Lake
Umpqua	Diamond Lake	
Rogue	Willow Reservoir	
Willamette	Blue Lake	
Deschutes	Suttle Lake	

SOURCE: "1990 Water Quality Status Assessment Report", Appendix A, Department of Environmental Quality, Portland, Oregon, 1990.

Several water quality parameters may indicate excessive algal growth, including chlorophyll a, dissolved oxygen, pH and phosphorus. Chlorophyll a is a measure of phytoplankton or "floating" algae. The chlorophyll a criteria for the purpose of preventing nuisance phytoplankton growth is 0.010 or 0.015 mg/l, depending on the type of waterbody (OAR 340-41-150). If a waterbody exceeds the criteria, it may not support beneficial uses and the Department is to conduct an investigation.

Dissolved oxygen (DO) and pH measurements can also be used to detect algal growth. Excessive algal growth may cause large fluctuations in DO or pH throughout the day, and DO supersaturation (i.e., greater than approximately 110-130 percent saturation). As photosynthesis occurs during daylight hours, dissolved oxygen increases, carbon dioxide is taken up and pH rises. Then, during the night, respiration and decomposition deplete the dissolved oxygen so that by early morning DO and pH may be quite low.

High nutrient levels, particularly phosphorus, also indicate a potential algae or plant growth problem. The phosphorus criteria recommended by EPA and DEQ to prevent nuisance algal growth are discussed above.

The 1990 Water Quality Assessment (DEQ) summarizes the water quality monitoring data collected by the Department from 1979-1989. These data are on streams because the Department does not routinely monitor lakes. Chlorophyll a and phosphorus samples were collected primarily between April and October. Phosphorus values in the following streams exceeded the 0.10 mg/l criteria in at least 25 percent of the samples (only sites with at least 10 samples are included here):

- Little Butte Creek
- Elk Creek
- Bear Creek
- Rogue River
- Coast Fork Willamette R.
- Willamette River
- Pudding River
- S. Yamhill & Yamhill R.
- Tualatin River & tribs.
- Columbia Slough
- Deschutes River
- Owyhee River
- Malheur River
- Powder River
- Grande Ronde River
- Umatilla River & tributaries
- Crooked River
- Klamath River & tributaries
- S. Umpqua & Umpqua Rivers

Cholorphyll a concentrations in the following streams exceeded the 0.015 mg/l criteria in at least 10 percent of the samples taken (only sites with at least 10 samples are included here):

- Yamhill River
- Tualatin River & tribs.
- Columbia Slough
- Malheur River
- Calapooia River
- Willamette River
- Klamath River & tributaries

If streams with at least 5 samples taken are included, the Owyhee and Miami Rivers would be added to this list.

High chlorophyll a concentrations are less frequently detected than high phosphorus levels for several reasons. First, water monitoring samples are taken from the water column and, therefore, measure only phytoplankton algae, not periphyton algae or macrophytes, which grow attached to stream bottoms. Therefore, if a stream is dominated by periphyton algae, this will not show up in chlorophyll a measurements. Periphyton algae are more common in shallow, moving streams. Some water quality limited streams in Oregon dominated by periphytons include the South Umpqua River, Umatilla River, Grande Ronde River and Bear Creek.

Second, the Department does not test for chlorophyll a as frequently and there is simply not as much data available. Unlike nutrient concentrations, chlorophyll a has not historically been a standard ambient monitoring test. Finally, some rivers have high phosphorus but do not experience excessive algal growth due to turbidity or shade, which limit the availability of light, or due to the speed of the water movement which prevents the algae from accumulating.

Nitrogen-fixing algae are abundant or dominant in the Klamath, Umatilla, South Umpqua, Tualatin, and Grande Ronde Rivers, and many lakes (Sweet, 1985). When this occurs, phosphorus must be controlled to limit algal growth. The algae are obtaining the nitrogen they need from the atmosphere.

Total Maximum Daily Loads

The Department of Environmental Quality has identified 13 streams and Garrison Lake as priority waterbodies to receive total maximum daily loads (TMDLs). These waterbodies, listed in Appendix D, Table D-1, are water quality limited as defined by the Federal Clean Water Act. To date, phosphorus TMDLs have been established, or identified as being needed, for 8 of the 13 streams and Garrison Lake. These phosphorus TMDLs are being established to eliminate violations of dissolved oxygen and pH standards caused by excessive algal growth. In addition, the Department has established phosphorus TMDLs for Clear and Collard Lakes (near Florence) to control the potential impacts of future development. After the priority TMDLs are completed, the Department will begin work on the remaining water quality limited waterbodies in the state.

Phosphorus TMDLs have been established for three streams, the Yamhill and Tualatin Rivers and Bear Creek. The largest sources of phosphorus in these basins are the wastewater treatment plants. In the Tualatin and Bear Creek, phosphorus allocations were also given to nonpoint sources, including runoff from urban, agricultural and forest lands. The Department has also established phosphorus TMDLs for Clear Lake and Garrison Lake. The sources being regulated in these basins include WWTP effluent, septic systems and urban runoff.

Nutrient Limitation in Oregon Waters

A few studies of nutrient limitation have been conducted on Oregon waterbodies. A study of Devils Lake (KCM, 1983) stated that phosphorus was probably the limiting nutrient. Algal assays (biological tests) in Garrison Lake found that both nitrogen and phosphorus were limiting in August of 1988 (SRI, 1990). Algal assays conducted in Clear Lake (Cooper Consultants, 1985) found that phosphorus was limiting algal growth. EPA research in several Oregon bays shows that phosphorus is typically the limiting nutrient in riverine portions of estuaries.

In Bear Creek, phosphorus appears to be the nutrient in limiting proportions in nonpoint loads and background conditions. Below the City of Ashland's wastewater treatment plant (WWTP), neither nutrient is limiting. Nitrogen appears to be the nutrient in limiting proportions (the nitrogen to phosphorus ratio is low). This situation results from the discharge of relatively large amounts of phosphorus from the WWTP.

Algal assays conducted for the Tualatin River indicate that a target concentration of 0.05 to 0.10 mg/l total phosphorus is needed to reduce algal growth. The instream phosphorus criteria established by the Environmental Quality Commission is 0.07 mg/l.

A US Geological Survey study of the Willamette River in 1977 (Hines et al.) found that phosphorus was the nutrient in limiting proportions in the Willamette River, but that algal growth was not being limited by a nutrient at that time.

III. NUTRIENT SOURCES

SOURCES OF PHOSPHORUS AND NITROGEN TO OREGON WATERWAYS

Nitrogen and phosphorus sources can be placed into three general categories: point sources, nonpoint sources and natural sources. Point sources include wastewater treatment plants (WWTPs), combined sewer overflows (CSOs), and direct industrial discharges. Nonpoint sources are diffuse and are carried to a stream or lake by overland runoff rather than through a pipe or ditch. Nonpoint sources include agricultural, forestry and urban runoff and septic system drainage.

It is difficult to quantify how much of the nutrient load to a particular stream is from point sources and how much is from nonpoint sources. The DEQ has estimated that in the Tualatin basin, less than 15-20 percent of the total phosphorus load to the Tualatin River is from nonpoint sources. The proportions will vary from basin to basin, however, depending on the physical characteristics, land uses and point sources present in a particular basin.

WWTPs are the largest point sources of phosphorus discharges to Oregon waters. There are over 275 WWTPs in Oregon, with a total design capacity of approximately 300 million gallons per day, that discharge effluent to surface waters. WWTP effluent contains an average of 5 - 7 mg/l phosphorus. The sources of nutrients to WWTPs are discussed in more detail below.

The types of industries that typically discharge nutrients include food processors, log ponds, and manufacturers using phosphorus compounds for metals cleaning. These direct industrial discharges are a relatively small portion of the total phosphorus load in Oregon. Direct industrial discharges are suspected pollution sources for four of the 15 priority rivers and lakes to receive TMDLs. Municipal WWTPs are suspected sources for all 15 waterbodies.

There are a variety of nonpoint sources of nutrients. Agricultural nonpoint sources include the runoff of animal waste and fertilizer, and the erosion of soil particles which may have phosphorus adsorbed to them. Another agricultural source is irrigation return flow. Some forestry practices cause phosphorus from decomposing vegetation or soil erosion to be carried to surface waters. Forestry fertilizers may be a source of nitrogen, but do not typically contain phosphorus. Urban fertilizer use also contributes nutrients to runoff.

On-site sewage treatment systems, such as septic system drain fields, can be a nonpoint source of nutrients. It is commonly understood that septic systems can be a source of nitrogen to groundwater and surface waters; in some situations they can also be a source of phosphorus. This may occur when a system is failing (the sewage is seeping to the surface of the ground). It may also occur when septic systems exist close to a waterbody, such as development along the shoreline of a lake, in sandy soils. Phosphorus readily adsorbs to soil particles, but the soils between the drain field and the lake may become saturated with phosphorus. As the soils become saturated with phosphorus, the concentrations of phosphorus passing through the soil would increase.

SOURCES OF PHOSPHORUS TO WWTP INFLUENT AND EFFLUENT

Phosphorus loads entering municipal WWTPs come from residential, industrial and commercial sources. Residential sources of phosphorus include human waste, laundry detergent, automatic dishwashing detergent, garbage disposals and other household cleaners. Industrial and commercial sources usually originate from food or forest product processing wastes, or some type of detergent or cleaner.

The relative proportion of phosphorus coming from various sources is assumed to be the same in the WWTP effluent as in the influent. Once the wastewaters are mixed in the plant, it is not possible to determine the source of the phosphorus. Therefore, estimates of the relative contribution of sources to effluent phosphorus are based on the influent sources.

The Unified Sewerage Agency (USA) estimates that an average of 85 percent of the phosphorus entering four of their plants in the Tualatin River basin is from residential and commercial sources.

An average of 15 percent of the influent phosphorus load is from industrial sources (Tualatin Basin Consultants, 1990).

Table 4 presents general estimates of the current phosphorus loads entering municipal wastewater treatment plants in areas without restrictions on phosphate detergent use. The percentage of the influent phosphorus contributed by each source is also shown.

Table 4 shows that household laundry detergents contribute approximately 27 percent of the total phosphorus load to WWTPs. This estimate was calculated based on the typical amount of phosphorus found in detergents today. Manufacturers have reduced the amount of phosphorus in their detergents since the 1970's and, therefore, this source represents a smaller proportion of the total phosphorus load today than it did 15-20 years ago.

Observed reductions in influent phosphorus resulting from the elimination of a particular source may also be used to estimate the contribution of phosphorus from that source. This method is primarily available for laundry detergents. Twelve states and five regions have restricted phosphate detergents from 1972 to present. Since the late 1970's these bans have resulted in 23 to 38 percent reductions in influent phosphorus loads, with an average reduction of 29 percent observed (see Table 5).

The Unified Sewerage Agency estimates that the METRO phosphate detergent ban, effective February 1, 1991, will reduce the phosphorus loads to their plants in the Tualatin River basin approximately 30 percent.

The calculated estimates and results of prior bans support the conclusion that household laundry detergents account for approximately one-third of the total phosphorus load entering municipal wastewater treatment plants, and being discharged from plants that do not remove phosphorus.

SOURCES OF NITROGEN TO WWTPS

The primary source of nitrogen to municipal wastewater is human waste. This source generates an average of approximately 4.4 kilograms of nitrogen per capita per year in organic and ammonium forms (Organization for Economic Cooperation and Development, 1971).

Table 4

Estimated Phosphorus Loads to Municipal Wastewater Treatment Plants

Source	Phosphorus Load* (kg/capita/yr)	Percent of Total Load
Human Waste	0.6	44
Laundry Detergents	0.37	27
Automatic Dishwashing Detergent	0.098	7
Other Household Cleaners	0.013	1
Industrial & Institutional:		
• Cleaners	0.16**	12
• Finishers	0.05**	4
• Water Treatment Chemicals	0.05**	4
Denitrifices	0.005	0.4
TOTAL	1.35	

* These estimates are based on current detergent formulations.

** Industrial loads vary widely. These values are national averages, assuming that all the industrial phosphorus loads enter municipal treatment plants. In many cases, however, these sources will either not exist in a service area, be treated and discharged directly rather than entering a municipal plant, or they will undergo pretreatment before entering the plant.

SOURCE: Personal communication with Richard Sedlak, Soap and Detergent Association, New York, December 1990.

Table 5
Phosphate Detergent Ban Effects on Municipal Wastewater

State/Region	Influent P Reduction	Effluent P Reduction	Year Ban Effective
Indiana	60%	60%	1972
New York	48	--	1972
Michigan	23	24	1977
Minnesota	38 (Loading)	42 (Loading)	1978
Vermont	--	40 (Loading)	1978
Wisconsin	22	--	1983
Maryland	32	42 (Loading)	1985
Washington, DC	25	--	1986
North Carolina	23	44	1988
Virginia	30	51	1988
Missoula, MT	--	40 (Loading)	1988
Atlanta, GA/Georgia	35 (Loading)	40 (Loading)	1989/1990
Pennsylvania	Not Yet Available	Not Yet Available	1990
Ohio	Not Yet Available	Not Yet Available	1990
Spokane River Basin, WA	Not Yet Available	Not Yet Available	1990
Portland, OR	Not Yet Available	Not Yet Available	1991

NOTE:
Reductions were figured as a percent decrease in either concentration or mass load (which accounts for the discharge flow), as indicated.

SOURCE: Updated information from Findings of the Region-Wide Phosphate Detergent Ban Study. Staff report to the Council of the Metropolitan Service District of Oregon, Jim Morgan, Portland, Oregon, May 22, 1990.

Industries can also be sources of nitrogen to municipal WWTPs. For example, the Unified Sewerage Agency estimates that industrial sources contribute 2, 5, 6 and 19 percent of the ammonia nitrogen loads to four plants in the Tualatin basin (Tualatin Basin Consultants, 1990).

The largest source of nitrogen to WWTPs is residential, and the primary residential source of nitrogen is human waste. Therefore, there is limited opportunity to regulate or eliminate nitrogen loads to the plants.

SOURCES FOR POSSIBLE REGULATION OR ELIMINATION

Phosphate in detergents is a significant source of phosphorus which could be eliminated or greatly reduced through statewide regulation. The following portions of this report discuss the potential benefits and impacts of such a regulation.

The Task Force recognizes that for many waterbodies, a phosphate detergent ban would be only one component of a successful program to control algal growth. Other components could include water quality based permitting (TMDLs), the permitting of combined sewer overflows, and the control of nonpoint sources. Each of these activities is in an early stage, but making progress as part of the Department's water quality program.

Industrial sources of nitrogen to WWTPs could potentially be controlled at the source. This control option is not analyzed below because industrial sources of nitrogen to WWTPs are relatively small. The primary residential source of nitrogen, human waste, could not feasibly be reduced at the source. Nonpoint sources of nitrogen could also be controlled at the source. See Appendix E and F for information on nutrient control technologies and programs.

IV. THE IMPACTS OF ELIMINATING PHOSPHORUS FROM DETERGENTS

IMPACTS ON WATER QUALITY

Table 5 above shows that the amount of phosphorus in municipal treatment plant discharges to receiving waters (effluent) has decreased an average of 40 percent as the result of phosphate detergent bans implemented since the late 1970's. These figures represent results at plants that do not treat for phosphorus removal. Phosphorus load reductions will aid in improving water quality if in-stream concentrations are reduced to the levels required to prevent excessive algal growth.

While there have been many studies following detergent phosphate bans which document the reduction in phosphorus in the influent and effluent of wastewater treatment plants, fewer studies have been done on the resultant change in instream or in-lake phosphorus concentrations and other related water quality parameters. The literature that is available varies in its conclusions.

The effect of a reduced phosphorus load on water quality is difficult to predict quantitatively because of the variety among waterbodies and the many other environmental variables that influence the outcome. There are models which can be used to estimate the response of a given waterbody to a change in one factor, such as its phosphorus load. This requires that a set of data on a specific water body be collected and used to assemble the model. Studies and modelling of individual waterbodies to quantify the results of phosphorus control require time and expense.

IMPACTS ON OTHER NUTRIENT CONTROL STRATEGIES

In some waterbodies, a decrease in phosphorus loads from a phosphate detergent ban could be sufficient to allow discharge of WWTP effluent without prior phosphorus removal, or to delay the time when removal becomes necessary. Where nutrient and algal growth problems are severe, however, WWTPs will need to reduce their phosphorus loads by a very large amount. In these situations, detergent bans alone will not produce the required reduction and other measures must also be implemented. Additional information on nutrient control practices is provided in Appendix E.

There are over 420 wastewater treatment facilities in Oregon. More than 275 of these discharge effluent to surface waters and these facilities have a combined treatment capacity of over 300 million gallons per day (MGD). Currently, two plants (USA's Rock Creek and Durham), with a combined capacity of approximately 30 MGD, chemically remove phosphorus. Three additional plants (Lafayette, McMinnville and Ashland) are considering various phosphorus removal alternatives to achieve new discharge limits. As TMDLs continue to be established, phosphorus limits will be included in the permits of additional plants.

Phosphorus Removal at Treatment Plants

Phosphorus removal at the treatment plant is one method to reduce effluent phosphorus. This removal is typically accomplished by a chemical addition process using iron or alum which precipitates the phosphorus. The chemical treatment process generates additional sludge, which must then be removed and disposed.

Reduced influent phosphorus resulting from phosphate detergent bans typically affects the chemical removal process in the following ways:

1. The quantity of chemicals required for phosphorus removal is reduced in proportion to the decrease in influent phosphorus.

2. The quantity of sludge generated from the phosphorus removal process is reduced.

5. The need to add chemicals to correct for pH depression caused by alum treatment is reduced.

4. Biological rather than chemical removal may become more feasible.

5. Reduced chemical use would reduce the concentration of total dissolved solids (TDS) in the effluent. The Oregon Administrative rules for some basins

> state that instream TDS shall not exceed 100 mg/l. Potential exceedence of this standard is a concern in the Tualatin basin, for example, where it is anticipated that chemical removal will cause effluent TDS levels to increase by 100-300 mg/l (HDR Engineering, 1990).

WWTPs practicing phosphorus removal in other states reduced their chemical use, and therefore chemical costs, by an average of about 29-43 percent following the implementation of phosphate detergent bans. Based on the USA estimates below and additional information reported in Appendix G, the estimated savings from a 30 percent reduction in influent phosphorus range from approximately $100,000 to over $200,000 per year per 10 MGD.

The Unified Sewerage Agency of the Tualatin River basin estimates that it will save $389,000 per year in operating costs from a phosphate detergent ban (HDR Engineering, 1990). These savings, based on 1995 flow conditions, will be incurred at 2 plants having a planned 1995 capacity of 35 MGD. The estimate is based on a predicted 25 percent reduction in chemical use ($308,000), and reduced sludge handling ($81,000).

Biological nutrient removal (BNR) is being developed as an alternative to chemical removal. There are BNR systems operating in the eastern U.S. Typically, chemical treatment capabilities are constructed as backup at plants using biological removal.

Wetlands Polishing

The capacity of a wetland to assimilate inputs is finite (see Appendix E for information). As the sediment adsorption of phosphorus approaches saturation, the ability of the wetland to retain additional phosphorus will be reduced. If the load of phosphorus introduced to a wetland is decreased, the ability of the wetland to retain the nutrient will be prolonged.

Wastewater Reuse -- Irrigation

The value of wastewater for irrigation is not affected by decreasing the phosphorus concentration by approximately one-third, the expected reduction from a phosphate detergent ban. This would not influence a farmer's decision to use or not to use the water because the water itself is the primary value to the farmer (Jackson, 1990). (See Appendix E for additional information).

ECONOMIC IMPACTS

A phosphate detergent ban will yield an economic benefit through cost savings to WWTPs using chemical treatment to comply with a phosphorus discharge limit. These cost savings, associated with reduced chemical use and sludge handling, are discussed above and in Appendix G.

In addition, if the need for a treatment plant to add phosphorus removal facilities can be avoided or delayed, there would also be savings from avoided capital construction and operating costs. The potential for this as the result of a detergent phosphate ban has not been reliably predicted or quantified for Oregon.

A phosphate detergent ban could potentially increase the cost of distributing products to Oregon. No cost estimates on the effects of a phosphate detergent ban on the detergent industry are available. Such estimates are difficult to develop and include proprietary market information.

Based on reports from areas currently with phosphate detergent bans, these bans do not appear to increase the costs of laundry detergents to consumers. Consumer Reports (1987) rated the performance of laundry detergents across the country based on laboratory tests in hard water. Of the top 10 performers:

- 3 were liquids (non-phosphate), with an average cost of $0.23 per dose,

- 4 were phosphate containing powders, with an average cost of $0.20 per dose, and

- 3 were non-phosphate powders, with an average cost of $0.17 per dose.

Of all the laundry detergents rated, the average cost per dose for non-phosphate powders was 15.8 cents, for phosphate powders was 17.7 cents, and for liquids (non-phosphate) was 18.4 cents.

The cost to public agencies to implement and enforce a phosphate detergent ban is minimal. The implementation is primarily carried out by the product suppliers and enforcement has not been a problem in areas of existing bans.

See Appendix G for additional information on the economic impacts of a detergent ban.

IMPACTS ON THE FUNCTION AND EFFECTIVENESS OF DETERGENTS

Approximately 37 percent of the United States population now lives in areas where laundry detergent phosphates have been banned. The Task Force has found no reports or survey results that indicate that these citizens are dissatisfied with the effectiveness of the non-phosphate detergents they are now using.

OTHER ENVIRONMENTAL IMPACTS

Reducing concentrations of toxic metals in wastewaters is becoming a priority for WWTP operators. Metals in wastewater can settle into sludge or be discharged to surface waters with the plant effluent (EPA, 1982). A study of Seattle's municipal wastewater indicates that a significant proportion of many heavy metals originate from residential sources (Galvin, 1988).

A second study conducted for Seattle METRO considered whether laundry detergents were potential sources of heavy metals (Dickey, 1990). This study determined that increasing levels of phosphates in detergents correlated with increasing levels of heavy metals, although the relationship was statistically significant for only one metal, arsenic. The study concluded that laundry detergents were a significant source of arsenic to municipal wastewater.

