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Technical Memorandum

September 30, 2025

To:	J.R. Giska and Apollonia Goeckner, Oregon Department of Environmental Quality; Holly Dixon, PhD, Oregon Health Authority
From:	Deborah Proctor and Ann Verwiel, ToxStrategies LLC
Subject:	**Evaluation of Draft Proposed Toxicity Reference Value for "Silica, Amorphous and Other Non-Crystalline Forms" for Non-cancer Chronic Exposure for Cleaner Air Oregon**

To support the current review of the proposed draft inhalation toxicity reference values (TRVs) to be used in the Cleaner Air Oregon program, we have evaluated the draft proposed TRV for chronic non-cancer exposure for "Silica, Amorphous and Other Non-Crystalline Forms" that Oregon Department of Environmental Quality (ODEQ) and Oregon Health Authority (OHA) have presented to the Air Toxics Science Advisory Committee (ATSAC) for its consideration. **Table 1** briefly summarizes our conclusions, which are laid out in more detail in this memorandum.

Table 1. Summary of recommendations for proposed update to the chronic TRV for "Silica, Amorphous and Other Non-Crystalline Forms:

ODEQ Proposed TRV (µg/m^3)	Recommendations for Updates to Proposed TRVs
Chronic TRV 6.6	The chronic TRV is based on a value published by Texas Commission on Environmental Quality (TCEQ). We recommend that ODEQ withdraw the proposed acute TRV for amorphous silica because when reviewing the same study as TCEQ, Agency for Toxic Substances and Disease Registry (ATSDR), an authoritative source under ODEQ's rules, concluded that the information was insufficient for developing a quantitative toxicity value for any period of exposure for any form of amorphous silica. Relying on ATSDR's findings, which are explicit about the lack of data for amorphous silica, to withdraw the proposed acute TRV for amorphous silica, would be consistent with DEQ's authoritative source guidance for setting TRVs for the Cleaner Air Oregon program. If ODEQ continues to propose this value for further consideration, we recommend that ODEQ revise the acute TRV for amorphous silica to specify that it only applies to fumed amorphous silica rather than the broad toxic air contaminant (TAC) category that is currently published. Consistent with ATSDR's conclusions, it is not scientifically appropriate to use findings from studies on the fumed silica form of non-crystalline silica and to apply those findings to all silica forms.

"Silica, Amorphous and Other Non-Crystalline Forms"

Silica, or silicon dioxide, exists naturally in the environment and in synthetic forms (ATSDR 2020; TCEQ 2011). Silica is classified by its structure and designated as either crystalline silica or amorphous silica (non-crystalline silica) (ATSDR 2020). ATSDR (2019) reports that "According to the European Centre for Ecotoxicology and Toxicology of Chemicals Joint Assessment of Commodity Chemicals report (ECETOC 2006), ambient a-[amorphous] silica levels in the air range from 0.2 to 136 µg/m^3. As such the proposed TRV (6.6 µg/m^3) is well within the levels that may be considered background in ambient air.

Crystalline silica compounds contain repeating patterns of silica and nitrogen while amorphous silica compounds are less structured, non-repeating, and considered random by comparison (National Center for Biotechnology Information 2025). All silica that does not have a defined structure is considered non-crystalline silica. Crystalline silica is the most common form and trace amounts of crystalline silica are found in all soils (ASTDR 2019; ASTDR 2020). Common crystalline silica forms include quartz, cristobalite, and tridymite (ASTDR 2019; NIOSH 2002).

Amorphous silica forms include naturally occurring amorphous silica (i.e., diatomaceous earth, vitreous silica, opal), synthetic amorphous silica (i.e., pyrogenic silica (fumed silica), silica gel), and amorphous silica byproduct forms (i.e., silica fume) (ATSDR 2019). Diatomaceous earth, also known as diatomite, is a geological product of decayed unicellular organisms (IARC 1997). Vitreous silica, also referred to as fumed silica, can be

formed naturally by the fusion of siliceous earth after volcanic eruptions, lighting strikes, or meteoric impact (ATSDR 2019). It can also form intentionally and unintentionally as a byproduct from the process of melting and rapidly cooling crystalline silica.

Synthetic amorphous silica is manufactured intentionally and generally does not contain detectable amounts of crystalline silica (ATSDR 2019). Pyrogenic silica, also known as fumed silica, forms from the combustion of volatile silica at high temperatures (1,000 to 2000°C) or from the oxidization of organic or inorganic silicon compounds (ASTDR 2019). Precipitated silica and silica form from wet processes involving the precipitation from a vapor or solution (ATSDR 2019; Fruijtier-Polloth 2012). All these production processes are carried out with controlled physical parameters to generate the desired amorphous silica form (ATSDR 2019, Fruijtier-Polloth 2012). Silica fume, yet another form of amorphous silica, is an unintentional byproduct during the production of some industrial processes (i.e., silicon-containing alloy production) (ATSDR 2019; Fruijtier-Polloth 2012; IARC 1997). Silica fume can be formed intentionally during this production to be used in manufacturing processes if desired (ASTDR 2019).

Background on TCEQ's TRV

The proposed chronic non-cancer TRV for silica, amorphous and other non-crystalline forms (respirable) is based on the 2013 Texas Commission on Environmental Quality (TCEQ) reference exposure level (REL: 6.6 $\mu g/m^3$). TCEQ used Groth et al. (1981) as the basis for setting its REL. Groth et al. (1981) exposed rats, guinea pigs, and monkeys to 15 mg/m^3 of three forms of amorphous silica via an inhalation chamber, either fumed silica, silica gel, or precipitated silica . Animals were exposed at a rate of 5.5 to 6 hours per day for 5 days per week for 13 to 18 months. The authors reported a lowest-observed-adverse-effect level (LOAEL) of 15 mg/m^3 for pulmonary effects (i.e., respiratory impairment and histopathological changes) from fume silica (a form of amorphous silica). These effects were not observed for silica gel nor precipitated silica. Thus, the LOAEL for this study was the single dose of 15 mg/m^3 based on fume silica. A no-observed-adverse-effect level (NOAEL) was not established in this study.

TCEQ did not consider the implications of applying a LOAEL based on fume silica to all amorphous and other non-crystalline forms, which are more common than fume silica. While TCEQ is not one of Cleaner Air Oregon's authoritative sources, the Agency for Toxic Substances and Disease Registry's (ATSDR) is an authoritative source which came to very different conclusions than TCEQ, as discussed below.

ATSDR's Toxicological Profile for Silica

In 2019, years after TCEQ's work, Agency for Toxic Substances and Disease Registry (ATSDR) published its toxicological profile for silica. This profile reviewed both crystalline and amorphous or non-crystalline silica, including Groth et al. (1981). ATSDR did not establish inhalation or oral minimal risk levels (MRLs) for amorphous silica due to

insufficient data. ATSDR (2019) explained that the "results of the animal studies provide evidence that toxicological potency for respiratory effects can differ between different silica polymorphs. Given the potentially important role of surface chemistry characteristics in the toxicological potency of silica compounds, there is considerable uncertainty regarding identification of NOAEL or LOAEL values that could serve as the basis of development of inhalation MRLs, as values based on a single a-silica polymorph may not apply to all forms of a-silica [(amorphous silica)]."

When assessing database adequacy for acute, intermediate, and chronic inhalation MRLs, ATSDR states that all silica databases lacked studies evaluating the effects of inhalation exposure to amorphous silica at all exposure durations and highlighted that "only limited data are available regarding the relative potency of polymorphs" (ATSDR, 2019, p. 246).

Additionally, ATSDR states in their 2020 silica fact sheet that "there are no known health effects from exposure to amorphous silica at the levels found in the environment or in commercial products." ATSDR explains that although there are animal studies that suggest breathing specific forms of amorphous silica may cause lung inflammation and injury, amorphous silica "is less hazardous than crystalline silica."