Another study concluded that heavy metals contributed by a range of cleaning products contributed less than 1 percent of the current effluent limit for selected heavy metals other than arsenic (REED Corporation, 1990). The cleaners contributed in total, 0.5 parts per billion of arsenic to sewage effluent at an assumed sewage production rate of 100 gallons per capita per day. The presence of this amount of arsenic in sewage does not impair the ability of municipal discharges to meet water quality standards for arsenic.

SOCIAL IMPACTS

Oregonians are proud of the quality of their environment and publicly declare their commitment to preserving the state's natural resources. If a phosphate detergent ban is perceived to have an environmental benefit, it is likely to have strong public support.

A phosphate detergent ban may promote public awareness of the need for pollution control. It is a pollution prevention measure at the consumer or household level, an approach that should be encouraged. To the extent that consumers are aware of such measures, they will be able to recognize that they are part of a society which made this decision, and that they are contributing to the solution of an environmental problem.

POLLUTION PREVENTION

A phosphate detergent ban is a pollution prevention measure. Environmental foresight has proved prudent in the past, and has taught us to appreciate the value of pollution prevention over the treatment or cleanup of problems after they occur. While a phosphate detergent ban is only one component of a strategy to eliminate algal growth, it reduces human contributions to the wastestream.

In June, 1990, the Environmental Quality Commission adopted a Strategic Plan. One of the plan's nine goals is to:

> *Aggressively identify threats to public health or the environment and take steps to prevent problems which may be created.*

Similarly, one of the three high priorities identified for the DEQ's Water quality Program is to:

> *Implement aggressive source control and problem prevention programs based on the priorities established that explore and encourage use of environmentally sound alternatives for disposal of treated wastewater which do not adversely affect air, land, stream and groundwater quality.*

A ban on phosphates in detergents is consistent with these goals.

V. PHOSPHORUS CONTROL POLICY AND LEGISLATION

OREGON PHOSPHATE DETERGENT LAWS

In June of 1990, the Metropolitan Service District of Oregon passed a regional ban on detergent phosphates which will become effective on February 1, 1991 and will sunset on December 31, 1994. The METRO ban is similar to existing bans in other locations. It prohibits the sale of any cleaning agent with more than 0.5 percent phosphorus by weight, with listed exceptions. Automatic dishwashing detergents shall not exceed 8.7 percent phosphorus by weight.

The City of Ashland is considering a similar ordinance. Current Oregon law (ORS 468.760) requires the phosphorus content of synthetic cleansers to be labeled.

A statewide ban on the sale of phosphate detergents will be more manageable than local or regional bans. It would minimize the possibility of consumers unintentionally bringing phosphate detergents into areas with local bans.

AN OVERVIEW OF PHOSPHATE DETERGENT LAWS

A chart summarizing phosphate detergent ban legislation in other states and regions is provided in Appendix G. Many of the bans include similar provisions. Most prohibit the sale or distribution of household laundry detergents containing phosphates, although 7 areas also prohibit the use of these products. Many of the regulations prohibit phosphates in cleaning products and list exceptions. Most allow up to 0.5 percent incidental phosphorus in laundry detergents. All the laws allow dishwashing detergents to contain phosphorus, typically limiting them to 8.7 percent. Some bans include fines for violations.

Typical products exempted from the phosphate bans include detergents used to clean dairy and food processing equipment, detergents used in hospitals and health care facilities, and industrial cleaning products. Some of the bans exempt all detergents used for cleaning hard surfaces.

OTHER PHOSPHORUS CONTROL POLICIES AND REGULATION

There are a multitude of federal, state and local regulations aimed at controlling nutrient inputs to surface waters for the purpose of limiting algae and weed growth. These policies, some of which are described in Appendix F, range from point source discharge limits to technologies and management practices designed to reduce nonpoint sources of nutrients.

REFERENCES

Consumer Reports, 1987. The Great Soap Opera. Consumer Reports, July, 1987, 413-422.

Cooper Consultants, Inc., 1985. Limnology and Nutrient Dynamics of Clear Lake, Oregon. Portland, Oregon.

Dickey, P., 1990. A Database of Safer Substitutes for Hazardous Household Products. METRO, Seattle, Washington.

Department of Environmental Quality (DEQ), 1990. Draft Water Quality Status Assessment Report (305b Report). Portland, Oregon.

Environmental Protection Agency (EPA), 1982. Fate of Priority Pollutants in Publicly Owned Treatment Works, Final Report. U.S. EPA 440/1-82-303. Washington D.C.

EPA, 1986. Quality Criteria for Water. Office of Water Regulations and Standards, Washington D.C.

Galvin, ~~D~~., 1988. "Household Hazardous Wastes in Municipal Wastewaters and Storm Drains," IN Proceedings of the 3rd EPA National Conference on Household Hazardous Waste Management. Boston, MA.

HDR Engineering, Inc., 1990. Letter from Bruce Willey, HDR Engineering, to Jim Morgan, METRO, May 11, 1990. Portland, Oregon.

Hines, W.G. et al, 1977. Algal Conditions and the Potential for Future Algal Problems in the Willamette River, Oregon. U.S. Geological Survey Circular 715-G. Arlington, Virginia.

Jackson, 1990. Letter from John Jackson, Unified Sewerage Agency of Washington County, to Eleanor Phinney, October 18, 1990. Portland, Oregon.

Kramer, Chin and Mayo, Inc. (KCM), 1983. Devils Lake Diagnostic and Feasibility Study. Portland, Oregon.

Morgan, J., 1990. Findings of the Region-wide Phosphate Detergent Ban Study. Staff report to the Council of the Metropolitan Service District of Oregon, May 22, 1990. Portland, Oregon.

Organization for Economic Cooperation and Development, 1971. Scientific Fundamentals of the Eutrophication of Lakes and Flowing Waters, with Particular Reference to Nitrogen and Phosphorus as Factors in Eutrophication. Paris, France.

REED Corporation, 1990. The Contribution of Heavy Metals to Wastewaters from Household Cleaning Products. Prepared for the Soap and Detergent Association, New York, New York.

Ryding, S.O. and W. Rast (eds), 1989. The Control of Eutrophication of Lakes and Reservoirs. Man and the Biosphere Series, Volume 1. UNESCO and the Parthenon Publishing Group, Park Ridge, New Jersey.

Scientific Resources, Inc., 1990. Garrison Lake and watershed Assessment 1988-1989, Volume I: Diagnostic and Restoration Analysis. Lake Oswego, Oregon.

Sweet, J.W., 1985. An Analysis of Phytoplankton of Oregon Lakes. Report to U.S. EPA. Seattle, Washington.

Tualatin Basin Consultants, 1990. Draft Wastewater Facilities Plan, Volume 1, Technical Report. Prepared for Unified Sewerage Agency of Washington County. Hillsboro, Oregon.

APPENDIX A

GLOSSARY OF TERMS

activated sludge: biologically active solids produced in wastewater treatment systems, which grow through the consumption of organic wastes and nutrients present in the wastewater.

algal assay: studies in which algae are exposed to a substance and the response of the algae is monitored over time; the studies are used to identify substances that affect algal growth.

alum: a common name for commercial-grade aluminum sulfate, a material used to remove impurities from drinking water and wastewater.

biological phosphorus removal: use of selected bacteria to incorporate high concentrations of phosphorus during wastewater treatment, often such processes can be operated to remove other nutrients besides phosphorus, in which case they are generically referred to as "biological nutrient removal."

chemical phosphorus removal: use of chemicals to precipitate phosphate out of wastewater during treatment.

chlorophyll-a: a pigment present in all green plants and algae; measurements of this pigment are used as an indicator of plant and algal biomass.

combined sewer overflow: in municipal wastewater systems that collect both sewage and storm runoff, these are discharges of combined wastewater and storm runoff that occur prior to treatment as a result of storm events which cause flows to exceed the capacity of the treatment plant.

dissolved oxygen: oxygen dissolved in water.

effluent: treated wastewater discharged <u>out</u> of a wastewater treatment plant.

eutrophication: the process occurring in bodies of water particularly lakes, characterized by nutrient richness, luxurious aquatic plant growth, and low oxygen levels.

heavy metals:	metals with high atomic weight, such as lead, cadmium, or arsenic; these are often toxic at higher concentrations.
influent:	wastewater flowing <u>into</u> a wastewater treatment plant.
irrigation return flow:	irrigation water that runs off irrigated fields and is collected in channels for discharge.
loading:	the quantity of material carried into a body of water or a treatment plant. Expressed as mass per unit time (e.g. pounds per day), rather than concentration (e.g. milligrams per liter).
nitrogen-fixing algae:	algae that can take nitrogen gas from the atmosphere and change it into nitrogen-containing compounds necessary for growth.
nutrient:	any substance assimilated by an organism which promotes growth and replacement of cellular constituents.
nonpoint source:	diffuse sources of pollution, or a large number of small dispersed sources, carried to surface waters via overland or subsurface flow.
orthophosphate:	a common form of phosphate that is considered more biologically-available.
periphyton:	algae attached to streambeds and rocks in fresh waters.
pH:	a term used to describe the hydrogen-ion activity of a system; pH 0 to 7 is acid, pH of 7 is neutral, pH 7 to 14 is alkaline.
phosphate:	a generic term for any compound containing the phosphorus and oxygen group (PO_4^{-3}); in nature, phosphorus always exists as a form of phosphate.
phosphorus:	a naturally occurring element essential to all plant and animal life that can, when in excess in surface waters, lead to excessive plant growth; phosphorus usually infers 'total phosphorus' which includes all of its forms.
phytoplankton:	algae floating on the surface or in the water column.

point source:	a source of pollution where a single discharge point can be identified, such as municipal or industrial wastewater discharge pipe.
precipitate:	the solid material formed in a water or wastewater treatment process which can then be separated from the water.
sludge:	the accumulated solids separated from wastewater during treatment.
standard:	see "water quality standard"
TMDL:	a Total Maximum Daily Load is the maximum load of a particular substance allowed to be discharged into a receiving body of water; these are set by environmental management agencies for a water body designated as "water quality limited".
total dissolved solids (TDS):	the total amount of solids in water or wastewater that is in solution or is non-filterable.
water quality standard:	provisions of State law which consist of designated uses for the waters of the State and water quality criteria necessary to protect the uses. Water quality standards are to protect the public health or welfare, enhance the quality of water and serve the purposes of the Federal Clean Water Act (40 CFR 130.2-3).

APPENDIX B

TASK FORCE MEMBERS LIST

Mr. Jim Buckley
Clackamas County Public Health, Oregon City
representing the Conference of Local Health Officials

Mr. Dave Degenhardt
Oregon Dept. of Forestry, Salem

Mr. Tom Donaca
Associated Oregon Industries, Portland/Salem

Mr. Dell Isham
Devils Lake Water Improvement District, Lincoln City

Mr. Francis Kessler
Willow Lake Treatment Plant, Salem
representing the Association of Oregon Sewerage Agencies

Ms. Sue Knight
representing the Oregon Environmental Council, Portland

Mr. Jim Morgan
Metropolitan Service District, Portland

Ms. Eleanor Phinney
River Watch, West Linn

Mr. Chris Reive
Bogle & Gates
representing Oregonians for Food & Shelter, Portland

Mr. Richard Sedlak
Soap & Detergent Association, New York, New York

Dr. Benno Warkentin, Chair
Water Resources Research Institute, Oregon State University, Corvallis

ALTERNATES:

Paul Cosgrove
Lindsay, Hart, Neil & Weigler, Portland
representing the Soap & Detergent Association

Mr. Jim Whitty
Associated Oregon Industries, Portland/Salem

A-Engrossed
Senate Bill 1079

Ordered by the Senate May 9
Including Senate Amendments dated May 9

Sponsored by Senators COHEN, ROBERTS, SHOEMAKER, Representatives BAUMAN, CARTER, STEIN

SUMMARY

The following summary is not prepared by the sponsors of the measure and is not a part of the body thereof subject to consideration by the Legislative Assembly. It is an editor's brief statement of the essential features of the measure.

[Prohibits sale of laundry detergent containing phosphate. Prescribes exemptions. Defines "cleaning agent".]
[Prescribes effective date.]
Requires Department of Environmental Quality to establish task force on phosphorus and other nutrients in state waters. Prescribes membership and duties. Requires department to report findings to Sixty-sixth Legislative Assembly. Requires Legislative Assembly to determine whether to ban phosphates in detergents.

A BILL FOR AN ACT

Relating to phosphate.

Be It Enacted by the People of the State of Oregon:

SECTION 1. (1) The Department of Environmental Quality shall establish a task force on phosphorus and other nutrients in the waters of the state. The task force shall include representatives of municipal waste water treatment agencies, nonmunicipal point source dischargers, agriculture, forestry, manufacturers of consumer cleansing products and citizens. The task force shall assist the Department of Environmental Quality in identifying the sources of phosphorus and other nutrients contributing to the growth of algae in the waters of the state that the Department of Environmental Quality identifies in which algae growth is adversely affecting water quality. When appropriate, the task force shall assist the Department of Environmental Quality in identifying:

(a) Nutrient sources in waste ater treatment plant influent;

(b) The relative contribution of these nutrient sources on waste water treatment plant effluent; and

(c) The potential impact of regulating or eliminating phosphorus from detergents and other sources on potential nutrient control strategies and water quality.

(2) The Department of Environmental Quality shall report to the Sixty-sixth Legislative Assembly regarding the findings of the task force established under subsection (1) of this section. Based on the findings of the report, the Legislative Assembly shall determine whether it is appropriate to eliminate specific sources of phosphorus, including but not limited to, imposing a ban on phosphates in detergents.

NOTE: Matter in **bold face** in an amended section is new; matter *[italic and bracketed]* is existing law to be omitted.

APPENDIX C

STUDIES OF THE RELATION OF ALGAL GROWTH TO NUTRIENTS

Laboratory studies have shown the relationship between phosphorus concentration and algal growth when other factors are not limiting. These controlled experiments generally show that when phosphorus concentrations are below 0.07 mg/l, algal growth is very low. Between 0.07 and 0.15 mg/l, there is a linear relationship between the two factors; as the phosphorus concentration increases, so does algal mass. Above 0.15 mg/l, further increases in phosphorus produce no further increase in algal mass. Growth is then limited by other factors.

Field studies attempting to quantify the relationship between phosphorus and algal growth have not been consistent in their results, probably due to the large number of variables present in the natural environment.

Algae use nutrients in approximate atomic ratios of 106 C (carbon) to 16 N (nitrogen) to 1 P (phosphorus). This reduces to 7.2 N:P on a concentration basis. Ratios and absolute concentrations both need to be evaluated to determine potential limiting nutrients. The ratio of N:P measured in water should indicate whether N or P would limit growth. The concentrations indicate whether both or neither one are actually limiting growth. If the N:P ratio is less than 7:1, N is potentially limiting, if it is greater than 7:1, P is potentially limiting. Blue-green algae (cyanobacter), that fix their own nitrogen from the atmosphere, are rare where N:P ratios exceed 30:1. They grow competitively at low nitrogen concentrations.

The N and P fractions that should be measured are those that are biologically available, generally considered to be the soluble fractions. These are dissolved phosphate, and the ammonia, nitrate and nitrite forms of nitrogen. Phosphate is generally measured as "soluble" and "particulate" fractions, separated by passing through 0.05 um filter. It is assumed that soluble phosphate is biologically available, and that the particulate fraction replenishes the soluble fraction when the later is used. Phosphate concentrations are usually much larger in sediments than in water because of the strong adsorption of phosphate to clays.

The proportion of total phosphorus that is in a biologically available form is: 70 to 90 percent in wastewater effluent, 3-10 percent in eroded sediments, 10-90 percent in runoff as a whole, and 25-90 percent in atmospheric phosphorus. Sewage effluents have N:P ratios of about 5:1, while nonpoint sources range from 15:1 to 30:1.

References:

Lewis, W.M. et al. (eds), 1984. Eutrophication and Land Use. Springer-Verlag, New York.

This Dillon Lake symposium contains some more recent measurements.

Likens, G.E. (ed), 1972. Nutrients and Eutrophication: The Limiting Nutrient Controversy. Allen Press, Lawrence, Kansas.

This contains a paper by Duthrie on detergents and several papers relating algal growth and eutrophication to phosphorus concentrations.

Middlebrooks, E.J. et al. (eds), 1984. Modeling the Eutrophication Process. Ann Arbor Science Publ., Ann Arbor, Michigan.

This contains some background material on phosphorus as well as information on modeling.

Ryding, S.O. and W. Rast (eds), 1989. The Control of Eutrophication of Lakes and Reservoirs. Man and the Biosphere Series, Volume 1, Parthenon Publishing Group, UNESCO, 314 pages.

This book takes a management approach and interprets the available information in terms of management alternatives.

Sandgren, C.D. (ed), 1984. Growth and Reproductive Strategies of Freshwater Photoplankton. Cambridge Univ. Press, New York.

This has more detail on bluegreen algae growth and a set of good references.

Schindler, D.W., 1977. Evolution of Phosphorus Limitation in Lakes. Science 195, 260-267.

This is a paper on which a lot of the thinking about phosphorus and algal growth is based. It shows the relationship of phosphate concentration to chlorophyll-a for a number of lakes and establishes the limit of approximately 8 milligrams per cubic meter.

APPENDIX D

WATER QUALITY DATA FOR OREGON - NUTRIENTS AND ALGAL GROWTH

This Appendix provides water quality data for Oregon supplemental to that provided in Section II of this report.

Statewide Data

Table D-1 lists the priority waterbodies to receive TMDLs in Oregon, the identified or potential TMDL parameters, and additional information. Phosphorus is a parameter identified for 8 of the 10 rivers and both lakes included on this list. Five phosphorus TMDLs (3 rivers and 2 lakes) have been established to date.

Figures D-1 & D-2 are maps from the 1988 Oregon Statewide Assessment of Nonpoint Sources of Water Pollution (DEQ, 1988). Figure D-1 shows the stream segments and lakes in the State identified as having moderate or severe nutrient problems. Phosphorus was the parameter used for the nutrient assessment. Figure D-2 shows the stream segments and lakes identified as having moderate or severe plant growth problems. Plant growth problems were identified based on either chlorophyll-a measurements or observations completed by DEQ staff or others.

Of the total stream miles in the State, 45 percent either had no water quality problem or had no information available. The remaining 55 percent were found to have some type of water quality problem, 24 percent based on data and 31 percent based on observation. Due to the fact that not all the stream miles were evaluated, and due to the limitations of chlorophyll-a as a measure of algal growth (discussed in the Section II of the report), Figure D-2 does not necessarily show all waterbodies experiencing excessive algal growth.

Water Quality Trends

As part of the 1990 statewide water quality assessment, the Department performed trend analyses on 62 stream sites (DEQ, 1990, Appendix I). To be selected for analysis, a stream site had to have a minimum of 5 years of data with continuity.

Statistically significant phosphorus and chlorophyll-a trends were found at some sites, but no statewide conclusion can be made due to the limited number of sites and the varied results. Figure D-3 is an example, the Deschutes River, where chlorophyll-a levels have increased significantly over the last ten years.

Longitudinal Data

DEQ has longitudinal data available for the Willamette River and some of the water quality limited rivers for which the Department has conducted water quality studies. Longitudinal data are data for a number of sites along the river by river mile.

Figure D-4 shows the total phosphorus concentration by river mile for the Willamette River as a "box plot." Each box represents the data collected at a particular site and the width of the box represents the number of samples collected at that site. The dotted line is the median data point, half of the data points fell above and half below this value. The height of the box represents the range of the middle 50 percent of the samples, and the lines extending from the boxes represent the range of all the data points.

As can be seen in Figure D-4, the total phosphorus concentration in the Willamette River increases downstream and exceeds the 0.10 mg/l criteria frequently below approximately river mile 50. Plots for additional rivers are shown in Figures D-5 to D-7.

Lake Data

Table 3, shown in Section II of the report, lists the Oregon lakes identified in DEQ's 1990 Water Quality Assessment as having algae, weed or related problems and septic drainage as a suspected source.

Diagnostic studies have been completed on 5 Oregon lakes as part of EPA's Clean Lakes Program: Garrison Lake (SRI, 1990), Blue Lake (Beak Consultants, 1983), Devils Lake (KCM, 1983), Klamath Lake (Klamath Consulting Service, 1983) and Lake Oswego (SRI, 1986). The studies show that all the lakes have algal growth problems and phosphorus concentrations exceeding the criteria level for lakes (0.025 mg/l). Nitrogen-fixing blue-green algae species were abundant or dominant in the lakes at least part of the year. Lake restoration plans for all these lakes recommended phosphorus reduction as the means by which to control the algal growth and eutrophic conditions.

Clear Lake, near the Oregon Coast, is not a eutrophic lake, but was studied in order to assess the potential impacts of future development on the lake. As a result, a TMDL was recently established for the amount of phosphorus entering Clear Lake.

The Department has also established a phosphorus TMDL for Garrison Lake, located on the Oregon coast. Garrison Lake is a heavily enriched lake with excessive phytoplankton populations (SRI, 1990). Municipal wastewater effluent and septic system drainage will be controlled in order to reduce the phosphorus loading to the lake.

Figure D-8 is a graph from the study by SRI (1990) showing how phosphorus, depth and residence time are related to trophic status for a number of Pacific Northwest lakes. Lakes above the permissible and excessive lines on the graph tend to be highly enriched and have algal and plant growth problems (eutrophic).

In 1974-75, the U.S. Environmental Protection Agency surveyed 8 Oregon lakes and reservoirs: Brownlee Reservoir, Diamond Lake, Hells Canyon Reservoir, Hills Creek Reservoir, Lake Owyhee, Oxbow Reservoir, Suttle Lake and Waldo Lake (EPA, 1978). Nitrogen was found most often to be the limiting nutrient based on lake data collected during the spring, summer and fall. Four of the lakes were phosphorus limited during one season. Algal assays were performed for three lakes. The assays indicated that nitrogen was the limiting nutrient in two lakes and phosphorus in the third.

References:

Beak Consultants Inc., 1983. Blue Lake Clean Lakes Program Phase I Diagnostic/Feasibility Study. Portland, Oregon.

Department of Environmental Quality (DEQ), 1988. 1988 Oregon Statewide Assessment of Nonpoint Sources of Water Pollution. Portland, Oregon.

DEQ, 1990. Draft Water Quality Status Assessment Report (305b Report). Portland, Oregon.

Klamath Consulting Service, Inc., 1983. The Upper Klamath Lake EPA 314 Clean Lakes Program 1981-1983.

Kramer, Chin and Mayo, Inc. (KCM), 1983. Devils Lake Diagnostic and Feasibility Study. Portland, Oregon.

Scientific Resources, Inc. (SRI), 1986. Oswego Lake Improvement Project: Preliminary Analysis. Portland, Oregon.

SRI, 1990. Garrison Lake and Watershed Assessment 1988-1989, Volume I: Diagnostic and Restoration Analysis. Lake Oswego, Oregon.

U.S. Environmental Protection Agency (EPA), 1978. National Eutrophication Survey, Working Papers 287-834. Washington, D.C.

Table D-1. Oregon TMDL Parameters and Status, 1990

RIVER/LAKE	INTENSIVE WQ STUDY	TMDL STATUS	PARAMETERS OF CONCERN	TMDL PARAMETERS	SOURCES
Tualatin	Yes	Final	DO, pH, algae	Phosphate Ammonia Nitrogen	STPs nonpoint
Yamhill	Yes	Final	pH, algae fecal bacteria turbidity	Phosphate	STPs nonpoint
Bear Creek	Yes	Final	DO, pH, algae fecal bacteria ammonia toxicity	Ammonia Nitrogen BOD Phosphate	STP log ponds nonpoint
Umatilla	Yes	Preliminary	pH, algae fecal bacteria	Phosphate	STPs nonpoint
Pudding	In Progress	Preliminary	DO fecal bacteria	BOD	STP, Agripac, nonpoint
S. Umpqua	No	Preliminary	DO, algae fecal bacteria	Phosphate Ammonia Nitrogen	STP nonpoint
Grande Ronde	No	Preliminary	algae fecal bacteria	Phosphate	STPs, nonpoint, log ponds
Klamath	In Progress	Preliminary	DO pH, algae	BOD Ammonia Nitrogen	STP, Weyerhauser, Klamath Lake, nonpoint
Columbia Slough	In Progress	Preliminary	pH, algae, bacteria, toxins	Bacteria Ortho-Phosphorus Toxins [a]	nonpoint, landfill, CSOs, point sources
Coquille	In Progress	Preliminary	DO fecal bacteria algae	BOD	STPs log ponds nonpoint
Coast Fork Willamette	Yes	Preliminary	DO, pH, algae, bacteria	BOD Phosphorus	STPs, nonpoint misc. point sources

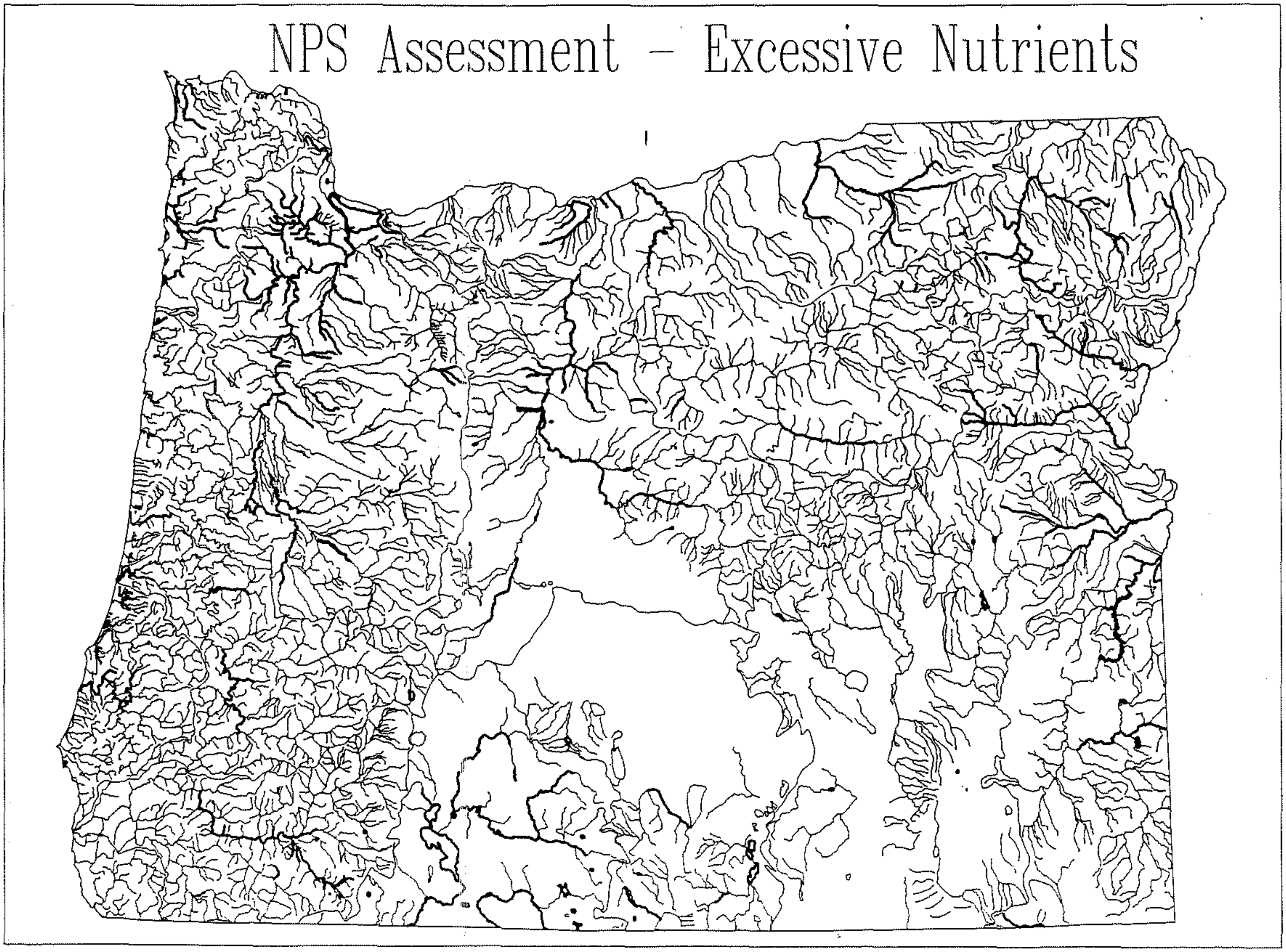
(continued next page)

Table D-1. Oregon TMDL Parameters and Status, 1990

RIVER/LAKE	INTENSIVE WQ STUDY	TMDL STATUS	PARAMETERS OF CONCERN	TMDL PARAMETERS	SOURCES
Rickreall Cr.	In Progress	Preliminary	DO	BOD	STPs
Columbia River	No	Preliminary	TCDD	TCDD	pulp & paper mills, STPs, nonpoint
Clear Lake	Yes	Final	algae	Phosphorus	septic systems
Garrison Lake	Yes	Final	pH, algae macrophytes	Phosphate	STP nonpoint

[a] Preliminary TMDLs are proposed for toxins: PCBs, lead, zinc, mercury, arsenic, dioxin, copper, cadmium and chromium.

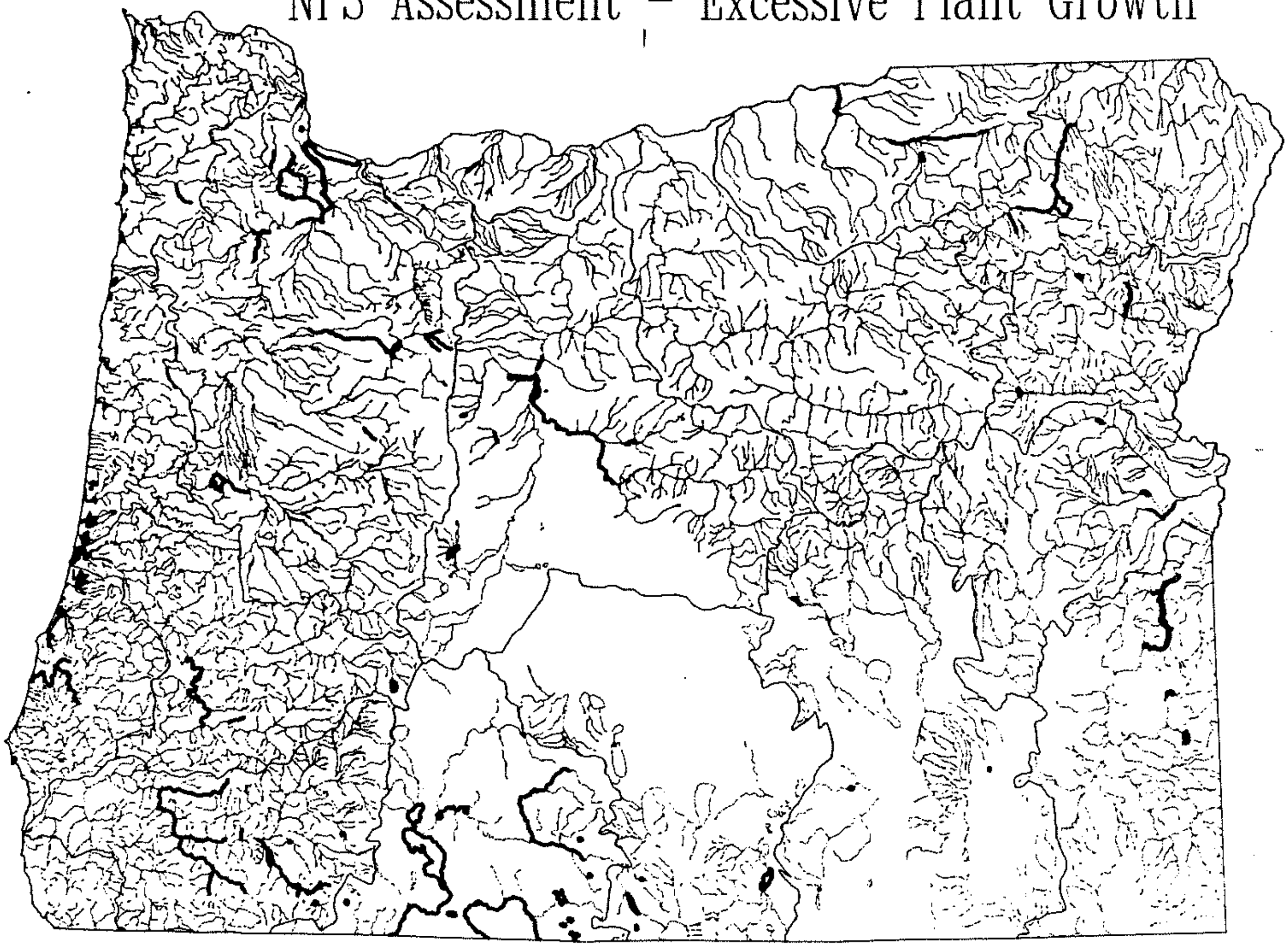
FIGURE D-1



SOURCE: 1988 Oregon Statewide Assessment of Nonpoint Sources of Water Pollution - Department of Environmental Quality - August 1988

FIGURE D-2

NPS Assessment - Excessive Plant Growth



SOURCE: 1988 Oregon Statewide Assessment of Nonpoint Sources of Water Pollution - Department of Environmental Quality - August 1988

FIGURE D-3

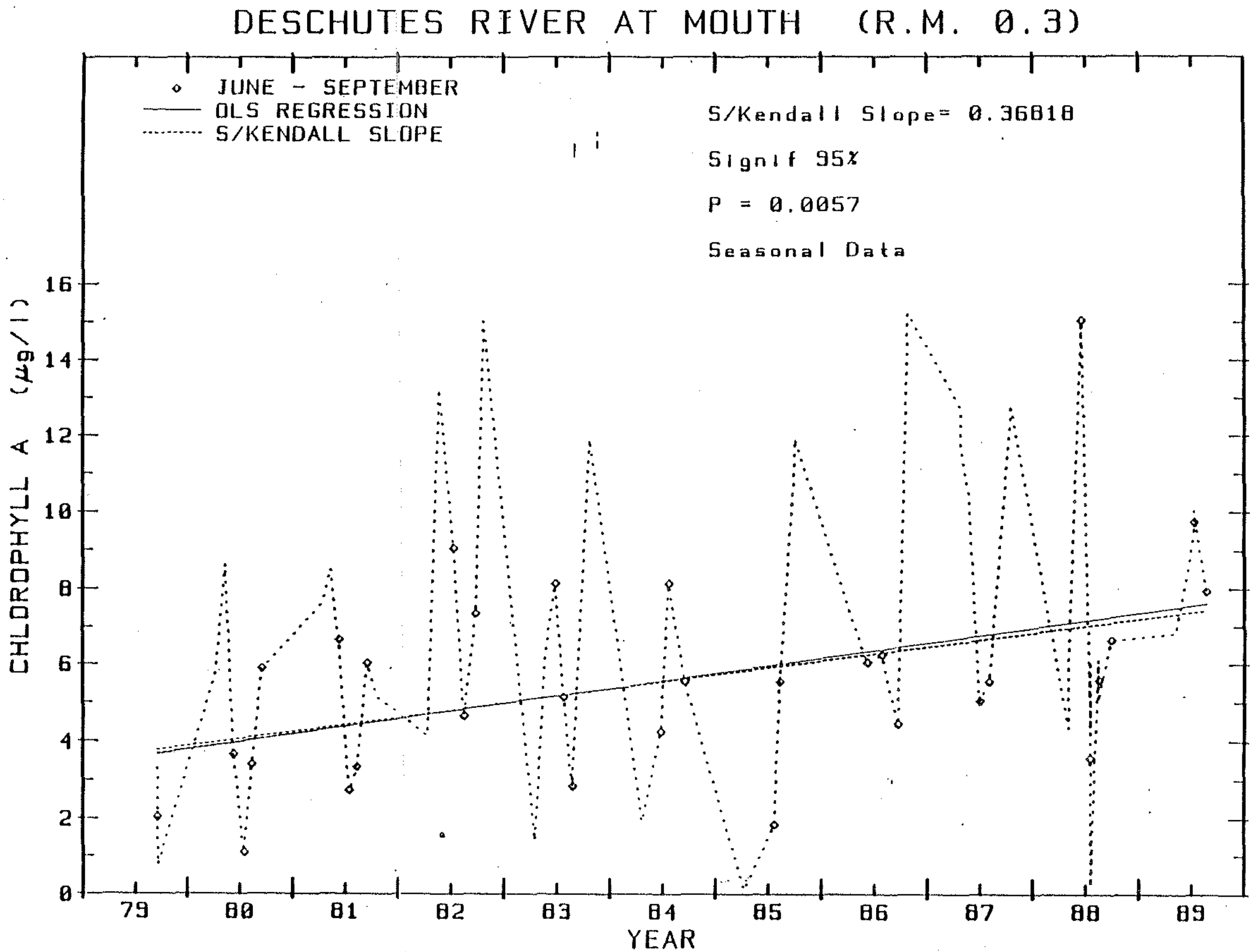
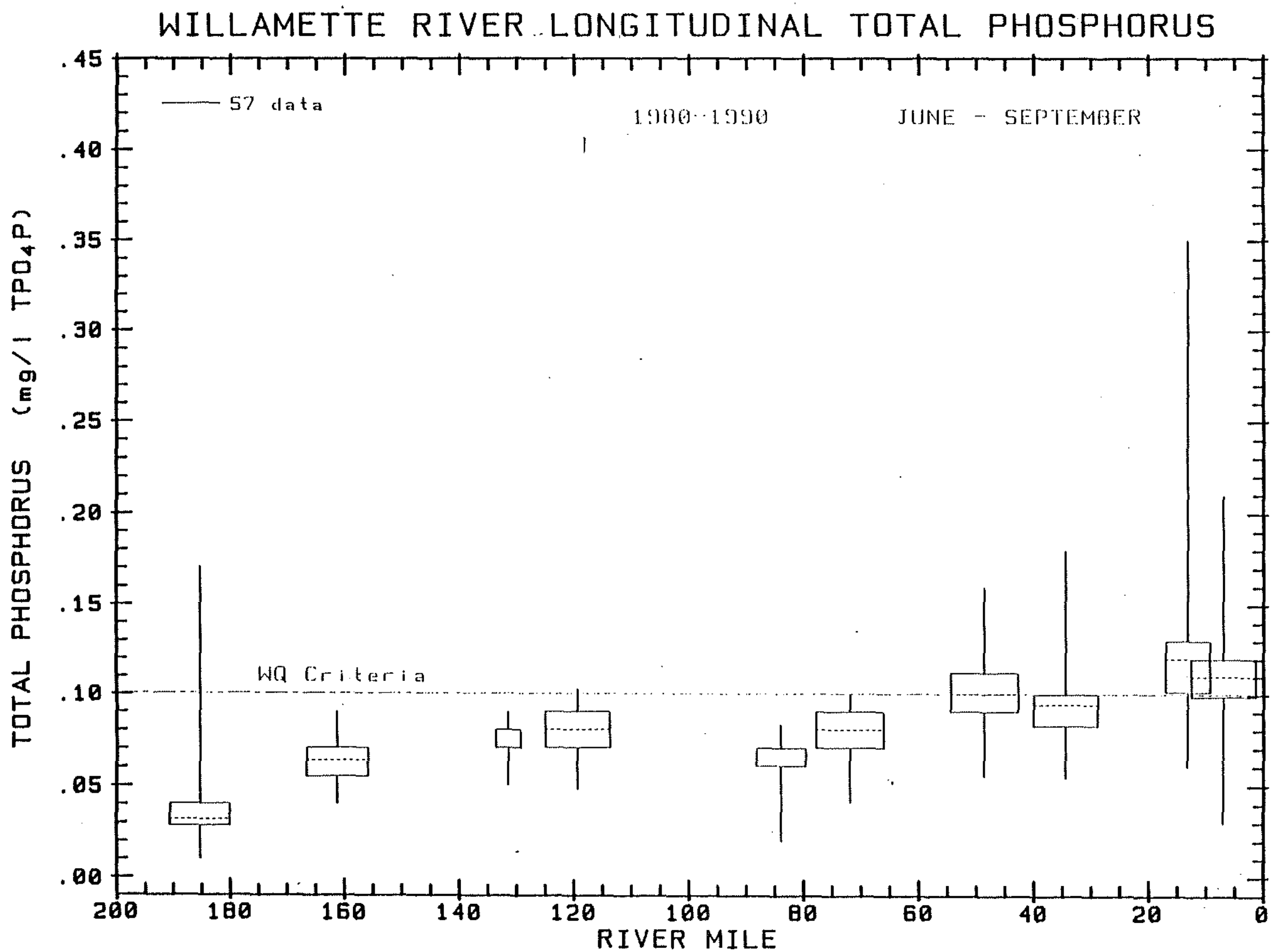

DESCHUTES RIVER AT MOUTH (R.M. 0.3)
JUNE - SEPTEMBER
OLS REGRESSION
S/KENDALL SLOPE
S/Kendall Slope= 0.36818
Signif 95%
P = 0.0057
Seasonal Data
CHLOROPHYLL A (μg/l)
0
2
4
6
8
10
12
14
16
79
80
81
82
83
84
85
86
87
88
89
YEAR

FIGURE D-4



WILLAMETTE RIVER LONGITUDINAL TOTAL PHOSPHORUS
57 data
1980-1990
JUNE - SEPTEMBER
WQ Criteria
TOTAL PHOSPHORUS (mg/l TPO4P)
.45
.40
.35
.30
.25
.20
.15
.10
.05
.00
200
180
160
140
120
100
80
60
40
20
0
RIVER MILE