Proposed Chronic Non-cancer TRV for "Silica, Amorphous and Other Non-Crystalline Forms"

The proposed chronic TRV for "silica, amorphous and other non-crystalline forms" is based on the TCEQ REL. The TCEQ REL is based on a LOAEL established by a study that evaluated exposures to fume silica. However, ATSDR (which, unlike TCEQ, is a Cleaner Air Oregon authoritative source) later reviewed all available silica toxicity information, including the key study cited by TCEQ. Significantly, ATSDR did not find sufficient evidence to establish any MRLs for amorphous or non-crystalline silica due to the limited data and the "potentially important" differences between the multiple forms (polymorphs) to be considered.

Consistent with the Cleaner Air Oregon regulations, ODEQ should look first to authoritative sources such as ATSDR in setting (or not) TRVs, especially when an authoritative source explicitly considers the toxic air contaminant of interest and newer toxicity data is not available for evaluation. In this case, TCEQ relied on the same study (Groth et al., 1981) as ATSDR, but TCEQ did not acknowledge the limitations in the data in developing a chronic REL for a broad category of silica polymorphs. ATSDR later reviewed TCEQ's work and concluded that the data set relied upon by TCEQ (which was limited to a specific polymorph, i.e., fume silica) was insufficient for developing quantitative toxicity criteria. Additionally, it is not appropriate to use the LOAEL from one form of silica and apply the results to all forms of silica. More research is needed before ODEQ can develop a TRV for the broad category of amorphous and non-crystalline silica.

If ODEQ finalizes the proposed TRV, the compound name should be specific to fumed silica rather than inappropriately generalized to all forms of amorphous silica.

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To:	J.R. Giska and Apollonia Goeckner, Oregon Department of Environmental Quality; Holly Dixon, PhD, Oregon Health Authority
From:	Deborah Proctor and Ann Verwiel, ToxStrategies LLC
Subject:	**Evaluation of Draft Proposed Updates to Chromium(III) TRVs for Cleaner Air Oregon**

To support the current review of the inhalation toxicity reference values (TRVs) used in the Cleaner Air Oregon program, we have evaluated the draft proposed TRVs that the Oregon Department of Environmental Quality (ODEQ) and Oregon Health Authority (OHA) have presented to the Air Toxics Science Advisory Committee (ATSAC) for its consideration for soluble and insoluble chromium(III) (CrIII). This memorandum discusses in more detail the proposed CrIII TRVs, and **Table 1** below briefly summarizes our comments.

Table 1. Summary of Recommendations for Proposed Updates to Chromium(III) TRV

ODEQ Proposed TRV ($\mu g/m^3$)	Recommendations for Updates to Proposed TRV
Chronic TRV Soluble: 1.4 Insoluble: 0.06 **Acute TRV** Soluble: 7 Insoluble: 0.14	We recommend: • Consistent with authoritative sources, do not proceed with the acute TRVs for soluble and insoluble Cr(III). • Consistent with authoritative sources, do not proceed with the chronic TRV for insoluble Cr(III). • Consistent with authoritative sources, exempt chromium in alloy and metalloid forms from regulation under Cleaner Air Oregon (CAO).

The acute noncancer TRVs for soluble and insoluble Cr(III) and the chronic insoluble Cr(III) TRV are not scientifically supportable, and are not consistent with approach of the cited authoritative source, ATSDR.

Withdraw Proposed Insoluble and Soluble Cr(III) Acute TRVs

For soluble and insoluble Cr(III), we request that the Agency for Toxic Substances and Disease Registry (ATSDR)'s intermediate minimal risk level (MRL) not be used as an acute exposure TRV. The intermediate MRL is intended for exposures of 14 to 365 days, which is much longer than the duration for an acute TRV (24 hours). In addition, ATSDR clearly states that available studies regarding acute exposure to Cr(III) were not adequate for deriving an acute MRL for either soluble or insoluble Cr(III).