FIGURE D-5

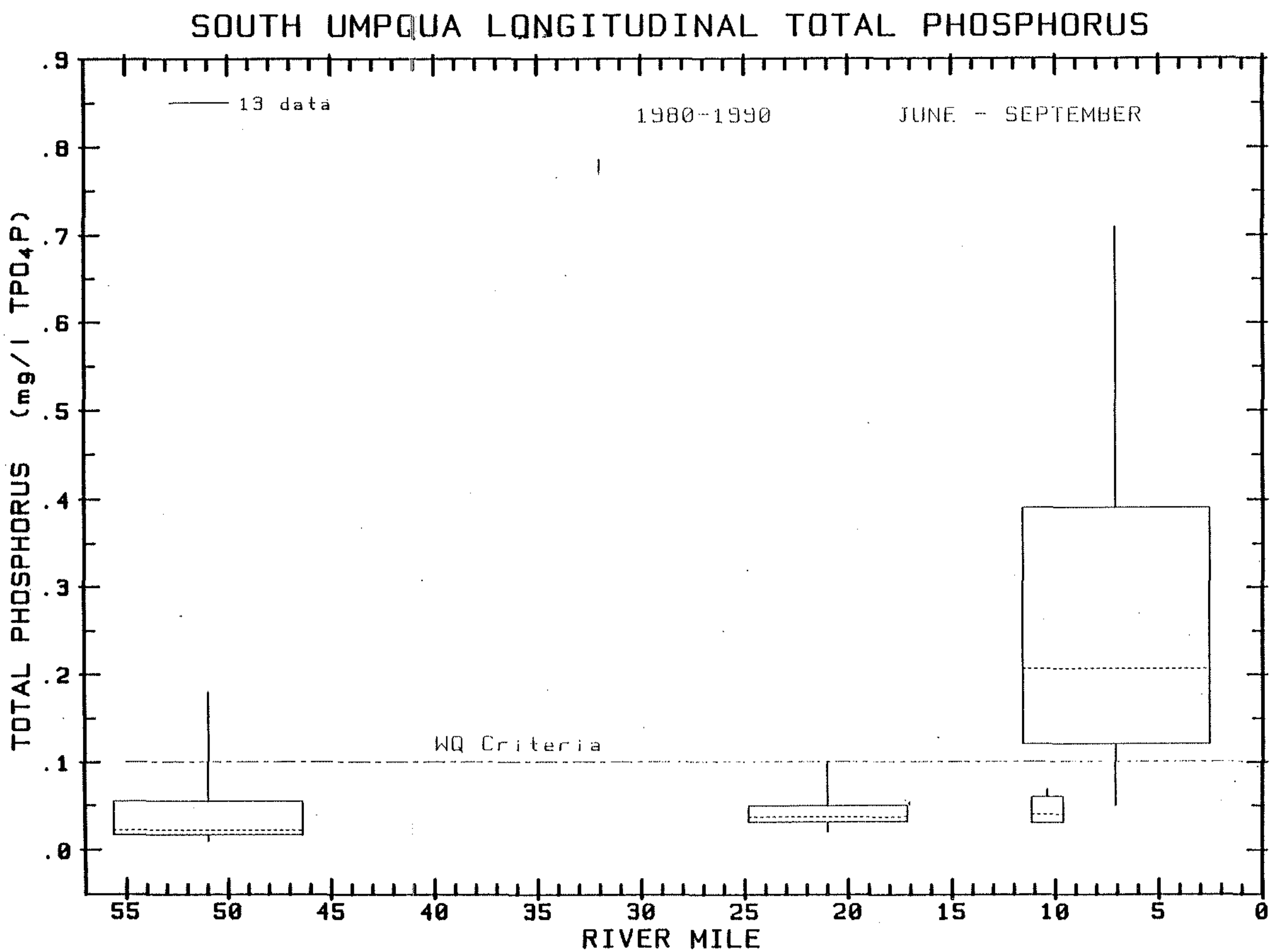
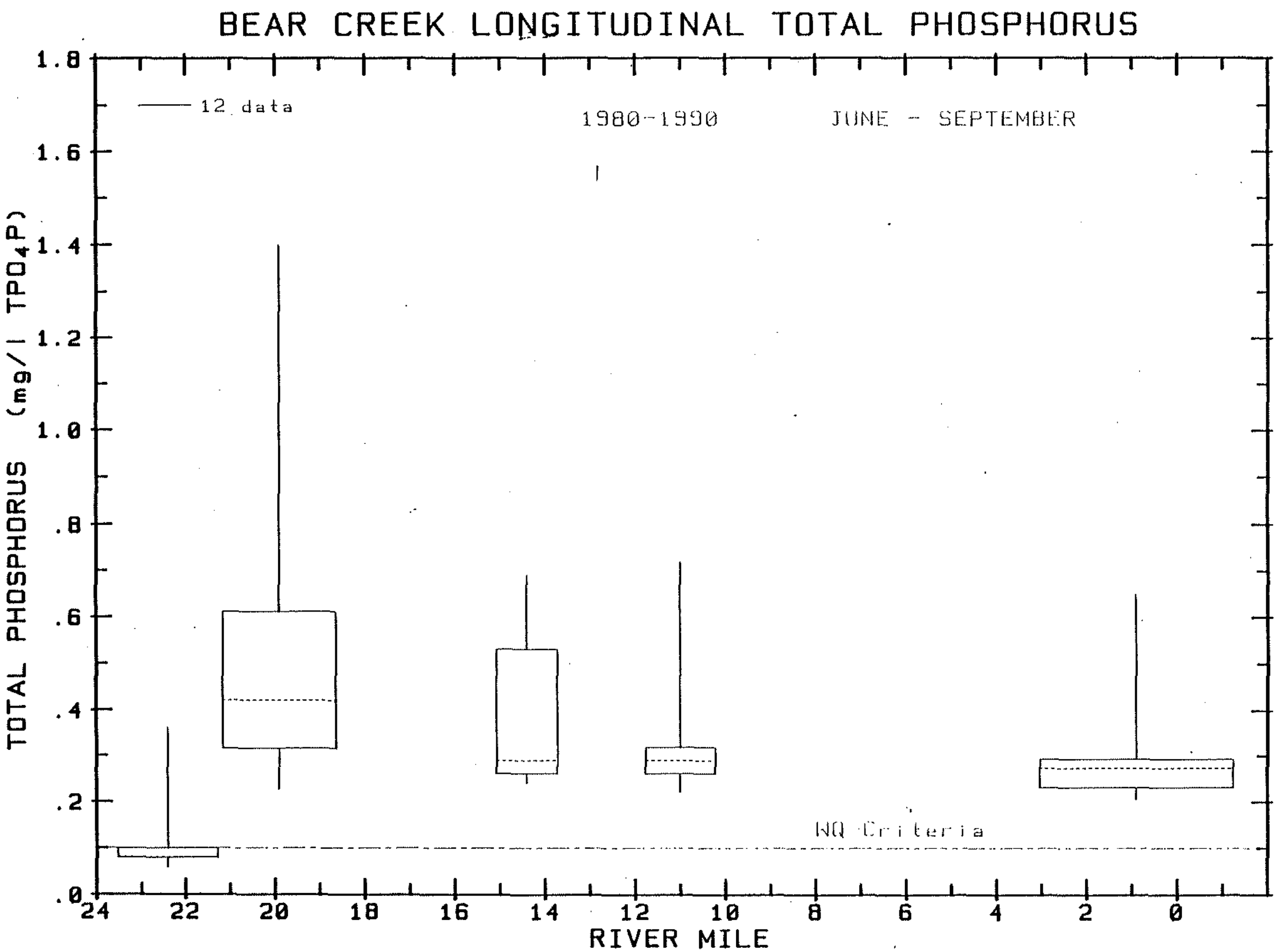

SOUTH UMPQUA LONGITUDINAL TOTAL PHOSPHORUS
13 data
1980-1990
JUNE - SEPTEMBER
WQ Criteria
TOTAL PHOSPHORUS (mg/l TPO4P)
.9
.8
.7
.6
.5
.4
.3
.2
.1
.0
55
50
45
40
35
30
25
20
15
10
5
0
RIVER MILE

FIGURE D-6



BEAR CREEK LONGITUDINAL TOTAL PHOSPHORUS
12 data
1980-1990
JUNE - SEPTEMBER
WQ Criteria
TOTAL PHOSPHORUS (mg/l TPO_4P)
RIVER MILE
1.8
1.6
1.4
1.2
1.0
.8
.6
.4
.2
.0
24
22
20
18
16
14
12
10
8
6
4
2
0

FIGURE D-7

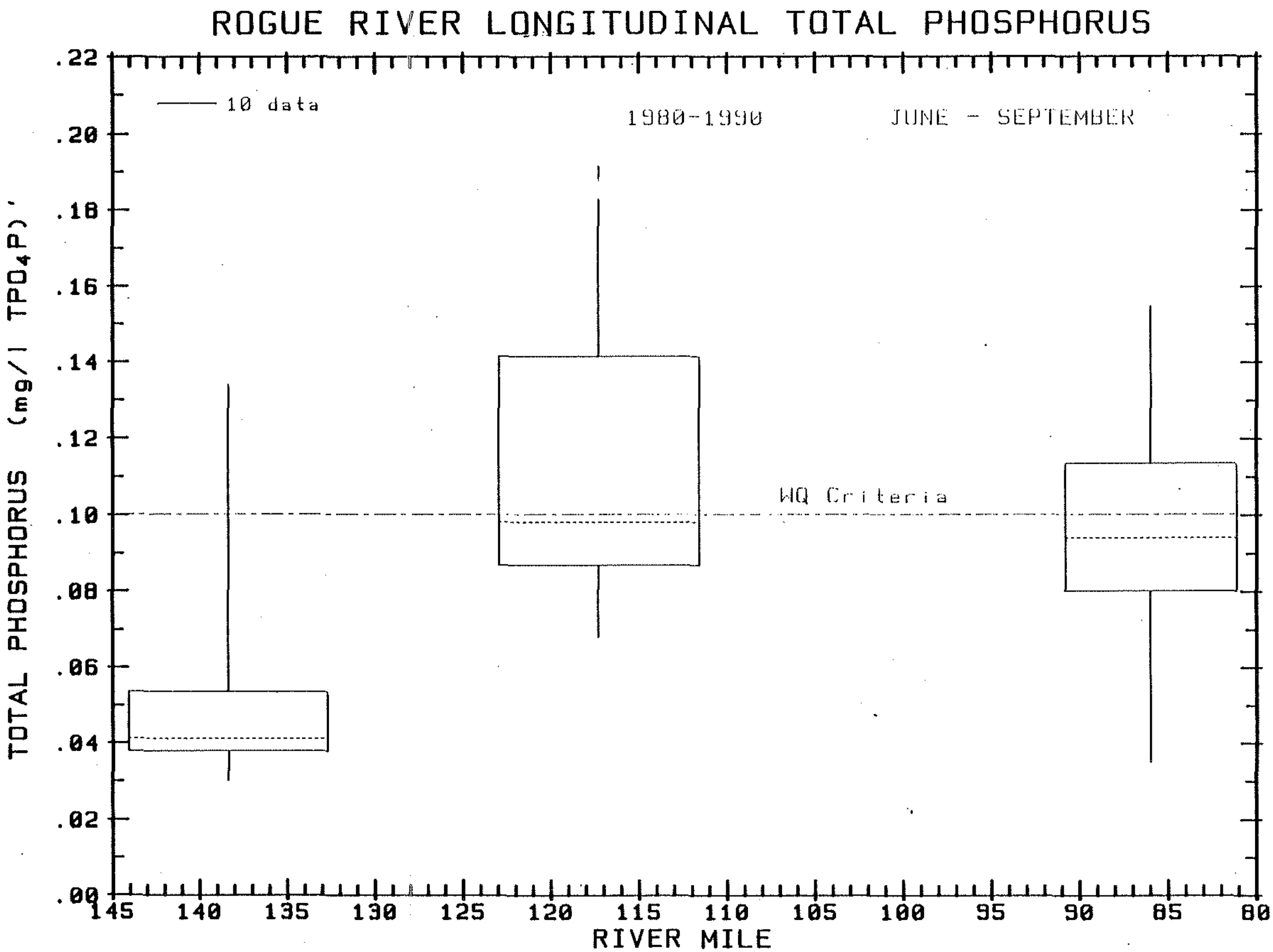
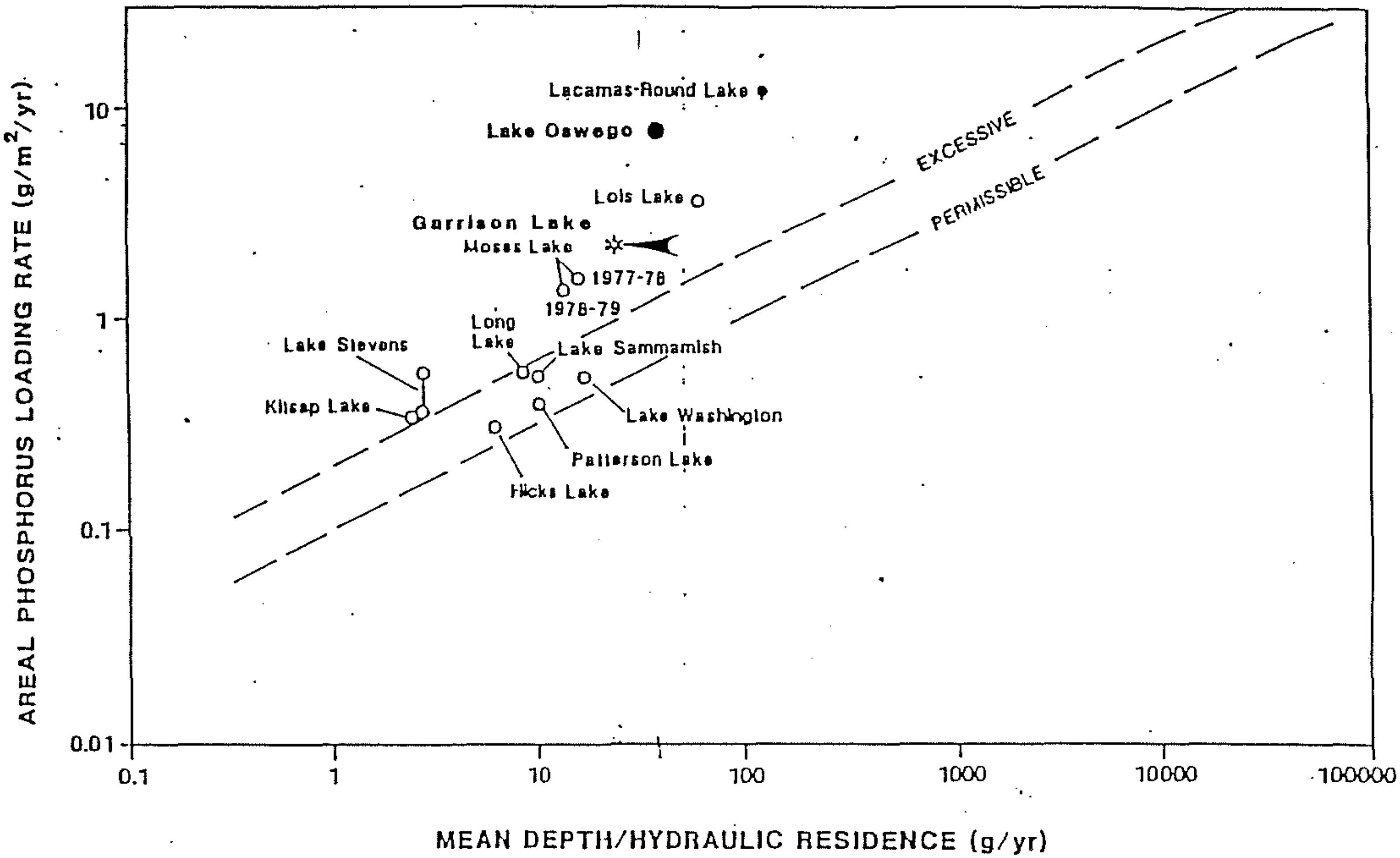

ROGUE RIVER LONGITUDINAL TOTAL PHOSPHORUS
10 data
1980-1990
JUNE - SEPTEMBER
WQ Criteria
TOTAL PHOSPHORUS (mg/l TPO4P)
.22
.20
.18
.16
.14
.12
.10
.08
.06
.04
.02
.00
145
140
135
130
125
120
115
110
105
100
95
90
85
80
RIVER MILE

FIGURE D-8

Vollenweider graph (1976) showing the relative position of Garrison Lake in relation to other Northwestern lakes with respect to annual total phosphorus loading.



SOURCE: Garrison Lake and Watershed Assessment 1988-89.

Scientific Resources, Inc., Portland, Oregon, 1990.

APPENDIX E

NUTRIENT TREATMENT AND CONTROL PRACTICES

Phosphorus Control Alternatives for Wastewater Treatment Plants

There are currently two general methods of process control employed for the removal of phosphorus at wastewater treatment plants. These are chemical/physical and biological nutrient removal. The following are the common chemical removal systems:

a. Precipitation with aluminum salts - precipitation of phosphorus compounds can be accomplished through the addition of aluminum salts such as aluminum sulfate. The resulting aluminum phosphate compound is allowed to thicken and settle in tanks for later processing. Aluminum salts are the most commonly used and are the most effective at removing phosphorus to very low levels.

b. Precipitation with iron salts - phosphorus can be removed through precipitation with iron salts such as ferric chloride. The reaction results in a sludge which is thickened in tanks for later processing.

c. Precipitation with lime - calcium carbonate (lime) can be used to remove phosphorus through a two stage addition to the waste stream. This addition raises the pH of the wastewater and forms a precipitate which will settle in tanks. The waste stream will then typically need to have the pH adjusted to a more neutral level. The sludge that is generated is typically different than the sludges generated through alum or ferric chloride addition and may require a different type of processing.

Biological nutrient removal systems are also used to remove phosphorus from the waste stream. These are typically not as efficient as chemical removal systems in removing phosphorus to very low levels. This process involves the selection of microorganisms capable of accumulating excess quantities of phosphorus during cellular metabolism. This selection process requires special tanks where varying environmental conditions can be maintained. These environmental conditions are required to stimulate the phosphorus uptake and microorganism selection.

In addition to removal during the wastewater treatment plant processes, phosphorus can be removed through post treatment use. The following methods may be employed:

a. Wetlands polishing - Wastewater treatment plant effluent may be polished, and phosphorus removed, through circulation across constructed or natural wetlands. The capacity to remove phosphorus is dependent on the size of the wetland, various plant species in the wetland, and the detention time of the wastewater in the wetland. Wetlands have a finite capacity to remove inputs and can reach a saturation level at which the wetland will have a reduced ability to assimilate pollutants. The large amount of land required for wetlands and the difficulty in insuring high levels of phosphorus removal will prevent the use of wetlands in many instances.

b. Wastewater effluent reuse for irrigation - The use of treated municipal wastewater for irrigation is both practical and safe. Wastewater effluent phosphorus levels should not present a problem in overloading the soil when the effluent is used for irrigation. Phosphates added to the soil may be taken up by the crop, accumulated by the solid phase of the soil in sorption or precipitation reactions, or lost from the system in percolation and runoff waters or by erosion. Reactions with the soil, and crop removal, account for the largest fraction of the phosphorus removed.

Management Practices to Control Nonpoint Sources of Phosphorus

In addition to point source contributions, such as wastewater treatment plants, of phosphorus to waterbodies, there are less easily quantifiable and controllable nonpoint sources. Phosphorus contribution percentages from point to nonpoint sources vary depending on land use but both can have detrimental water quality effects. Nonpoint sources include runoff from agricultural and forest lands, stormwater runoff, and erosion. The following are management practices used to control nonpoint sources of phosphorus.

a. Agriculture - Control of pollution from fertilizers and concentrated animal feeding operations reduces nonpoint sources. Management of discharges from feedlots, liquid wastes, runoff, and land application of wastes reduces contributions of phosphorus to water bodies. Also helpful in managing agricultural nonpoint sources are farm specific nutrient management plans and the establishment of forested buffer strips along stream channels adjoining croplands.

b. Forestry - Best management practices on forest lands include erosion control involving road construction, unstable slopes, and streamside areas. Good management during fertilization programs on forest lands must also be practiced.

c. Stormwater - Best management practices for stormwater runoff, and sediment deposition, include capturing the runoff in retention basins or detention facilities. Discharge from these detention facilities must then meet specific criteria.

d. Rangeland - Best management practices for rangeland have the dual objectives of maintaining and improving desirable vegetation for grazing and providing adequate cover to prevent soil erosion. Practices include timing of animal grazing, streambank protection and grass seeding.

<u>General References:</u>

Hetling, L.J. and I.G. Carcich, 1973. Phosphorus in waste water. Water and Sewage Works, Vol. 120, No. 2, pp. 59-62.

Porcella, D.B., P.A. Cowan and E.J. Middlebrooks, 1973. Detergent and nondetergent phosphorous in sewage. Public Works, Vol. 104, No. 9, pp. 126-128.

APPENDIX F

NUTRIENT CONTROL PROGRAMS AND POLICIES

This appendix provides examples of nutrient control programs and policies outside of Oregon. This is not an exhaustive summary of all programs. Programs and policies being implemented in Oregon are not included.

Comprehensive Programs

Regional Programs

The United States and Canada agreed in 1978 to establish phosphorus target loads for each of the Great Lakes. First, the emphasis was placed on a 1 mg/L total phosphorus discharge limit for point sources and phosphorus reductions in laundry detergents, but it later became apparent non-point source control measures were also needed. Non-point management techniques emphasized include accelerated adoption of conservation tillage, better management of livestock waste, and better management of nutrients used for crop production (Great Lakes Water Quality Board Report to the Intentional Commission - 1981).

The Chesapeake Bay states and the District of Columbia agreed in 1987 to achieve by 2000 at least a 40 percent reduction in both nitrogen and phosphorus entering the Bay. (Chesapeake Bay Agreement - December 14, 1987). Each jurisdiction is responsible for reducing its own nitrogen and phosphorus inputs by 40% each. Each state has determined its own "mix" of point and non-point controls to achieve the required reductions.

State Programs

North Carolina - The Nutrient Sensitive Waterway (NSW) designation has been established for waterways subject to excessive growths of vegetation which substantially impair the use of the water (NCAC 2B.0214). The NSW designation requires the development and implementation of a nutrient management strategy. The process involves identification of nutrient sources, establishment of nutrient reduction goals, and development and implementation of a nutrient reduction strategy.

Innovative approaches are being utilized in these strategies. For example, the Tar-Pamlico River Basin NSW experimental implementation strategy will provide the option of allowing operators of expanding wastewater treatment plants to meet nutrient load reduction goals by funding the implementation of Best Management Practices (BMPs) for agricultural non-point source (NPS) runoff (EPA Non-point Source News - Notes, 1990).

Idaho - Legislation adopted in 1989 requires the Department of Health and Welfare to develop a comprehensive nutrient management plan on a hydrologic basin unit basis (Nutrient Management Act - Chapter 308). Each plan will identify nutrient sources, the dynamics of nutrient removal, nutrient use and dispersal, and preventative or remedial actions to protect surface water. The plan will guide the state agencies in developing programs for nutrient management. Local management plans must be consistent with the state plan.

Florida - Under the Surface Water Improvement and Management Act, enacted in 1987, each water management district prioritizes water bodies based on criteria that consider violations of water quality standards, amounts of nutrients entering the water body, trophic state, etc. Surface water improvement and management plans are then developed. The plans include a list of all point and non-point source owners, recommendations and schedules for bringing all sources into compliance with state standards, a description of strategies for restoring and then maintaining the quality of the water body and funding estimates. All plans are reviewed by the Departments of Game and Fresh Water Fish, Agriculture, Consumer Services, Community Affairs and Natural Resources.

Nonpoint Source Programs

Federal

The Water Quality Act of 1987 authorized the expenditure of up to $400 million in federal funds to assist the states in designing and implementing programs to reduce non-point source pollution.

The Conservation Title of the 1985 Food Security Act established the Conservation Reserve Program, which retires highly erodible land from production for ten years in return for rental payments to farmers to compensate for lost income. The Act also requires farmers producing on highly erodible land to develop and implement conservation programs to reduce soil erosion or else lose farm program benefits.

State Programs

Kansas - Legislation adopted in 1989 authorized a dedicated source of funding for the State Water Plan. Implementation Guidelines and Procedures for the NPS Pollution Control Fund were issued in January, 1990 and set forth local non-point source pollution management plan requirements. Plans are to be prepared on a watershed or drainage area basis. All sources of non-point source pollution must be considered, and anyone affected should participate in the development of the plans. Work plans are to be prepared for waters needing protection or restoration. Work plans can include planning, designing, monitoring, evaluation, assessment, demonstration projects, and educational programs as well as implementation activities involving construction of NPS pollution control practices. Technical and financial assistance is available.

State Programs Directed at Specific Nonpoint Sources

Agricultural Sources

Arizona - Best management practices are required to reduce pollution from nitrogen fertilizers and concentrated animal feeding operations (Regulated Agricultural Activities Program - 1986). BMPs have been established for managing discharges from feed lots, liquid wastes, the management of runoff, and land disposal of wastes. Failure to comply could subject individuals to enforcement actions and extensive permitting procedures. Technical assistance and training is available.

Maryland - the Maryland Agricultural Water Quality Management Program, published in 1987 as the state's revised 208 plan, included outreach and technical assistance to farmers, information and education, cost-share funding for BMPs, research, and enforcement. Farm-specific management plans are developed to address all nutrient input to farmland, including fertilizers, animal wastes, sewage sludge, etc. Programs will encourage the widespread use of farm specific nutrient management plans and the establishment of forested buffer strips along stream channels adjoining cropland.

Pennsylvania - The non-point source control program consists of financial, technical, educational and planning assistance (Chesapeake Bay Non-point Source Programs - January, 1988). Program eligibility is established by conducting a watershed assessment to identify non-point nutrient sources and prioritize areas for financial assistance. Fifteen BMPs had been approved by January 1988 to reduce nutrient loadings, including BMPs for animal waste management, soil and manure analysis, fertilizer management, soil erosion, etc. Manure management practices are regulated and enforced. (Clean Streams Law - 25 PA Code, Chapters 101 and 102).

Virginia - The Chesapeake Bay Preservation Act (Sec. 10-313 et seq, Code of Virginia) requires farmers within designated preservation areas to develop soil and water quality conservation plans on their farms by 1995. The plans will address proper nutrient management and integrated pest management as well as traditional soil erosion concerns. Buffer strips are required along permanent watercourses. Soil and Water Conservation personnel will assist land owners in meeting the requirements.

Forestry

Washington - The Forest Practices Act (1974) provides both voluntary and regulatory tools to protect water quality. BMPs address road construction, maintenance and abandonment, unstable slopes, streamside areas, etc.

Urban Growth

District of Columbia - In January 1988, the District adopted regulations requiring BMPs for all new development and redevelopment (Chesapeake Bay Program - District of Columbia Nutrient Reduction Strategy - July 1988.)

Virginia - The Chesapeake Bay Preservation Act (Sec.,10-313 et seq. Code of Virginia) called for a determination of the ecological and geographic extent of Chesapeake Bay Preservation Areas and called for criteria to be established for use by local governments in granting, denying or modifying requests to rezone, subdivide or to use and develop land in these areas. Funding was provided to encourage landowners to convert lands having high pollution potential.

Stormwater

Florida - Under the Florida Stormwater Rule, stormwater runoff is now being captured in retention basins or detention facilities in urban areas across the state. To release stormwater to a surface water body, developers must apply for a state discharge permit, assuring the state that the discharge will not cause a violation of water quality standards.

Maryland - State Stormwater Management regulations were implemented in 1983, and counties and municipalities were required to enact ordinances to require that post-development runoff rates and volumes meet specific criteria. The program has been expanded to cover existing development and maintenance of stormwater management BMPs.

Virginia - Legislation was enacted that established permit requirements for stormwater discharges from certain systems, based on population served (Public Law. 100-1, Section 405).

Stormwater/Sediment

Delaware - The Stormwater and Sediment Control law enacted in June 1990 provides for stormwater and sediment control. The stormwater component provides for the management of water quantity and water quality. The program will be integrated with sediment control and will include regulatory and fee structure elements. Designated watersheds or subwatersheds may be established to promote a watershed plan and provide for implementation of practices to reduce existing flooding problems or improve existing water quality. The development or stormwater utilities by local governments, Conservation Districts or the state is authorized. Utility charges are to be reasonable and equitable so that each contributor of runoff to the system, including state agencies, shall pay to the extent to which runoff is contributed.

Rangeland

Washington - BMPs for rangeland focus on the dual objectives of maintaining and improving desirable vegetation for grazing and providing adequate cover to prevent soil erosion (Washington Nonpoint Source Assessment and Management Program - October 1989). Practices include timing of animal grazing to allow vegetation to become well established, streambank protection, seeding, etc.

<u>Point Source Programs</u>

Pennsylvania - A 2.0 mg/L total phosphorus effluent limit was established in 1970 for all new and modified point sources discharging to the Susquehanna River and its tributaries (Chesapeake Bay Program - Pennsylvania Nutrient Reduction Strategy - July 1988).

Maryland - The state's projected approach to achieve a 40% reduction in point source nutrients is to require biological nutrient removal at all sewage treatment plants larger than 0.5 million gallons per day, which should achieve 2 mg/L phosphorus and 8 mg/L nitrogen effluent levels (Chesapeake Bay Program - Maryland Nutrient Reduction Strategy - July 1988).

Virginia - In 1987, funding was provided for three nutrient removal demonstration projects at wastewater treatment plants. A Point Source Policy for Nutrient Enriched Waters was approved, which established a 2 mg/L phosphorus effluent limit for existing dischargers authorized to discharge 1 million gallons per day or more and new dischargers greater than 0.05 million gallons per day. Nitrogen removal will be required at all of Virginia's major municipal treatment plants below the fall line. Both phosphorus and nitrogen removal projects will be given priority for funds available from the State Revolving Loan Fund (Chesapeake Bay Program - Virginia Nutrient Management Strategy - July 1988).

APPENDIX G

ECONOMIC AND ENVIRONMENTAL IMPACTS OF A PHOSPHATE DETERGENT BAN

This appendix provides additional information on the potential economic and environmental impacts of implementing a ban on detergent phosphates.

Economic Impacts on Wastewater Treatment Plants

The economic benefit to a wastewater treatment plant (WWTP) resulting from a phosphorus detergent ban will vary with the method of phosphorus removal used at the plant. Plants that use iron or aluminum salts to remove phosphorus will experience the greatest reduction in operating costs when influent phosphorus is reduced. These are the most common methods of removal used today.

Wastewater treatment plants that remove phosphorus through only biological means, with the addition of lime, or through land disposal of the effluent, do not have costs proportional to the amount of phosphorus in their influent. Therefore, there will be essentially no economic benefit from reduced influent phosphorus at these plants.

Permit requirements also affect the amount of economic benefit resulting from a phosphate detergent ban. For example, there is uncertainty about the degree to which chemical dose is dependent on the amount of phosphorus to be removed when plants must meet very low effluent phosphorus levels (i.e. <0.5 mg/l).

Operational Expenses

Operational expenses are driven by the cost of chemicals, how the chemicals are added to the wastestream, and how the chemicals and precipitated phosphorus are removed from the wastestream prior to discharge. Cost savings result from reductions in the quantity of chemicals purchased, the quantity of chemical/phosphorus solids to be removed, and quantity of sludge requiring treatment and disposal. Chemical addition during treatment increases the amount of sludge and can change its chemical character, making it more difficult to dispose. Phosphorus removal generates an estimated additional 25 to 40 percent more sludge than typically produced through secondary wastewater treatment (EPA, 1987).

Some examples of operational cost savings following the implementation of bans include the following. Four WWTPs in Maryland reported 30 to 57 percent reductions in average monthly chemical dose requirements (Jones and Hubbard, 1986). Calculated estimates of Maryland's chemical cost savings statewide are $4.5 million annually (Sellars et al., 1987). Similarly, Michigan reported chemical use reductions at 9 WWTPs ranging from 12 to 49 percent with an average reduction of 29 percent (Hartig and

Horvath, 1982). Washington D.C. reported an actual chemical use reduction of 40 percent and an estimated annual cost savings of $6.5 million from chemical use and sludge processing reductions (Bailey, 1988). The Washington D.C. plant processes 306 million gallons of wastewater per day. Observed cost savings at Wisconsin plants were equivalent to $0.05 to 0.26 per capita per year (Foth and Van Dyke, 1981, 1984). North Carolina also projected operations cost savings (DiFiore, 1988).

Cost savings from reduced influent phosphorus can also be realized at biological treatment systems, although they may be less direct. Biological systems usually have chemical systems as backup. By reducing phosphorus loads, it is possible that reliance on the chemical backup systems could be reduced or eliminated. There are no biological treatment systems operating in Oregon.

Construction Expenses

The phosphorus removal system at a wastewater treatment plant is designed based on a number of factors, including: the volume of water to be treated, the quantity of phosphorus to be removed, and the discharge limits. To date, designs have been based primarily on the volume of water to be treated. A phosphate detergent ban will reduce the quantity of phosphorus that must be treated, but will not affect the other factors.

It is possible that a phosphate detergent ban may reduce the concentration of phosphorus in the wastewater enough to delay or prevent the need for phosphorus removal. Because of the expense of capital improvements, such a delay could result in cost savings.

Other Potential Impacts

Potential additional economic and environmental impacts from reduced influent phosphorus include:

- Reducing the volume of sludge to be landfilled, thus increasing existing landfill life and allocating that volume of landfill space for other beneficial purposes.

- Increasing sludge disposal options due to the removal or reduction of potential contaminants (i.e. the metals used in chemical removal) from the sludge.

- Decreasing the long-term environmental costs associated with chemical production and increased sludge generation, such as fuel for sludge transport and possible air contamination during disposal.

References:

Bailey, W., 1988. Impact of the Regional Phosphate Detergent Ban on Washington D.C.'s AWT Plant at Blue Plains. Washington Suburban Sanitary Commission, Washington D.C.

DiFiore, R.S., 1988. The Phosphate Detergent Ban and Its Impacts on Wastewater Treatment Plants in North Carolina. Presented at the North Carolina AWWA/WPCA Conference, Durham, North Carolina.

EPA, 1987. Design Manual: Phosphorus Removal, EPA 625/1-87/001.

Foth and Van Dyke and Associates, Inc., 1981 and 1984. The Effects of the Detergent Phosphorus Ban on Municipal Wastewater Treatment Plants in the State of Wisconsin. Report to the FMC Corporation.

Gates, D.D., C. Luedecke, S.W. Hermanowicz and D. Jenkins, 1990. Mechanism of Chemical Phosphorus Removal in Activate Sludge with AL (III) and FE(III). Presented at ASCE 1990 National Conference on Environmental Engineering, Arlington, Virginia.

Hartig, J.H. and F.J. Horvath, 1982. A Preliminary Assessment of Michigan's Phosphorus Detergent BAn. Journal of the Water Pollution Control Federation, 54(2).

Jones, E.T. and S.D. Hubbard, 1986. Maryland's phosphate ban - History and early results. Journal of the Water Pollution Control Federation, 58, 816-822.

Luedecke, C., S.W. Hermanowicz and D. Jenkins, 1989. Precipitation of ferric phosphate in activated sludge: A chemical model and its verification. Water Science and Technology, 21, 325-337.

Sellars, Jr., R.B., D.S. Bauer, J.L. Rein and M. Jiang, 1987. Effect of a Phosphate Detergent Ban on Municipal Treatment Plants in Maryland. Water Management Administration, Maryland Office of Environmental Program.

APPENDIX H

A SUMMARY OF PHOSPHATE DETERGENT LAWS

Table H-1 provides a summary of phosphate detergent laws in the United States. To date, 12 states and 5 regions have banned or restricted the use of phosphates in detergents. Most of the bans include similar provisions as discussed in section 5 of this report. Table H-1 may not be complete.

Table H-1: Phosphate Detergent Laws in the United States

Jurisdiction: State/Locality	Date Effective	Definition	Exemptions	Fine
Metropolitan Service Districts Portland, OR	1991 Sunset 1994	No person may sell of distribute for sale within the MSD any cleaning agents containing more than 0.5 percent phosphorus, by weight, except agents used in automatic dishwashing machines. Dishwashing products are limited to 8.7 percent phosphorus.	• Dairy, beverage, food processing products. • Detergents used in hospitals, vet hospitals, health care facilities, or used in commercial laundries serving hospitals and health care facilities. • Agricultural and electronic production. • Detergents for metal cleaning and conditioning. • Cleaning hard surfaces — windows, sinks, counters, and food preparation areas. • Water softners used in heating and cooling boilers.	May levy fine of up to $500 a day for violation of this ordinance.
Connecticut	1972	No person, firm, or corporation shall sell, offer, or expose for sale, give or furnish and synthetic detergent or detergent in any form that contains more than 7 grams of phosphrus per recommended dose.	• Detergent used for medical, scientific, or special engineering purposes and for use in machine dishwashers. • Detergents for dairy equipment, beverage equipment, food processing equipment. • Industrial cleaning equipment.	Information not available.
Georgia	1989	Mandate the use of low phosphate detergents. Allows 0.5 percent phosphorus (incidental to manufacturing) or more. Dishwashing products limited to 8.7 percent phosphorus.	Same as Maryland, except industrial and institutional detergent provisions.	Any violations of ordinance shall result in fine not to exceed $500. Each sale shall be a separate offense.
Indiana	1972	It is unlawful to use, sell, or otherwise dispose of detergent containing phosphorus, except for up to 0.5 percent incidental to manufacturing.	• Detergents for cleaning in places of food processing, and dairy equipment. • Sanitizers, brighteners, acid cleaners, and metal conditoners. • Detergents for use in dishwashing equipment — household or commercial. • Institutional laundry detergents.	Not Available.
Maryland	1985	Prohibit the sale, use distribution, manufacturing of cleaning products that contain phosphates of 0.5 percent (incidental to manufacturing) or more. Dishwashing products may contain 8.7 percent phosphorus or less.	• Detergents used in dairy, food, beverage processing equipment. • Metal sanitizers, brighteners, acid cleaners, or metal conditioners. • Detergents used in hospitals, vet hospitals, health care facilities, clinics, agricultural products. • Industrial detergents for metal conditioning or cleaning. • Detergent stored, manufactured, or distributed for use outside the state. • Detergent used in biological, chemical, engineering labs.	• User-fine not to exceed $100. • Seller/Manufacture not to exceed $1,000.

Table H-1: Phosphate Detergent Laws in the United States (Continued)

Jurisdiction: State/Locality	Date Effective	Definition	Exemptions	Fine
Maryland (Continued)			• Commercial laundries serving hospitals, health care facilities.	
Michigan	1977	A person shall not sell or distribute a household landry detergent which contains phosphorus in any form in excess of 0.5 percent by weight. Dishwashing products are limited to 8.7 percent phosphorus.	Same as Pennsylvania, except industrial and institutional provisions.	None.
Minnesota	1977	No person shall sell, offer expose for sale, or use in Minnesota a cleaning agent or chemical water conditoner that contains 0.5 percent or more phosphate (incidental to manufacturing). Machine dishwashing detergents not to exceed 11.0 percent. Chemical water conditioners not to exceed 20.0 percent phosphorus.		None.
Missoula, Montana	1989	Prohibits sale of certain products containing phosphorus within city limits (or 3 miles of city) of 0.5 percent (incidental to manufacturing or more). Dishwashing products — 8.7 percent or less. Metal conditioning — 20.0 percent or less.	• Detergents used in food or beverage processing. • Detergents used in medical or surgical cleaning or dairy equipment. • Existing stocks may be sold for 6 months after ordinance in passed.	Upon discovery of sale or district, offender shall be notified of noncompliance. If situation still persists after 10 days, a fine will be levied of $50 to $500.
North Carolina	1988	Prohibit the sale, use, distribution, or manufacturing of cleaning products that contain phosphate of 0.5 percent (incidental to manufacturing or more). Dishwashing products are limited to 8.7 percent phosphorus.	Same as Georgia and Pennsylvania. Detergents used for cleaning hard surfaces, sinks, windows, counters, and food preparation surfaces.	• User-Fine not to exceed $10. • Seller/Manufacture not to exceed $50.
New York	1973	Prohibition and restriction of the distribution, sale, offering or exposing for sale cleaning products containing phosphate of 0.5 percent (incidental to manufacturing) or more. All products may contain 0.1 percent or less. Dishwashing products — 8.7 percent or less.	• Detergents used in food and beverage. • Detergents used in dairy equipment.	None.
Ohio Counties (applies to approximately 50 percent of the counties in the State)	1990	No person shall sell, offer for sale, or distribution for sale in listed counties any household laundry detergent containing phosphorus in any form in excess of 0.5 percent.	• A cleanser, rinsing aid, or sanitizer agent intended primarily for use in automatic machine dishwashers. • A metal brightener, rust inhibitor, etchant, surface conditioner.	Not Available.

Jurisdiction: State/Locality	Date Effective	Definition	Exemptions	Fine
Ohio Counties (Continued)			• A disinfectant or detergent used in hospitals or clinics or commercial laundries that serve them. • Detergents used in food processing.	
Pennylvania	Partial 1990 Statewide 1991 Sunset 1992	Prohibit the sale, use, or distribution of cleaning products that contain phosphates of 0.5 percent (incidental to manufacturing) or more. Dishwashing products limited to 8.7 percent phosphorus.	Same as Maryland. Water softners, antiscale agents, and corrosion inhibitors.	• User-Fine not to exceed $100. • Seller/Manufacture not
Vermont	1978	Applies to commercial establishments, household cleansing productgs that contain phosphates of 0.5 percent (incidental manufacturing). 8.7 percent phosphorus limit in automatic dishwashing detergent.	• Food, drug, and cosmetics, including personal care items, such as toothpaste, shampoo and handsoap. • Products labeled, advertised, marketed, and distributed for use primarily as economic poisons as defined in Section 911(5) of Title 6.	None.
Virginia	1988	Prohibits the use, sale, manufacture, or distribution of any cleaning agent that contains phosphorus; allows up to 0.5 percent incidental to manufacturing. Dishwashing products limited to 8.7 percent phosphorus.	• Cleansers used in dairy beverage or food processing.	Not Available.
Washington, DC	1986	Ban the use, sale or furnishing of detergents that contain more than a trace amount of phosphorus. 8.7 percent phosphorus limit for machine dishwashing detergent.	• Surface cleaning — counters, sinks, and windows. • Detergents for use in hospitals, vet hospitals, and health care facilities. • Detergents for metal cleaning and conditioning. • Lab use — biological, chemical, engineering.	Fines for sale or furnishing: $500, 1st offense; $1,000, 2nd offense.
Spokane, WA	1990	No person may sell, offer, or expose for sale or distribute any laundry cleaning product that exceeds 0.5 percent (incidental to manufacturing) or more.	Allow for depletion of existing stocks.	None.
Wisconsin	1983	Restrict sale of cleaning agents containing phosphorus of 0.5 percent (incidental to manufacturing) or more. Agents for machine dishwashing or cleansing of medical equipment restricted to 8.7 percent phosphorus. Water conditioners restricted to 20 percent phosphorus.	Detergents used in industrial processes and dairy equipment.	Any violation of this ordinance shall result in a fine not to exceed $100.

Leaking fuel tanks prompt DEQ action

DEQ pushes probe of creosote plant

Service stations and other sites in Government Camp, Hoodland, Boring and Gresham are on the Department of Environmental Quality's "leaking underground storage tank" cleanup list.

The 18 sites are in various stages of identification and cleanup. As problems at each site are eliminated, the DEQ will remove the site from the list.

• Zim's Shopping Center, 223rd Avenue and ... taminated so... removal of ar... tank. The soil ... site to be aera...
• Former M... Main Ave., G... groundwater ... a release of pe...

DEQ will take over creosote ...nt cleanup

S.E. Stark St., ...re decommis- ... Industries also ... e site to aerate other contaminated soil, but before the DEQ would approve such a plan, the company must show that such a use is compatible with land use laws.

DEQ offers voluntary cleanup ...gram

...artment of Environment... ...Q) is now accepting a... ...r participation in a volu... ...dous substance cleanu...

DEQ drilling monitoring wells

DEQ will use wells to track chemicals

DEQ as...

The departme... serve as cond...

By BARBARA PESCHIERA
Correspondent, The Oregonian

...by DEQ

...cessed in the Corn... ...ea. Cornucopia is ...istrict in the Wallow... ...ns approximately 1... ...th of Halfway.

...*ination*

...y, the Forest Servic... developing recreatio... the Cornucopia are... ...de a new trailhea... ...ea and hiking, pac...

Leak...

DEQ...

Eighteen locations in various stages

DEQ To Assess Health Risks of N...

DEQ TO INVESTIGATE

...start

examining

DEQ planning Alkali Lake probe

Department of Environmental Quality (DEQ) has decided to conduct another round of testing from samples to be gathered from the Cornucopia Mine's tailing piles.

In early August, the Forest Service made public results of testing of mine tailing sampl... indicate t... concentrat... heavy me... Accordi...

...pen house ...procedure

...nowing more about the ... the Oregon Department ...will hold an open house ...:30 to 8:30 p.m. at the St. ...427 N. Central. The public ...meet the staff who will be ...ore about the ... ick & Baxter ...and at the St. ...st... or at the ...Lo... ...rd.

DEQ investigation will measure impact on groundwater, soils, riverwater, air

OREGON ENVIRONMENTAL CLEANUP PROGRAM:

1991 REPORT TO THE LEGISLATURE

Environmental Cleanup Division
Department of Environmental Quality

Oregon

DEPARTMENT OF
ENVIRONMENTAL
QUALITY

January, 1991

This report is submitted to the Oregon Legislature in fulfillment of ORS 465.235. The report summarizes the accomplishments of the environmental cleanup program, identifies major issues, and concludes with a four-year plan of action.

Oregon's environmental cleanup law was adopted in 1987. The law requires establishment of a comprehensive program to protect public health and the environment by identifying and cleaning up sites contaminated by the release of hazardous substances.

Hazardous substance releases have contaminated land, tainted drinking water supplies and destroyed wildlife habitat. Both legal and illegal practices have resulted in damage we must now either live with or clean up. Cleanups range from a few weeks and a few thousand dollars for a simple site to several million dollars and twenty or more years of work for complex sites.

The price of not cleaning up sites is that contamination will migrate, cleanup costs will escalate, public health will continue to be threatened, and productive use of land and water resources will be precluded. Therefore, a fundamental issue for Oregon's program is how to identify and clean up more sites without sacrificing the level of protectiveness envisioned by the legislature when it adopted the environmental cleanup law.

Significant progress has been made towards implementing the state environmental cleanup laws. We are pleased to present this report and look forward to hearing your comments.