Using the intermediate MRLs as acute TRVs is particularly flawed in the case of Cr(III) because the effects reported in the 13-week exposure group of the key study (Derelanko et al., 1999) used by ATSDR as the basis for the intermediate soluble and insoluble Cr(III) MRLs were not observed following five days of exposure under the same conditions in the very same study. The key study was a subchronic 13-week inhalation exposure study by Derelanko et al. (1999), wherein rats were dosed six hours per day for five days per week—which is 390 hours of exposure—to basic chromium sulfate (soluble) or chromic oxide (insoluble). One-third of the animals were included in a 13-week recovery group. Black insoluble chromium pigment was still present in the lungs of the insoluble chromium oxide-treated animals, and, to a lesser extent, in the basic chromium sulfate-treated animals after the 13-week recovery period. The authors of the Derelanko et al. (1999) study attributed the effects observed at very high exposures to insoluble chromic oxide to insoluble particle loading of the rat lung due to the exposure conditions. The health effects driven by insoluble particle overloading in a subchronic exposure study for insoluble Cr(III) are not relevant to environmental exposure conditions that occur for 24 hours, the exposure duration of the acute TRV.

This study used as the basis for the intermediate MRL also included a 5-day exposure group, and the effects observed at 13 weeks—the basis of the ATSDR MRL—were not observed following the 5-day exposures in the same study. Results observed following the 5-day exposures, and those due to insoluble chromic oxide in the 13-week exposures, were not dose-dependent, suggesting that they were due to the insolubility and acidity of the chromium forms administered, not Cr(III). Clearly, the results of the 13-week exposures reported in Derelanko et al. (1999) are not relevant to acute (24-hour) exposures.

ATSDR, the authoritative source cited as the basis of the acute Cr(III) TRVs, specifically states that "studies evaluating the effects of acute exposure of humans to chromium(III) compounds were not identified" (ATSDR, 2012, p. 38) and "data [from animal studies] are not adequate to characterize the exposure-response relationship for respiratory effects" (ATSDR, 2012, p. 38). In short, ATSDR did not find that the available data are sufficient to set acute an MRL for soluble or insoluble Cr(III). In making that determination, ATSDR reviewed and considered the 5-day exposure data from the Derelanko et al. (1999) study.

ATSDR did not substitute their intermediate value, or use the 13-week Derelanko et al. (1999) study data, to set an acute MRL. ATSDR noted that the lack of a dose response in either study may be due to the insoluble and/or highly acidic nature of the Cr(III) forms administered. By ignoring these concerns from ATSDR, ODEQ is not following the guidance of the authoritative source in setting the acute TRVs, which is a misuse of the authoritative source guideline under CAO.

Also, ODEQ's guidance recognizes that developing acute TRVs from chronic studies is not preferred, and in the case of Cr(III), where the exposures were subchronic, the same principle applies. Specifically, ODEQ states:

> "We acknowledge that deriving acute TRVs from chronic TRVs is not ideal and, where appropriate and possible, we would prefer to derive an acute TRV from a study with an acute exposure duration" (ODEQ, 2023, p. 2).

In consideration of all the information, we recommend that ODEQ withdraw the proposed acute TRVs for insoluble and soluble Cr(III).

Withdraw Proposed Insoluble Chronic TRV For Cr(III)

We request that the chronic TRV for insoluble Cr(III) be withdrawn because, similar to the acute TRV, ATSDR did not find any chronic inhalation exposure studies for Cr(III) alone. California's Office of Environmental Health Hazard Assessment (OEHHA), another authoritative source, also did not develop a chronic reference exposure level (REL) for insoluble Cr(III) because the data were insufficient, and no dose-response was observed in the key study (Derelanko et al., 1999).