Respectfully submitted,

William P. Hutchison, Jr.
Chair
Environmental Quality Commission

Fred Hansen
Director
Department of Environmental Quality

811 SW Sixth Avenue
Portland, OR 97204-1390
(503) 229-5696

LEGISLATIVE REPORT

OREGON'S ENVIRONMENTAL CLEANUP PROGRAM

JANUARY 1991

Submitted to:

Governor Barbara Roberts

The 66th Oregon Legislative Assembly

Oregon Environmental Quality Commission

Submitted by:

Fred Hansen, Director
Oregon Department of Environmental Quality

Michael Downs, Administrator
Environmental Cleanup Division

PRINTED ON RECYCLED PAPER

INTRODUCTION

ORS 465.235 requires the Department of Environmental Quality to submit a report to the Governor, the Legislative Assembly and the Environmental Quality Commission. Specifically, the legislature directed that each year a quantitative and narrative description be prepared which includes information regarding the following environmental cleanup activities:

- facilities with a suspected release of hazardous substances added to the Department's database;
- facilities with a confirmed release of hazardous substances;
- facilities added to or removed from the inventory of sites requiring further action;
- hazardous substance removals;
- preliminary assessments;
- remedial investigations;
- feasibility studies; and
- remedial actions, including environmental and institutional controls, initiated and completed.

In addition, beginning with the current year and every fourth year thereafter, ORS 465.235 requires development of a four-year plan of action. The plan must include estimates regarding the number of preliminary assessments, remedial investigations, feasibility studies and remedial actions to be initiated and completed, and funding and staffing levels necessary for implementation.

REVIEW OF ACCOMPLISHMENTS

The Environmental Cleanup Division (ECD) was established in 1988 by the Department of Environmental Quality (DEQ) and charged with implementing Oregon's environmental cleanup laws. The Division's mission is to discover, assess, investigate and clean up sites contaminated by a release of hazardous substances. The following information summarizes accomplishments since adoption of Oregon's environmental cleanup law.

Public Information About Sites

Public information is an important and legislatively mandated component of Oregon's environmental cleanup program. Required public information about environmental cleanups includes:

1) listing sites with a confirmed release of hazardous substances;

2) identifying sites requiring further investigation or action; and

3) ranking sites according to the relative threat to public health and the environment posed by the hazardous substance release.

These requirements are addressed, respectively, by the following DEQ-maintained sources of public information: the Confirmed Release List, the Inventory of Sites Requiring Further Action, and the ranking of sites on the Inventory. Oregon's Environmental Quality Commission (EQC) adopted rules pertaining to the Confirmed Release List and Inventory of Sites Requiring Further Action in June 1990. Rules for how sites placed on the Inventory will be ranked were proposed for public comment in November 1990 and are scheduled for adoption in early 1991.

DEQ began issuing notice letters informing owners of the intent to list facilities on the Confirmed Release List and the Inventory in August 1990. By the end of the current biennium, owners of an estimated 120 sites will have been notified of the intent to propose the facility for placement on the Confirmed Release List. 80 of the sites will also be proposed for the Inventory.

In addition, DEQ has established an electronic filing system of sites with suspected or confirmed releases of hazardous substances. This "Site Discovery Database" tracks data and activities on reported releases.

Site Discovery

Properties with suspected or confirmed contamination are discovered through review of DEQ files, reports from the public and other state and federal agencies and field activities by DEQ staff. Through June of 1991, DEQ estimates about 983 suspected or confirmed sites will be identified. Of these, approximately 228 sites will be added to the Department's database during the current biennium.

Site Assessment

When DEQ receives information indicating a potential release of hazardous substances, the Department performs an evaluation to determine whether, in fact, a release has or may have occurred. This evaluation is brief and intended to screen out sites where it is readily apparent that additional investigation is not required. The site evaluation process conserves resources for sites requiring further action.

For sites not screened out, a preliminary assessment or equivalent is conducted to develop as complete a picture of the site as possible--primarily from existing information. In some instances, additional soil or water samples are taken to document the presence or absence of hazardous substances at the site.

The purpose of the "preliminary assessment" is to determine if the release poses a significant threat to public health or the environment. Preliminary assessments address current and past management of hazardous substances at a site, the type and concentration of the substances released, potential pathways for migration, and the potential effects of the substances. DEQ has developed a phased preliminary assessment process to help ensure sufficient information is collected to recognize when continued investigation is warranted.

By June 1991, DEQ estimates about 123 preliminary assessments will have been initiated, with 101 completed. Of these, 81 will have been initiated and 77 completed during the current biennium.

Simple Site Investigations

Cleanups can be either complex or simple. When hazardous substances are present in groundwater, investigations generally require extensive study to determine the boundaries of contamination and potential methods for control and removal of the contamination. On the other hand, some cleanups may be relatively simple because they are limited to soil and can be studied and cleaned up in a matter of weeks or months.

Opportunities for "simple site cleanup" have been dramatically demonstrated by Oregon's Underground Storage Tank (UST) cleanup program. While petroleum is also a hazardous substance, its well-defined characteristics and the widespread use of USTs, especially at gasoline stations, have resulted in development of a discrete process for petroleum cleanups.

To maximize the cleanup of other hazardous substances and to respond to private sector demand, DEQ has undertaken a program called voluntary cleanup initiative (VCI). When fully employed, VCI will help streamline methods of overseeing relatively simple hazardous substance cleanups. VCI will be discussed in more detail later in this report.

Complex Site Investigations

If DEQ determines hazardous substances have been released and a cleanup is needed, a remedial investigation and feasibility study may be required. The purpose of a remedial investigation (RI) is to determine the full nature and extent of the contamination. An RI provides for completion of a more thorough characterization of the site's hazardous substances, hydrogeology and geology, and an assessment of risks to public health and the environment.

A feasibility study (FS) develops options for remedial action. Typically, options considered range from total cleanup to no action. The FS evaluates the various options for practicability and cost effectiveness. The RI/FS may be conducted separately or as a single, integrated phase. An RI/FS typically requires one to three years, since this is the phase during which site conditions, chemical transport mechanisms, risk assessment and remedial action options are comprehensively evaluated.

For the biennium ending June 1991, DEQ estimates there will be 19 initiated and 10 completed remedial investigations, along with 10 initiated and 6 completed feasibility studies.

Cleanup

Information developed during the RI/FS, along with public comments regarding potential cleanup alternatives, is used by DEQ's director to determine the cleanup level and method. State rules stipulate the goal is to clean contaminated sites to background (e.g., naturally-occurring) levels for contaminants of concern. If that is not feasible, the goal is the lowest concentration determined to be feasible. The feasibility requirement means remedial actions must be cost effective, possible to implement and effective. Selected actions must also exhibit a preference for permanent solutions and the use of alternative or resource recovery technologies.

Remedial Design and Remedial Action

Specifics of selected remedial actions are designed and engineered during the phase known as "remedial design". Remedial design and remedial action are typically the longest and most expensive phases of the environmental cleanup process and may last for many years. During the current biennium, 6 sites have progressed to the remedial design or remedial action phase.

Removals

Removals may occur at any time during the investigation and cleanup process, and may be done prior to, in conjunction with, or in lieu of remedial action. Removals usually involve off-site disposal of contaminated materials, but may also entail measures to stabilize and contain contaminants on-site until a remedial investigation and remedial action can be completed. Security fencing, provision of alternative drinking water supplies and similar activities are additional examples of "removal actions".

Removals generally take from 6 to 18 months to complete. The cost of removals ranges from several hundred thousand dollars to more than a million dollars. During the current biennium, DEQ estimates it will have initiated 3 and completed 7 removals.

Underground Storage Tanks and Petroleum Contamination

Petroleum cleanups from leaking underground storage tanks are handled separately from other hazardous substances because petroleum has well-defined characteristics and the use of underground tanks is widespread. For the biennium ending June 30, 1991, about 1653 releases will have been discovered and 1243 investigations and 508 cleanups completed.

Spill Response

Programs previously discussed deal primarily with releases of hazardous substances that occurred sometime in the past. However, there are "contemporary" instances where hazardous substances are accidentally or intentionally spilled or otherwise discarded into the environment. Responsible parties are required to report these releases to DEQ and clean up spills.

DEQ performs three roles related to spill response: 1) technical support to local emergency response teams charged with protecting public health and safety from immediate danger; 2) oversight of work performed by responsible parties to ensure that long-term public health, safety, welfare and environmental concerns are properly addressed; and 3) in instances where a responsible party cannot be identified or the party will not clean up the spill, DEQ may task a contractor to complete the required corrective action.

For the current biennium, DEQ estimates about 400 incidents will qualify as significant hazardous substance spill response incidents and, of these, approximately 81 will require use of a contractor to complete cleanup activities.

Drug Lab Cleanup

In the mid-1980s a new law enforcement and public health danger appeared in Oregon. Using readily available hazardous chemicals, clandestine drug lab operators have created a steadily increasing problem by contaminating houses and leaving behind hazardous substances.

DEQ provides assistance to law enforcement agencies in cleaning up drug lab chemicals, as authorized by the Oregon legislature in 1987. At the request of law enforcement agencies, arrangements are made for packaging and disposal of wastes confiscated at illegal drug lab sites.

As with the spill response program, DEQ's principal roles in illegal drug lab cleanup are to provide technical assistance, oversee the cleanup work, or perform the work where necessary. By June 1991, about 275 drug lab cleanups will have been completed in the current biennium alone.

Conclusion

DEQ has made significant progress during the past four years in identifying and cleaning up sites contaminated by hazardous substances. The effectiveness of state programs is reflected by the steadily growing number of sites which have been cleaned.

For additional information regarding accomplishments since the initiation of the environmental cleanup program, including case studies of sites currently undergoing environmental investigations and cleanups, please refer to the appendices.
DEQ plans to refine and streamline the established environmental cleanup processes. As discussed in the following section, these changes will address voluntary cleanups, orphan sites, spill response and drug labs.

DISCUSSION OF ISSUES

The following section addresses some of the key issues emerging after nearly four years of implementing Oregon's Environmental Cleanup Law. Issues highlighted include: the voluntary cleanup initiative, orphan site cleanup, spill response, and drug labs.

The Voluntary Cleanup Initiative

In March of 1990, DEQ began a major new project, known as the voluntary cleanup initiative. The purpose of the initiative is to address issues of emerging importance as the environmental cleanup program matures, specifically: 1) availability of staff to respond in a timely manner to requests for oversight of environmental investigations and cleanups; and 2) expediting the environmental cleanup process where practical.

The first of these issues is DEQ's acknowledged inability to respond in a timely manner to a large number of requests by property owners, lenders, buyers and others for review of investigations and cleanups. During the initial two years of the program, it was often possible for DEQ to provide oversight for new projects, even though the demand for assistance sometimes required shifting work assignments. For example, to accommodate development plans for the Oregon Convention Center, DEQ was able to provide oversight for investigation and cleanup work by temporarily reassigning staff from other projects. More recently, with an increasing number of environmental priority projects, most new requests for DEQ oversight must be turned away.

The second issue is an interest on the part of DEQ and others to streamline the environmental cleanup process, particularly for simple sites. For example, DEQ is evaluating the use of numeric soil cleanup standards for some individual hazardous substances. If recommended for adoption, numeric standards and/or simplified risk assessment procedures promise to significantly reduce the time and expense of establishing cleanup standards for each individual site. Another effect of cleanup standards is that they will serve as a benchmark for evaluating the effectiveness of cleanups which occur without DEQ oversight.

To help DEQ address these issues, the Department established the Voluntary Cleanup Initiative Task Force with representatives of industry, environmental and public interest groups, lending institutions, environmental consultants, attorneys, and local governments. In June of 1990, DEQ and the Task Force completed work on a conceptual plan for the voluntary cleanups based on the following principles:

- the voluntary cleanup program should be fully self-supported by those who use the program;
- the type and extent of work performed by responsible parties will be significantly increased;
- DEQ needs to hire additional staff to provide oversight of investigations and cleanups; and
- simple sites should allow for streamlined approaches for investigation and cleanup while complex sites will continue to use a more comprehensive approach.

The Environmental Quality Commission has recognized the voluntary cleanup initiative as a high priority for Department action. In June 1990, the Commission approved DEQ's Strategic Plan which states that DEQ should:

> "[E]nhance the environmental cleanup program to include a non-complex cleanup process (with an appropriate regional component) that will promote voluntary cleanups by responsible parties with limited DEQ oversight."

In July 1990, the Legislative Emergency Board authorized 9 positions to begin implementation of the VCI. The E-Board will consider authorizing additional staff as the demand for DEQ oversight increases. This determination will be based on written requests from responsible parties. So far, 7 applications have been received. DEQ intends to begin oversight of these projects in February 1991.

Orphan Site Cleanup

Sometimes responsible parties are unknown, unable or unwilling to pay for environmental cleanup activities. In these cases, DEQ spends state funds for the cleanup. Occasionally, responsible parties can be found as the cleanup progresses and sources of the contamination are identified.

To augment funding for orphan site cleanups, the 1989 Legislature created an Orphan Site Account. This account may be used for remedial action expenses at sites where DEQ determines the responsible party is unknown, unable or unwilling to undertake the required actions and/or for grants and loans to local government units for remedial action. Three fees, each designed to generate up to $1 million annually, were authorized to support bonds sold to pay for those cleanups or to pay directly for the cleanups. The fees are: 1) the hazardous substances possession fee; 2) petroleum withdrawal fee; and 3) solid waste tipping fee.

In mid-1991, DEQ will request approval to sell pollution control bonds for financing cleanup of orphan sites. Legislative approval would trigger collection of fees for the Orphan Site Account.

Spill Response

Securing sufficient funding for the cleanup of hazardous substance spills remains a challenge for Oregon. For the period June 1989 through December 1990, a total of 81 hazardous substance spills required full or partial funding by the state at a cost of about $446,921. Revenue to support these activities was not made available. Currently, spill response activities are funded by the Hazardous Substance and Remedial Action Fund (HSRAF). HSRAF is primarily intended to address past practices and releases of hazardous substances, rather than contemporary spill response incidents.

Because of limited financing and staffing levels, DEQ currently operates a minimal spill response program that must be cut back further if funding is not provided.

Drug Labs

As with spill response activities, finding a stable and adequate source of funds to support drug lab cleanups has proven difficult. Costs can rarely be recovered successfully because: 1) confiscated property may cost more to clean up than the property is worth; and 2) in most cases, law enforcement agencies have not been able to pay for their legislatively mandated 50% share of cleanup and disposal costs. Thus far, General Funds and cost share repayments have been used to support DEQ's drug lab cleanup work.

Conclusion

During the past four years, Oregon's environmental cleanup program has evolved rapidly in response to a wide range of sources of hazardous substance releases. New challenges and opportunities related to voluntary cleanups, orphan site cleanups, spill response and drug lab cleanup have been recognized. The following section discusses the tools which DEQ believes are necessary to meet these challenges and opportunities.

FOUR-YEAR PLAN FOR ENVIRONMENTAL CLEANUP

ORS 465.235 requires submittal of a four-year plan of action for the state's environmental cleanup program. The plan must include estimates regarding the number of certain environmental cleanup activities--specifically, preliminary assessments, remedial investigations, feasibility studies and remedial actions--which will be initiated and completed.

Preliminary assessments, remedial investigations, feasibility studies and remedial actions comprise only part of the Environmental Cleanup Division's activities. Therefore, the four-year plan incorporates related work including cleanups of leaking underground storage tanks, orphan sites, spill response, drug labs, and the voluntary cleanup initiative. Funding and staffing requirements for the four-year plan are also presented.

Four-Year Plan Activities

Much has been accomplished since the environmental cleanup law was adopted just four years ago. Because of these accomplishments, two major trends in the future of environmental cleanup activities can be anticipated. First, the total number of activities will increase because much of the infrastructure and rules for implementing the environmental cleanup program has been established. Second, a shift in the types of activities completed is expected as sites move from investigative to cleanup stages.

Figures 1-4 depict the number of preliminary assessments, remedial investigations, feasibility studies and remedial actions which DEQ estimates will be initiated and completed. Figure 1, for example, shows that the number of completed preliminary assessments is expected to climb from 77 in the current biennium to approximately 100 in 1991-93 and 200 in 1993-95. In contrast to the anticipated steady growth in completion of preliminary assessments, a different trend is anticipated for remedial investigations and feasibility studies. As shown in Figure 2, DEQ projects about 10 remedial investigations will be completed in the 1989-91 biennium, followed by 15 in 1991-93 and 8 in 1993-95. Likewise, approximately 6 feasibility studies will be completed in 1989-91, followed by 13 in 1991-93 and 5 in 1993-95 as shown in Figure 3. This anticipated short-term surge in completion of remedial investigations and feasibility studies reflects movement of sites currently under investigation to cleanup stages. Figure 4 demonstrates the combined effect of increasing environmental cleanup activity and the movement of individual sites from investigation to cleanup phases. As shown, DEQ estimates the number of completed remedial actions will increase from 2 in this biennium to 11 in 1991-93 with an additional 12 to be completed in 1993-95.