For chronic effects via inhalation exposure, ATSDR found there were "no studies evaluating the effects of chronic-duration inhalation exposure of animals to chromium(III) compounds alone" (ATSDR, 2012, p. 42). ATSDR evaluates chronic exposure for MRLs to represent "exposure to a chemical for 365 days or more" (ATSDR, 2012, p. 498). Data on mixtures of CrVI and insoluble CrIII are "not appropriate as the basis for a chronic-duration inhalation MRL for chromium(III) compounds due to concomitant exposure to chromium(VI)" (ATSDR, 2012, p. 42). As such, MRLs for chronic exposure to insoluble Cr(III) were not developed by ATSDR, and TRVs should not be pursued at this time by ODEQ. ODEQ outlines situations in which ODEQ, in consultation with the ATSAC, might derive a TRV. Insoluble Cr(III) does not meet these criteria, since it is of very low innate toxicity. It is highly unlikely to pose a health hazard to Oregonians, and there is inadequate scientific data available to derive a value.

When OEHHA (2022), set the chronic REL for soluble Cr(III), OEHHA recognized that the effects reported by Derelanko et al. (1999) for insoluble chromic oxide exposure were due to insoluble particle loading, resulting in no-dose response (OEHHA, 2022, Table 12). OEHHA elected to not set a chronic REL—actually any REL—for insoluble chromium based on this study. OEHHA determined that, overall, the data for insoluble chromium

were “insufficient to support the derivation of a REL” (OEHHA, 2022, p. 101). Again, by proposing values for insoluble Cr(III), ODEQ is not following the determination of OEHHA, one of its authoritative sources.

Cr(III) in Alloy Form Should be Exempted From TRVs

OEHHA states that the RELs for Cr(III) “are not applicable to Cr alloys (e.g., alloyed with iron, copper, or cobalt) and other chemicals comprised of Cr and another heavy metal (e.g., Cr-nickel eutectics) or metalloid because they often exhibit different toxicities when compared to other inorganic compounds containing Cr as the sole metal” (OEHHA, 2022, p. vii). If ODEQ persists in setting soluble or insoluble Cr(III) TRVs, despite the findings of the authoritative sources and our comments herein, the same exemption stated by OEHHA for chromium containing alloys and other metalloids should be included and Cr in alloys and metalloids should be exempt from CAO regulation.

In summary, the chronic noncancer insoluble Cr(III) TRV and both the insoluble and soluble acute non-cancer TRVs are, not supported by the authoritative sources cited for several reasons, and should not be recommended by ODEQ and OHA.

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To:	J.R. Giska and Apollonia Goeckner, Oregon Department of Environmental Quality; Holly Dixon, PhD, Oregon Health Authority
From:	Deborah Proctor and Ann Verwiel, ToxStrategies LLC
Subject:	**Evaluation of Draft Proposed Updates to Cobalt TRVs for Cleaner Air Oregon**

To support the current review of the inhalation toxicity reference values (TRVs) used in the Cleaner Air Oregon (CAO) program, we have evaluated the draft proposed TRVs that Oregon Department of Environmental Quality (ODEQ) and Oregon Health Authority (OHA) have presented to the Air Toxics Science Advisory Committee (ATSAC) for its consideration for soluble and insoluble cobalt. This memorandum discusses in more detail the proposed soluble and insoluble cobalt TRVs, and **Table 1** below briefly summarizes our conclusions and recommendations, which are discussed in more detail in this memorandum.

Table 1. Summary of Recommendations for Proposed Updates to Cobalt TRV

ODEQ Proposed TRVs (µg/m^3)	Recommendations for Updates to Proposed TRV
Cancer TRV Soluble: 0.00013 Insoluble: 0.0001 **Chronic TRV** Soluble: 0.1 Insoluble: 0.1 **Acute TRV** Soluble: 0.3 Insoluble: 0.3	• Withdraw the insoluble cancer, non-cancer chronic, and non-cancer acute TRVs because they are based on studies of exposure to cobalt forms that are freely soluble in lung biological fluids. The cobalt TRVs should be limited and specific to soluble cobalt forms. • Clarify in the cobalt TRV documentation that cobalt solubility in biological fluids (referred to as inhalation bioaccessibility), not water solubility, is a key determinant of cobalt's potential cancer and non-cancer toxicity. • Specify that *in vitro* inhalation bioaccessibility tests may be used with the soluble cobalt TRVs in the CAO program to assess cobalt's potential to be bioavailable and potentially pose a health concern. • Consistent with the guidance of the authoritative source, California's Office of Environmental Health Hazard Assessment (OEHHA), explicitly exempt cobalt in alloy form (e.g., steel) from the TRVs for insoluble and soluble cobalt because cobalt in alloy form is not soluble in biological fluids.