Figure 1

PRELIMINARY ASSESSMENTS

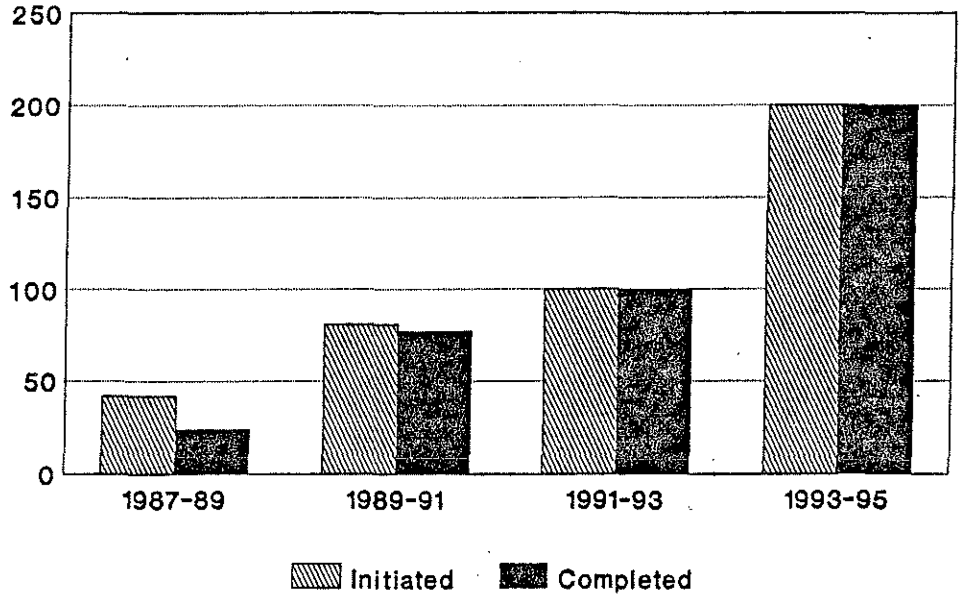


Figure 2

REMEDIAL INVESTIGATIONS

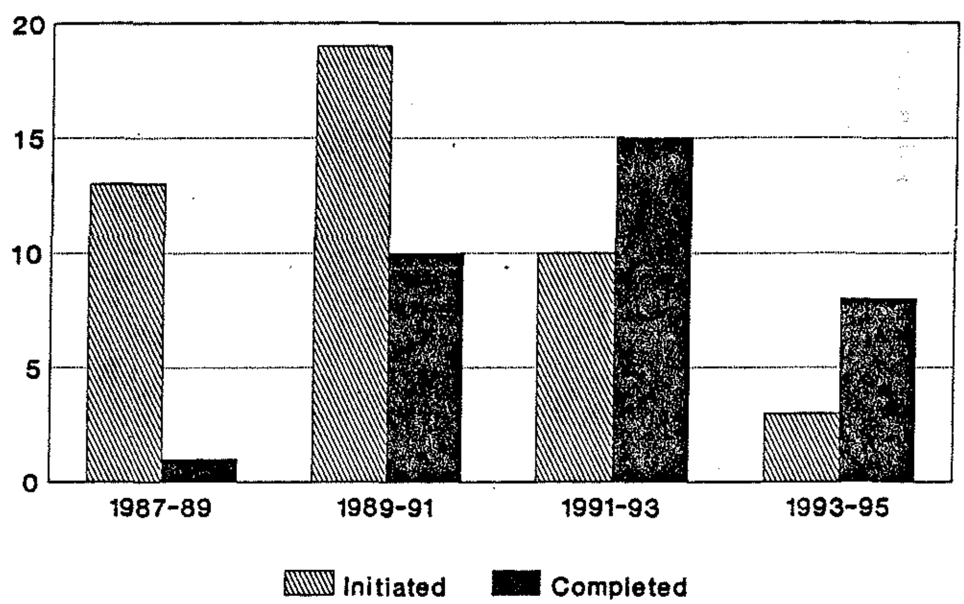


Figure 3

FEASIBILITY STUDIES

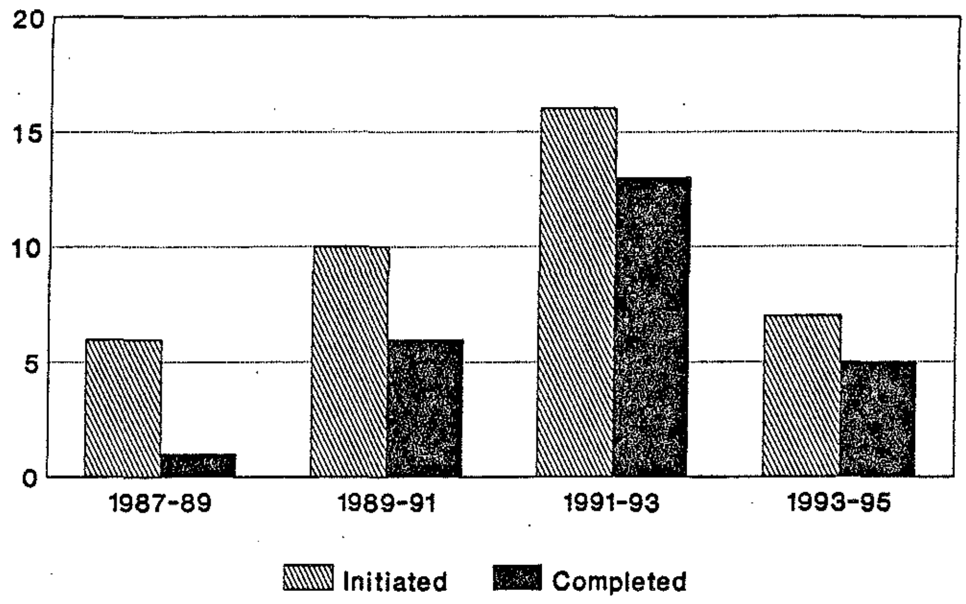
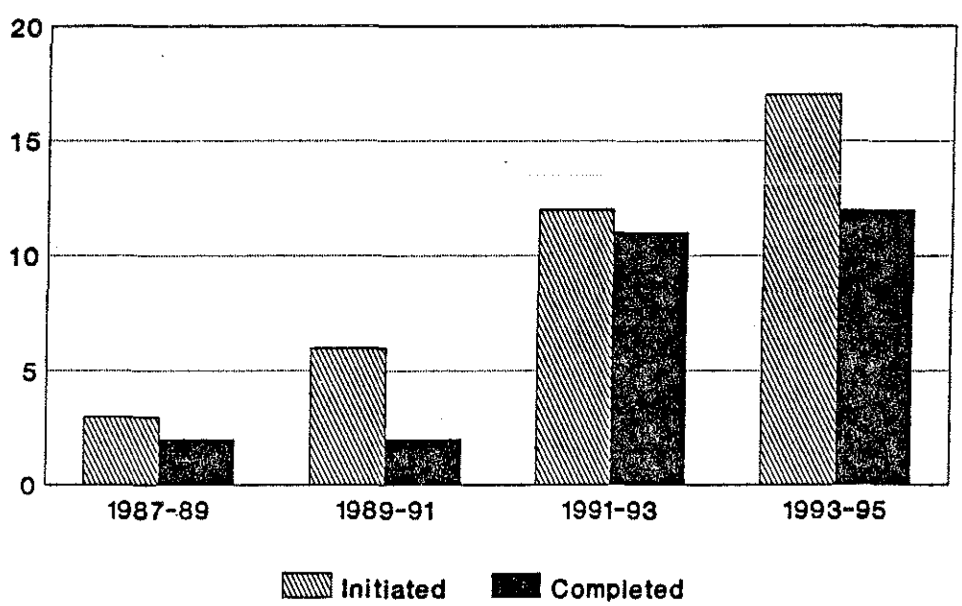
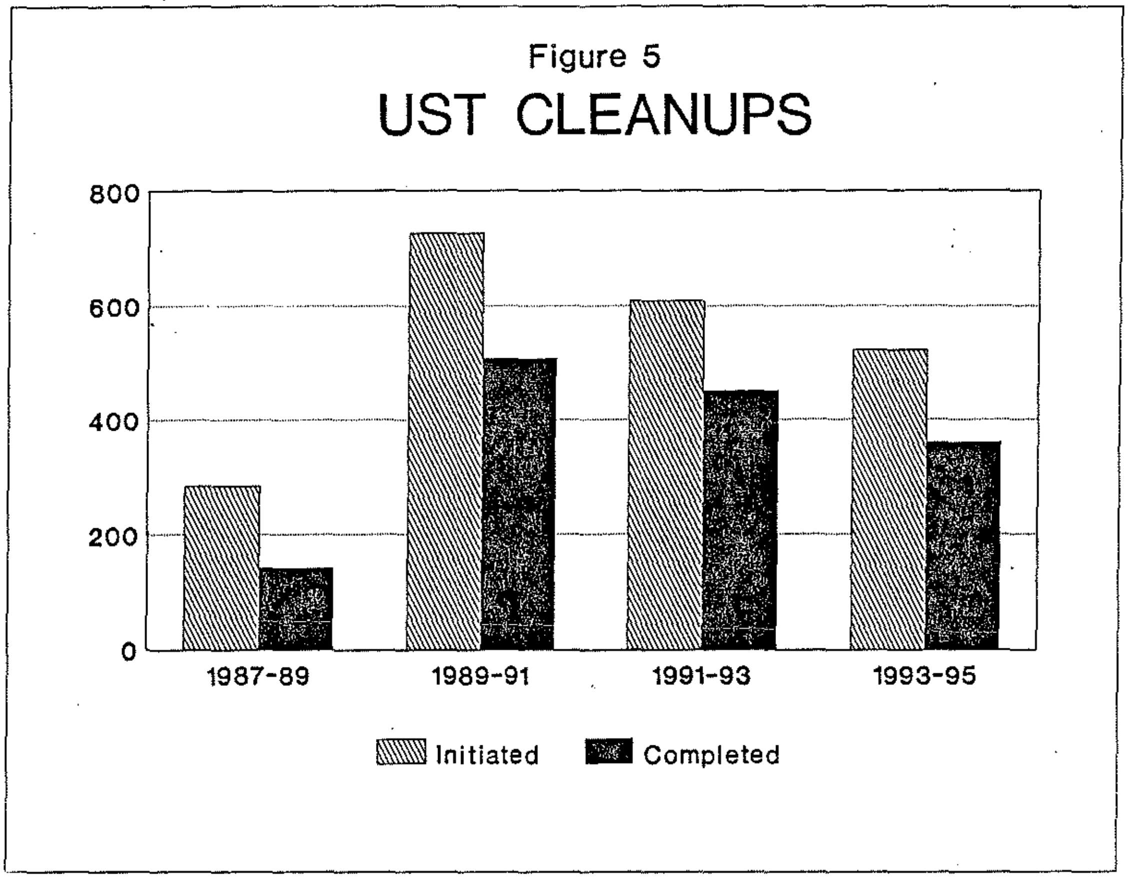


Figure 4

REMEDIAL ACTIONS





Other Activities

As previously discussed, Oregon's environmental cleanup programs have evolved in response to new issues and requirements.

For example, the Underground Storage Tank (UST) cleanup program has developed a relatively simple process for cleanup of eligible sites. Hundreds of sites contaminated by petroleum products have already been identified and cleaned up, primarily sites where petroleum product contamination has been limited to soils. Figure 5 summarizes the number of UST cleanups completed per biennium and projections for the program's future.

Other major activities include investigation of high-priority orphan sites, spill response, illegal drug lab cleanups and voluntary cleanups.

Funding and Staffing Levels

For the current biennium, environmental cleanup activities are funded with an approved budget of $14.8 million and 51.58 full time equivalent (FTE) staff. A general breakdown of expenditures and staffing by major program activities is presented on the following page.

Environmental Cleanup Program
Current Funding and Staffing
(1989-91)[1]

Activity	Approved Budget	FTE	Funding Source(s)
Cleanup of hazardous substances	$9.7 million	34.66	HSRAF[2], federal, cost recovery, and General Fund
UST cleanup	$3.5 million	16.42	Federal, HSRAF, petroleum loading and cost recovery
Spill response	$ .1 million	0.00	HSRAF, cost recovery, and Oil and Hazardous Materials Emergency Response Fund[3]
Drug lab	$1.5 million	.50	General Fund and law enforcement matching funds
TOTALS	$14.8 million	51.58	

[1]Includes legislatively approved budget and Emergency Board additions.

[2]Hazardous Substance Remedial Action Fund (HSRAF), derived from a $20/ton fee on all waste disposed at permitted hazardous substance incinerators and landfills, account for about $6.7 million. Federal Superfund revenue ($2.1 million), cost recovery ($800,000) and General Funds ($100,000) represent the balance of budgeted funds for hazardous substance cleanup activities.

[3]$119,436 authorized from Oil and Hazardous Materials Emergency Response Funds but all expenditures paid from HSRAF, including cost recovery.

If environmental cleanup programs are to be continued at present levels, the 1991-93 budget will require similar staffing and increased dollars to accommodate the shift from investigative phases to more resource-intensive engineering and remedial action selection. Increased dollars will be required because contractors will be used more extensively.

When reviewing environmental cleanup program costs, the following issues merit attention. First, only part of environmental cleanup activities are financed by General Funds. DEQ is prepared to forego current appropriations of about $100,000 in General Funds previously used for hazardous substance program activities. In addition, DEQ has examined options for replacing more than $1 million in General Funds used to finance drug lab cleanups.

Second, DEQ has prepared decision packages for Legislative consideration. If approved, the decision packages will: 1) convert existing limited duration positions to permanent status; 2) create a "regional presence" for environmental cleanup work, utilizing regional offices currently established by DEQ; 3) continue some of the current services provided under the drug lab and spill response programs; and 4) provide for partial implementation of the voluntary cleanup initiative. The Governor's recommended budget, including decision packages, provides for the following:

Environmental Cleanup Program
Governor's Recommended Budget
(1991-1993)[1]

Activity	Approved Budget	FTE	Funding Source(s)
Cleanup of hazardous substances	$13.36 million	52.9	HSRAF, federal, and cost recovery
UST cleanup	$ 4.18 million	26.0	Federal, HSRAF, petroleum loading, and oil heat and cost recovery
Spill response	$ .11 million	1.0	Petroleum loading and cost recovery
Drug lab	$ 1.97 million	1.0	General Fund and law enforcement matching funds
TOTALS	$19.62 million	80.9	

[1] Excludes positions in the Management Services Division.

Finally, DEQ will request authorization for the sale of bonds to provide for cleanup of orphan sites. If approved, bonds would be repaid by fees previously authorized. A request for authorization will be prepared for Legislative review during the 1991 session.

The 1991-93 orphan site authorization request will total approximately $11 million for orphan site activities and $600,000 for related staff.

The 1993-95 budget and staffing projections incorporate orphan site requirements, a fully operational voluntary cleanup program, and increases in the spill response and preliminary assessment activities. The 1993-95 projections for orphan site cleanups include new hazardous substance and petroleum storage projects not currently underway.

Environmental Cleanup Program
Budget and Staff Projections
(1993-95)

Activity	Projected Budget	Projected FTE	Funding Source(s)
Cleanup of hazardous substances	$18.18 million	77.9	HSRAF, federal and cost recovery
UST cleanup	$4.6 million	26	Federal, HSRAF, petroleum loading, and cost recovery
Spill Response	$1.23 million	4	Petroleum loading and cost recovery
Drug lab	$2.1 million	1	General Fund and law enforcement matching funds
Orphan site cleanups	$27.07 million	18	Pollution control bonds
TOTALS	$53.18 million	126.9	

These projections are based on program experience and estimates of future site requirements. The projections, of course, are subject to change as investigations proceed, additional releases of hazardous substances are discovered, and cleanup work advances.

APPENDICES

Activity	Actual Jan. 88 to June 89		Projection July 89 to June 91*		Projection July 91 to June 93		Projection July 93 to June 95	
PUBLIC INFORMATION	**ACTIVITIES**							
Suspected releases added to Database	755		228		NA		NA	
Added to Confirmed Release List	NA		120		NA		NA	
Facilities added to/removed from Inventory	NA		80/10		NA		NA	
HAZARDOUS SUBSTANCES REMEDIAL ACTION ACTIVITIES (Except petroleum)								
	Initiated	Completed	Initiate	Complete	Initiate	Complete	Initiate	Complete
Preliminary Assessments	42	24	81	77	100	100	200	200
Removals	8	2	3	7	3	4	3	3
Remedial Investigations	13	1	19	10	10	15	3	8
Feasibility Studies	6	1	10	6	16	13	7	5
Remedial Design, Remedial Action	3	2	6	2	12	11	17	12
UNDERGROUND STORAGE TANK CLEANUP ACTIVITIES (Petroleum)								
Releases discovered	409		1653		1400		1200	
	Initiated	Completed	Initiate	Complete	Initiate	Complete	Initiate	Complete
Investigations	NA	285	NA	1243	NA	1050	NA	900
Cleanups	285	142	727	508	609	450	522	360

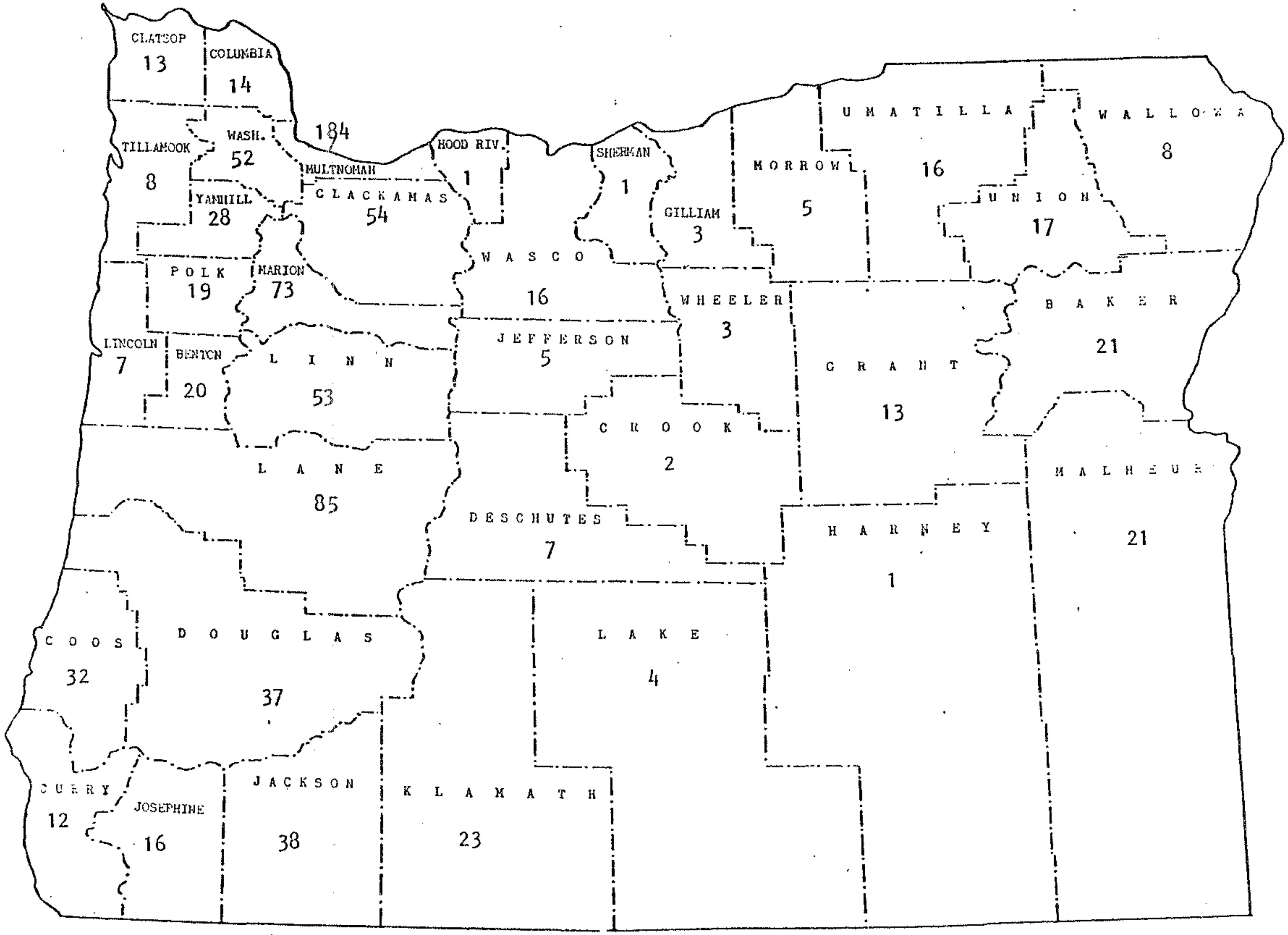
NA - Not applicable or not available.
* See "Detail for 1989-91 Biennium by Fiscal Year", Attachment B.

APPENDIX A
SUMMARY OF ENVIRONMENTAL CLEANUP ACTIVITIES
BY BIENNIUM

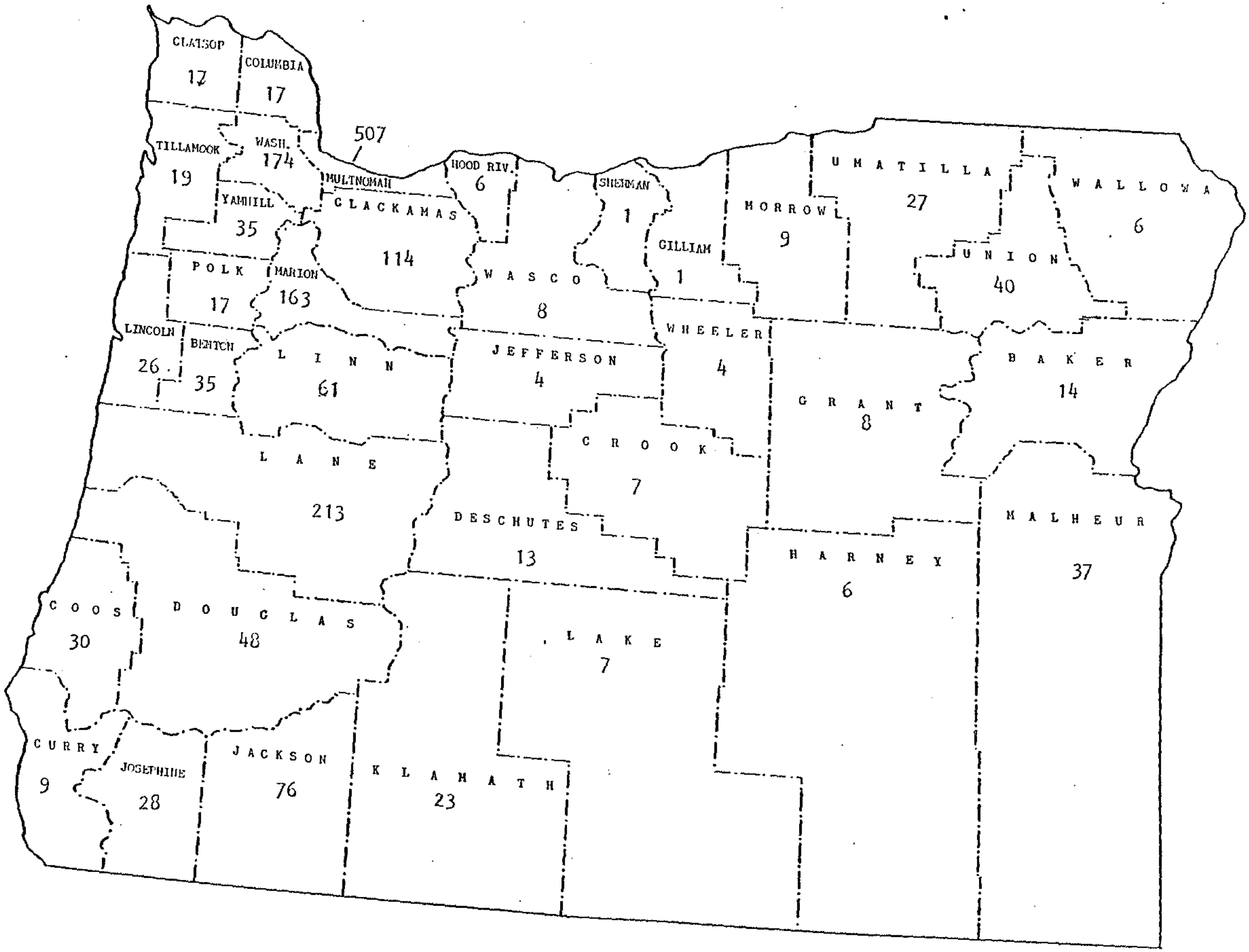
Activity	Actual July 89 to June 90		Projection July 90 to June 91	
PUBLIC INFORMATION ACTIVITIES				
Suspected releases added to Database	128		100	
Added to Confirmed Release List	NA		120	
Facilities added to/removed from Inventory	NA		80/10	
HAZARDOUS SUBSTANCES REMEDIAL ACTION ACTIVITIES (except petroleum)	Initiated	Completed	Initiate	Complete
Preliminary Assessments	31	27	50	50
Removals	3	4	0	3
Remedial Investigations	16	3	3	7
Feasibility Studies	7	2	3	4
Remedial Design, Remedial Action	4	1	2	1
UNDERGROUND STORAGE TANK CLEANUP ACTIVITIES (Petroleum)				
Releases discovered	843		810	
	Initiated	Completed	Initiate	Complete
Investigations	NA	634	NA	609
Cleanups	371	259	356	249

NA — Not applicable or not available.

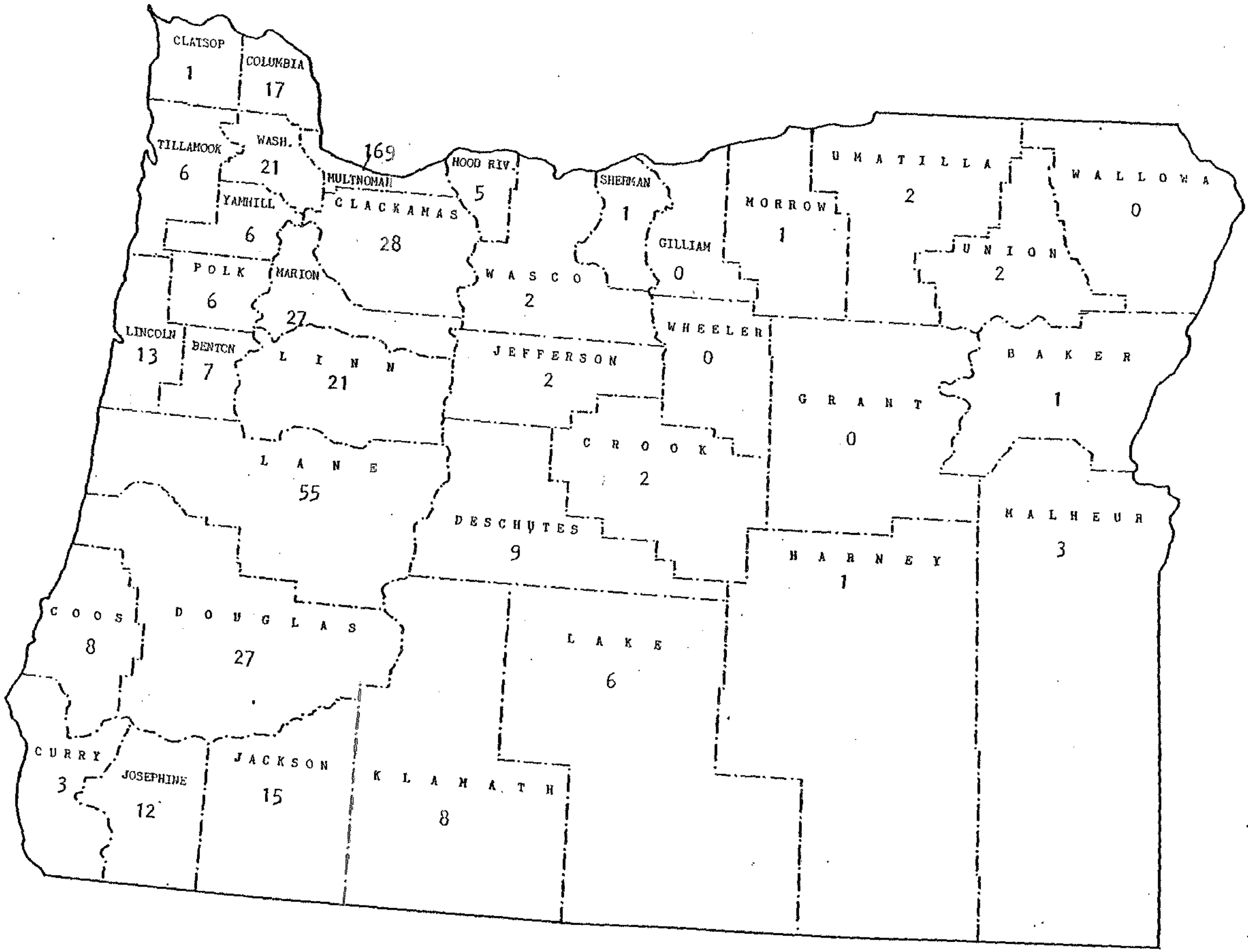
APPENDIX B
DETAIL FOR 1989-91 BIENNIUM
BY FISCAL YEAR



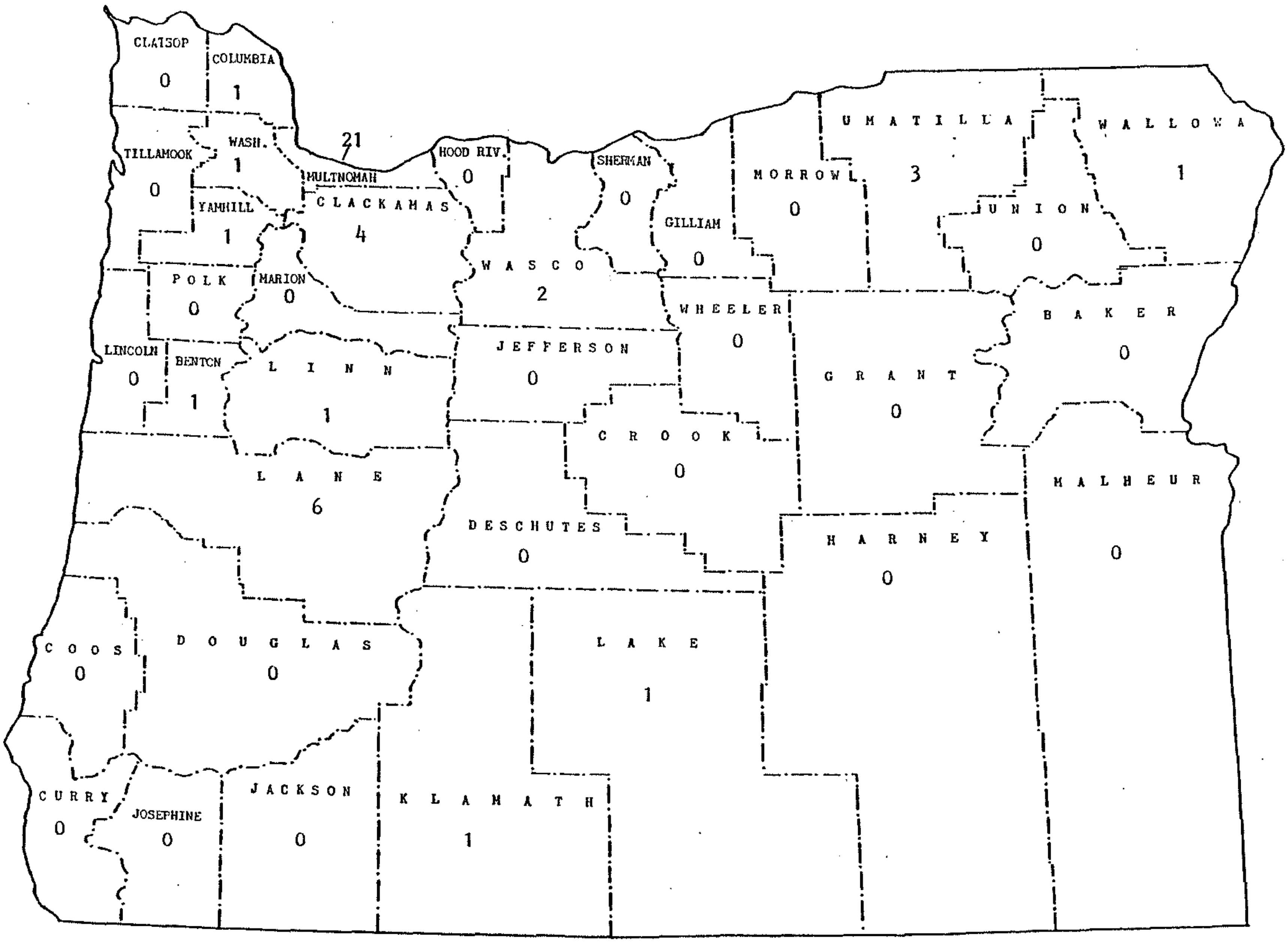
APPENDIX C
912 SITES WITH SUSPECTED OR CONFIRMED
HAZARDOUS SUBSTANCE RELEASES
(AS OF 12/90)



APPENDIX D
1810 SITES CONTAMINATED BY UST RELEASES



APPENDIX E
488 DRUG LAB CLEANUPS (AS OF 12/90)



APPENDIX F
44 SITES CURRENTLY IN REMEDIAL INVESTIGATION,
FEASIBILITY STUDY OR REMEDIAL ACTION PHASE (AS OF 12/90)

APPENDIX G
ENVIRONMENTAL CLEANUP CASE STUDIES

The following case studies illustrate the nature and complexities of conducting investigations and cleanups of contaminated sites.

PGE Station L. The Station L site is a former power generating facility on the western shore of the Willamette River in Portland. PGE operated the plant from the 1900s to 1975, and in 1986 donated 18 acres of the site to the Oregon Museum of Science and Industry (OMSI). During an investigation of the site for development, it was discovered that a transformer failure in 1971 caused PCBs to be released to the shore and riverbed of the Willamette River.

PGE removed 350 tons of contaminated soil and sediment from the shore and exposed riverbed in 1987. Although costly and time-consuming, this excavation was technically simple. Removal of contamination from submerged sediments, however, presented much greater problems. Various methods were examined for removal of PCBs without releases to the river, and most were deemed not feasible.

With DEQ technical assistance and oversight, PGE examined the possibility of using small-scale dredging techniques followed by construction of a protective "cap" within the river bed. This method was ultimately selected by DEQ for implementation.

Extensive monitoring and testing were required to ensure that no release of contaminated sediment occurred during the cleanup. Sediment dredged from the river was dried and sent to a hazardous waste landfill, while water was treated, tested and discharged back into the Willamette. Following completion of the dredging activities, verification sampling showed PCB concentrations dropped by as much as 99%.

After completion of the dredging activities, contaminated concrete surfaces were either removed or sealed, and the entire area was covered with a minimum 6-foot-thick layer of sand, gravel, and stone to isolate any residual contamination not removed by dredging. This protective cap was integrated into the shoreline stabilization planned for the new OMSI facility.

The riverbed cleanup was considered a success by all involved parties. A continuing investigation is addressing the adjacent "upland" portion of the Station L site.

McCormick & Baxter. The McCormick & Baxter Company has operated a wood treatment facility in north Portland at 6900 N. Edgewater Street since 1945. Environmental problems at the site were discovered in the early 1980s. The wood treating processes have involved chemicals such as creosote, asphalt-based petroleum oils, pentachlorophenol (pcp), water-borne solutions of chrome ammoniacal copper zinc arsenate (ACZA), and penta in butane. Between 1945 and 1969, the plant's wastewater was discharged directly into the Willamette River. Between 1968 and 1971 waste residues were disposed onsite.

DEQ obtained a consent agreement with McCormick & Baxter in 1987, requiring specific steps to clean up the site and prevent further releases of contamination. The company filed for bankruptcy protection under Chapter 11 in 1988, delaying implementation of many of the cleanup measures. In 1989, DEQ determined that an extensive investigation and cleanup was required to protect public health and the environment, and that work could not be delayed without significant adverse effects. DEQ decided to conduct the work with its own contractor, as McCormick & Baxter was unable to pay for the necessary work. As part of the bankruptcy settlement, DEQ will receive annual payments from McCormick & Baxter for cleanup costs. The company is also pursuing payment by its insurance carriers and is required to conduct future operations in an environmentally sound manner.

The DEQ investigation began in September 1990, and has identified extensive contamination of Willamette River sediments and areas of soil and groundwater contamination. Chemical, biological and physical testing results will allow DEQ to identify short-term and long-term cleanup options for the site. Cleanup probably will be conducted in stages, once key data has been assembled. McCormick & Baxter is an example of a site for which "Orphan Site" financing will be required for completion of cleanup activities.

PROJECT NAME/LOCATION	POTENTIAL RESPONSIBLE PARTY	LEAD & FUND SOURCE	PROJECT TYPE	PHASES	% COMPLETED	CONTAMINANTS OF CONCERN	MEDIA CONTAMINATED
Alkali Lake Alkali Lake, Lake Co	Under Investigation	STATE STATE	REMEDIAL ACTION	RI PD	<25% 100%	Chlorinated phenols, 2,4,-D, MCPA, dioxins, furans	Soil, groundwater, surfacewater
Allied Plating Portland	Stanley Hodes	FEDERAL FEDERAL	REMEDIAL ACTION	RI PD	<25% 100%	Heavy metals	Soil, groundwater
Bergsoe Metal Corporation St. Helens	List of 199 (available on request)	STATE STATE	REMEDIAL ACTION	RI PD	50% 100%	Lead, Cadmium, Chromium	Soil, groundwater
Broadway Cab Portland	City of Portland	STATE PRP	REMEDIAL ACTION	RI PD	<25% 100%	Polynuclear aromatics, Benzene, Toluene, Xylene	Soil, groundwater

Abbreviations

BTEX	Benzene, Toluene, Ethyl Benzene, Xylene
FS	Feasibility Study
PCB	Polychlorinated Biphenyls
PD	Pre-remedial Development, including negotiations
PM	Pre-remedial Measures, including removal
PRP	Potentially Responsible Party
RA	Remedial Action
RD	Remedial Design
RI	Remedial Investigation
TPH	Total Petroleum Hydrocarbons

APPENDIX H

SUMMARY OF CURRENT REMOVAL AND/OR REMEDIAL ACTION PROJECTS

PROJECT NAME/LOCATION	POTENTIAL RESPONSIBLE PARTY	LEAD & FUND SOURCE	PROJECT TYPE	PHASES	% COM-PLETED	CONTAMINANTS OF CONCERN	MEDIA CONTAMINATED
Carlton Company Milwaukie	Carlton Company	STATE PRP	REMEDIAL ACTION	PD	<25%	Trichloroethylene, 1,1-DCE, Vinyl Chloride, Perchloroethylene	Soil, groundwater
Cascade Corporation Troutdale	Cascade Corporation	STATE PRP	REMEDIAL ACTION	FS RI	<25% 50%	Trichloroethylene, Trichloroethane, TPH Dichloroethylene	Soil, groundwater, surfacewater
Coachman Industries, Inc. Hermiston	Coachman Industries, Inc.	STATE PRP	REMOVAL	PM	75%	Cadmium, Chromium, Lead, Mercury, solvents	Soil, groundwater
Columbia Steel/Joslyn Sludge Pond Portland	Joslyn Corporation Columbia Steel Casting Co.	STATE PRP	REMEDIAL ACTION	RI	<25%	Pentachlorophenol, Creosote, TPH	Soil, groundwater
Dant and Russell - Mill Site North Plains	Burlington Northern Railroad	STATE PRP	REMEDIAL ACTION	FS RI	50% 50%	Pentachlorophenol, Copper, Arsenic, Dioxin, Chromium, Creosote	Soil, groundwater, surfacewater
Doane Lake Study Portland	NL Industries, Inc. Gould, Inc. Liquid Air ESCO Rhone-Poulenc Schnitzer Pennwalt Pacific Northern Oil Wacker-Siltronic Koppers Northwest Natural Gas	STATE PRP	REMEDIAL ACTION	RI	50%	Polynuclear aromatics, pesticides, phenols, metals Volatile organic compounds,	Soil, groundwater, surfacewater
Dow Corning Corp. - Springfield Plant Springfield	Dow Corning Corporation	STATE PRP	REMEDIAL ACTION	PM	75%	1,1-Dichloroethane, 1,1-Dichloroethylene, Trichloroethylene, Perchloroethylene, 1,1,1-Trichloroethane	Soil, groundwater
East Multnomah County Troutdale	Unknown	STATE STATE	REMEDIAL ACTION	PD	<25%	Trichloroethylene, Trichloroethane, Dichloroethylene	Soil, groundwater, surfacewater

APPENDIX H (continued)

PROJECT NAME/LOCATION	POTENTIAL RESPONSIBLE PARTY	LEAD & FUND SOURCE	PROJECT TYPE	PHASES	% COMPLETED	CONTAMINANTS OF CONCERN	MEDIA CONTAMINATED
Forrest Paint Co. Eugene	Forrest Paint Co.	STATE PRP	REMEDIAL ACTION	FS RI PM	<25% 75% 100%	Toluene, Xylene, Ethyl Benzene, Methyl Ethyl Ketone	Soil, groundwater
Gould, Inc./N.L. Portland	NL Industries, Inc. Gould, Inc.	FEDERAL PRP	REMEDIAL ACTION	RA RD	<25% 75%	Lead, Zinc, Cadmium	Soil, groundwater surfacewater
Huntington Park Portland	Grayco Resources, Inc.	STATE PRP	REMEDIAL ACTION	RI PD	75% 100%	Perchloroethylene, Trichloroethylene, BTEX, long-chain hydrocarbons	Soil, groundwater
Illinois Tool Works, Inc. Milwaukie	Illinois Tool Works, Inc.	STATE PRP	REMEDIAL ACTION	PD	<25%	Trichloroethene	Soil, groundwater
J.H. Baxter Co. - Eugene Eugene	J.H. Baxter & Co.	STATE PRP	REMEDIAL ACTION	RI PD	25% 100%	Arsenic, Chromium, Copper, Creosote, Pentachlorophenol	Soil, groundwater
Joseph Forest Products Joseph	Joseph Forest Products	FEDERAL MIXED	REMEDIAL ACTION	RI PD	<25% 100%	Copper, Chromium, Arsenic	Soil, groundwater, surfacewater
L.D. McFarland Eugene	McFarland-Cascade L.D. McFarland Co.	STATE PRP	REMEDIAL ACTION	RI PD	<25% 100%	Pentachlorophenol, Polyaromatic Hydrocarbons	Soil, groundwater
Laurence-David, Inc. Eugene	Laurence-David, Inc.	STATE PRP	REMEDIAL ACTION	RI PD	<25% 100%	Chlorinated solvents, non-chlorinated solvents	Soil, groundwater
Malarkey Roofing Co. Portland	Herbert Malarkey Roofing Co.	STATE PRP	REMEDIAL ACTION	FS RI	25% 100%	Lead, Zinc	Soil

APPENDIX H (continued)

PROJECT NAME/LOCATION	POTENTIAL RESPONSIBLE PARTY	LEAD & FUND SOURCE	PROJECT TYPE	PHASES	% COMPLETED	CONTAMINANTS OF CONCERN	MEDIA CONTAMINATED
Marathon - N.W. Industrial St. Properties Portland	Marathon U.S. Realties, Inc.	STATE PRP	REMEDIAL ACTION	FS RI	25% 100%	Lead	Soil
Martin Marietta Reduction Facility The Dalles	Martin Marietta	FEDERAL PRP	REMEDIAL ACTION	RA RD	50% 100%	Cyanide, Fluorine, sulfates polyaromatic hydrocarbons	Soil, groundwater, surfacewater
McCormick & Baxter Portland	McCormick & Baxter Creosoting Co.	STATE STATE	REMEDIAL ACTION	FS RI	<25% <25%	Metals, Pentachlorophenol, PCB, solvents, petroleum products	Soil, groundwater, surfacewater, sediment, air
Milwaukie Public Water Supply Milwaukie	Unknown	STATE STATE	REMEDIAL ACTION	PD	<25%	TCE, chlorinated solvents	Groundwater
Nicolai Company Portland	Morgan Products, Inc.	STATE PRP	REMOVAL	PM	75%	Pentachlorophenol, PCB, solvents, petroleum products	Soil
Northwest Pipe and Casing - Clackamas Clackamas	Unknown	STATE MIXED	REMEDIAL ACTION	PD	75%	Polynuclear Aromatics, PCB, volatile organic compounds	Soil, groundwater, surfacewater
Northwest Pipe and Casing Co. - Portland Portland	Northwest Pipe and Casing Co.	STATE PRP	REMOVAL	PM	75%	Solvents, PCB, petroleum products, polyaromatic hydrocarbons	Soil, groundwater
Nu Way Oil Co. Portland	Delton Geary	STATE STATE	REMEDIAL ACTION	RI PD	<25% 100%	PCB, heavy metals, petroleum hydrocarbons	Soil
Pacific Detroit Diesel Allison Springfield	Pacific Detroit Diesel Allison	STATE PRP	REMEDIAL ACTION	PD	<25%	Trichloroethane, chlorobenzene, TPH	Soil, groundwater

PROJECT NAME/LOCATION	POTENTIAL RESPONSIBLE PARTY	LEAD & FUND SOURCE	PROJECT TYPE	PHASES	% COMPLETED	CONTAMINANTS OF CONCERN	MEDIA CONTAMINATED
Pendleton Grain Growers Hermiston	Pendleton Grain Growers	STATE PRP	REMEDIAL ACTION	FS RI PM	75% 100% 100%	Chlordane, 2,4-D, alachlor, atrazine, trifluarlin	Soil
Portable Equipment Salvage Co. Clackamas	Pacific Power and Light	STATE PRP	REMEDIAL ACTION	FS RI	75% 100%	PCB, Lead, Copper, Dioxin	Soil
Portland General Electric - Stn. L - Op. Unit 2 Portland	Portland General Electric	STATE PRP	REMEDIAL ACTION	RA RD	100% 100%	PCB	Sediment
Portland General Electric - Stn. L - Op. Unit 3 Portland	Portland General Electric	STATE	REMEDIAL ACTION	RI	75%	PCB, metals, polyaromatic hydrocarbons	Soil, groundwater
Rhone-Poulenc, Inc. Portland	Rhone-Poulenc AG Co.	STATE PRP	REMEDIAL ACTION	FS RI	<25% 25%	Pesticides, metals, volatile organic compounds, chlorinated benzenes, chlorinated phenolics	Soil, groundwater, surfacewater
Schnitzer Investment Corp. - Moody Portland	Schnitzer Investment Corp.	STATE PRP	REMEDIAL ACTION	FS RI PD	25% 75% 100%	PCB, pesticides, Cadmium, Lead, volatile organic compounds	Soil
Sixth & Klamath - Klamath Falls Klamath Falls	Unknown	STATE STATE	REMEDIAL ACTION	PD	50%	Perchloroethylene, Trichloroethylene, Trans-1,2 dichloroethylene	Soil, groundwater
South Waterfront Redevelopment - I Portland	Portland Development Commission	STATE PRP	REMEDIAL ACTION	RI	50%	Lead, Chromium, Copper, Zinc, Barium, petroleum hydrocarbons, PCB	Soil, groundwater
South Waterfront Redevelopment - II Portland	Cornerstone Columbia Development Company Portland Development Commission	STATE PRP	REMEDIAL ACTION	RA	50%	Metals, PCB, volatile organics	Soil, groundwater

PROJECT NAME/LOCATION	POTENTIAL RESPONSIBLE PARTY	LEAD & FUND SOURCE	PROJECT TYPE	PHASES	% COMPLETED	CONTAMINANTS OF CONCERN	MEDIA CONTAMINATED
Swift Adhesives Portland	Swift Adhesives	STATE PRP	REMEDIAL ACTION	FS RI PD PM	<25% <25% 100% 100%	1,1,1 Trichloroethane, 1,1 Dichloroethylene, Trichloroethylene, 1,1 Dichloroethane	Soil, groundwater
Taylor Lumber and Treating, Inc. Sheridan	Taylor Lumber and Treating, Inc.	STATE PRP	REMEDIAL ACTION	PD	50%	Pentachlorophenol, Arsenic, Zinc, polyaromatic hydrocarbons	Soil, groundwater, surfacewater
Teledyne Wah Chang Albany	Teledyne Wah Chang Albany	FEDERAL PRP	REMEDIAL ACTION	FS RI	25% 50%	Radionuclides, solvents, metals, PCBs	Soil, groundwater, surfacewater
Teledyne Wah Chang - Operable Unit #1 Albany	Teledyne Wah Chang Albany	FEDERAL PRP	REMEDIAL ACTION	RA RD FS RI	<25% 75% 100% 100%	Radionuclides, solvents, metals	Sludges
Umatilla Army Depot Activity Hermiston	U.S. Department of Army	FEDERAL PRP	REMEDIAL ACTION	FS RI PD	<25% 50% 100%	Explosives, metals, pesticides	Soil, groundwater
Union Pacific Railroad - The Dalles The Dalles	Union Pacific Railroad Co.	STATE PRP	REMEDIAL ACTION	FS RI PD	25% 25% 100%	Metals, PCP, creosote, volatile organic compounds	Soil, groundwater

PROJECT NAME/LOCATION	POTENTIAL RESPONSIBLE PARTY	LEAD & FUND SOURCE	PROJECT TYPE	PHASES	% COM-PLETED	CONTAMINANTS OF CONCERN	MEDIA CONTAMINATED
United Chrome Products, Inc. Corvallis	Marsh Family Insurance City of Corvallis	FEDERAL MIXED	REMEDIAL ACTION	OM	<25%	Chromium-6, Lead, metals	Soil, groundwater
				RA	<25%		
				RD	100%		
				RI	100%		
Viking Industries, Inc. Portland	Viking Industries, Inc.	STATE PRP	REMEDIAL ACTION	FS	25%	Diesel, Methylene Chloride	Soil, groundwater
				RI	50%		
				PD	100%		