Specifically Define Cobalt Solubility in TRV Documentation

Setting proposed TRVs for soluble and insoluble cobalt forms raises the question of how solubility is defined. Importantly, water solubility is not the determining factor dictating toxicity; rather, it is solubility in lung biological fluids (NTP, 2021). As discussed below, we recommend that additional clarity be added to the cobalt solubility definition to specify that it means solubility in simulated lung biological fluids[1]. Without further clarification, solubility likely may be assumed to refer to water solubility.

This important point seems to be lost in insoluble cobalt TRV development because all the insoluble cobalt TRVs are based on studies of cobalt freely soluble in simulated lung fluids. For example, the insoluble cancer TRV is based on exposure to metallic cobalt, which is water insoluble but 100% soluble (or bioaccessible) in lung lysosomal fluid (NTP, 2021). Distinguishing water insoluble cobalt metal from other water insoluble cobalt forms, such

[1]Simulated lung fluids include lysosomal, interstitial, and alveolar fluids. Extraction tests simulating lung conditions are available (e.g., Henderson et al., 2014).

as cobalt in an alloy form, is important, since those forms are not soluble in water or biological fluids, and, as such, are not bioavailable or carcinogenic in the lung.

As reviewed by the National Toxicology Program (NTP), cobalt carcinogenicity and toxicity are due to the availability of cobalt ions *in vivo* (NTP, 2016; 2021). Mechanistic toxicology research indicates that the release of cobalt ions *in vivo* is a key event for cobalt-induced carcinogenicity, and that cobalt metal and cobalt compounds that release cobalt ions *in vivo*, regardless of their solubility in water, act by similar modes of action to cause cancer (NTP, 2021). The NTP cancer bioassays conducted in rats and mice using soluble cobalt sulfate (NTP, 1998) and water-insoluble cobalt metal (NTP, 2014) both showed an increased occurrence of tumors, and are the underlying basis for OEHHA's risk assessment and ODEQ's cancer-based TRVs. Importantly, as noted above, although pure cobalt metal is not soluble in water, it is soluble in simulated lung fluids, and thus considered 'bioaccessible' upon inhalation exposure. NTP (2021) reports that while the water solubility of cobalt metal is 0.00029 g/cc, it is 100% bioaccessible in both gastric and lung lysosomal fluids.

As such, the cobalt bioavailability can be conservatively predicted by its solubility in biological fluids or its bioaccessibility (Heim et al., 2020). Cobalt forms that are not soluble in biological solutions are generally not considered to pose a cancer hazard (Taxell and Huuskonen, 2022), and cobalt forms have been categorized based on their solubility in lung fluids for the purpose of read-across (Verougstraete et al., 2022). In short, assessing cobalt's potential toxicity and carcinogenicity based on *in vitro* bioaccessibility tests in simulated lung fluid is well established. Therefore, should ODEQ decide to retain its soluble cobalt TRVs, it should clarify that cobalt solubility is clearly defined as solubility in lung biological fluids. Including TRVs for 'insoluble' cobalt in the CAO program is unnecessarily confusing.

Withdraw Proposed Insoluble Cobalt TRVs

Cancer TRV

As described in the previous paragraph, the proposed cancer TRV for insoluble cobalt is not necessary because the proposed value is nearly identical to the cancer TRV for soluble cobalt (0.0001 compared to 0.00013 $\mu g/m^3$) For this reason, the proposed cancer TRV for insoluble cobalt should be withdrawn, and only a value for cobalt that is soluble in biological fluids should be proposed.

Non-cancer Acute Insoluble Cobalt TRV

The proposed cobalt acute TRV for insoluble cobalt is based on the 2024 Agency for Toxic Substances and Disease Registry's minimum risk level (ATSDR MRL), which is from a study in which rats were exposed to cobalt sulfate heptahydrate, a freely soluble cobalt form. This MRL is not applicable to insoluble cobalt, and should only be used for soluble cobalt.

Non-cancer Chronic Insoluble Cobalt TRV

Further, the chronic insoluble TRV is based on a study of diamond polishers exposed to cobalt metal powder (ATSDR, 2024). Specifically, the proposed chronic non-cancer cobalt TRV is based on a study of diamond polishers who were exposed to cobalt sintered onto microdiamonds used as polishing wheels (Nemery et al., 1992; ATSDR, 2024). Cobalt solubility in biological fluids in this form is not known to us; however, ATSDR (2024) reports that airborne cobalt exposures among diamond cutters in this study was correlated with urine cobalt levels, indicating that cobalt was absorbed systemically and was bioavailable. Diamond-cutting wheels are made of sintered metals, including cobalt metal powder, and previous studies have shown that cobalt metal powder is highly bioaccessible in lysosomal lung fluid (Stopford et al., 2003; Hillwalker and Anderson, 2014). Using this study to set an insoluble chronic TRV for cobalt, then, is inappropriate.

As such, none of the proposed insoluble TRV values are applicable to cobalt forms that are insoluble in biological fluids. As discussed above, cobalt toxicity is determined by the release of cobalt ions in biological fluids; thus, the acute and chronic non-cancer TRVs, as well as the insoluble cancer TRV, are, at most, only relevant to cobalt soluble in lung biological fluids, and TRVs based on testing of soluble cobalt forms should not be applied to insoluble cobalt. For clarity, the insoluble cobalt TRVs should be removed from the proposed TRVs, and only the soluble cobalt TRVs included. Further, ODEQ should specify that *in vitro* bioaccessibility tests, such as the methods provided in Henderson et al. (2014), may be used to evaluate cobalt solubility in lung biological fluids for the CAO program.

Cobalt in Alloy Form Should be Exempted From TRVs

The primary end use of cobalt in the United States (US) is for superalloy production: 4,040 metric tons are used annually, which is 48% of all cobalt end uses in the US. Use in other alloys and steels is reported as 8.3% and 6.5%, respectively (NTP, 2021). Based on US production data, airborne emissions of insoluble cobalt as a superalloy and/or stainless steel likely represent a significant fraction of insoluble cobalt. Thus, cobalt emissions in Oregon are far more likely to contain insoluble cobalt in an alloy form rather than pure cobalt metal.

When cobalt is bound in an alloy, its bioaccessibility is highly limited; Hillwalker and Anderson (2014) report that cobalt's bioaccessibility in stainless steel and carbon steel in simulated lung lysosomal fluid were all non-detectable (<0.00027%). As such, unlike water soluble cobalt metal, insoluble cobalt in alloys does not pose a potentially significant non-cancer or cancer hazard because it does not readily release cobalt ions in biological fluids. Importantly, OEHHA, the authoritative source for the soluble and insoluble cobalt inhalation TRVs for cancer, specifically exempts cobalt in alloys and steel from its inhalation unit risk values. OEHHA states: "The cobalt [inhalation unit risks] IURs do not apply to steel and metal alloys that contain cobalt. In addition, the alloy-like hard metals, particularly cobalt-tungsten carbide hard metal, are not included." (OEHHA, 2023, p iii).

Cobalt in alloys is not soluble in simulated lung lysosomal fluids, and does not release cobalt ions *in vivo* upon exposure. The soluble cobalt TRVs should therefore be specifically amended and clarified to exempt cobalt alloy from the regulation.

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Technical Memorandum

September 30, 2025

To:	J.R. Giska and Apollonia Goeckner, Oregon Department of Environmental Quality; Holly Dixon, PhD, Oregon Health Authority
From:	Deborah Proctor and Ann Verwiel, ToxStrategies LLC
Subject:	**Evaluation of Draft Proposed Updates to Fluoride and Inorganic Compounds Acute TRV for Cleaner Air Oregon**

To support the current review of the inhalation toxicity reference values (TRVs) used in the Cleaner Air Oregon program, we have evaluated the draft proposed TRVs that Oregon Department of Environmental Quality (ODEQ) and Oregon Health Authority (OHA) have presented to the Air Toxics Science Advisory Committee (ATSAC) for its consideration for fluoride. This memorandum discusses in more detail the proposed acute TRV for fluoride and inorganic compounds. **Table 1** below briefly summarizes our conclusions.

Table 1. Summary of recommendations for proposed updates to fluoride TRVs

ODEQ Proposed TRV (µg/m^3)	Recommendations for Updates to Proposed TRV
Acute TRV **16**	• Revise the acute TRV to specify the toxic air contaminant (TAC) name as hydrogen fluoride or withdraw the proposed TRV for acute noncancer effects for fluorides and inorganic compounds because the underlying key toxicology studies are based on hydrogen fluoride and are not applicable to all forms of fluoride. • If the proposed acute TRV for fluoride and inorganic compounds is not revised or withdrawn, ODEQ should add a note to any final rule in which this value is adopted to clarify the limited applicability of the acute TRV to hydrogen fluoride. In the ATSAC Workbook 2: TRV Derivation provided by ODEQ/OHA to support derivation of the new TRVs, there is a note for the proposed acute TRV, which references the Office of Environmental Health Hazard Assessment (OEHHA)'s groupings of fluoride compounds to which the acute TRV, derived from the Agency for Toxic Substance Disease Registry (ATSDR)'s MRL for hydrogen fluoride, should apply. The note states: "No proposed change to acute TRV, however there are modifications to which fluoride compounds it should be applied to. This acute TRV should be applied to hydrogen fluoride, modified hydrogen fluoride, and selenium hexafluoride according to OEHHA groupings. We propose to apply the acute TRV derived from ATSDR according to OEHHA's groupings." The above note was not included in ATSAC Workbook 1: DEQ Proposed TRVs. This appears to have been in error. To reconcile the distinction between fluorides in general and hydrogen fluoride, a similar note regarding the limited applicability of the proposed acute TRV should be added to the proposed acute TRV to hydrogen fluoride.

ODEQ has adopted the acute minimal risk level (MRL) published by ATSDR for hydrogen fluoride as the proposed acute TRV for fluorides. The MRL is based on studies by Lund et al. (1997, 1999).

Lund et al. (1997) evaluated groups of seven to nine healthy, nonsmoking males (21 to 44 years of age) who were exposed to hydrogen fluoride for 1 hour. Test subjects performed a 15-minute ergometric test at a fixed work load of 75 W[1] over the last 15 minutes of their 1-hour exposure period. An average of the exposure concentration range was used to represent the exposure (0.4 mg/m^3, 1.7 mg/m^3, and 3.9 mg/m^3). No significant exposure-related alterations in lung function were observed; however, statistically significant increases in qualitative upper airway symptom scores and total symptom scores were observed in the low and high exposure groups but not in the middle group.

[1] In physics, the symbol "W" represents work, which is the force applied times the distance travelled, and is measured in joules (J) or newton-meters (N-m).

Lund et al. (1999) evaluated 15 healthy, nonsmoking males (21 to 44 years old) who were exposed to hydrogen fluoride for 1 hour. Again, test subjects performed a 15-minute ergometric test at a fixed work load of 75W over the last 15 minutes of their 1-hour exposure period. There were three exposure groups represented by the average exposure concentrations (<0.6 mg/m^3, 1.6 mg/m^3, and 3.9 mg/m^3). Bronchoalveolar lavage (BAL) was performed at least 3 weeks before and 24 hours after the exposure. The BAL results before and after the exposure were compared, and the test subjects served as their own controls. Indications of an inflammatory response were observed. For example, there was a significant increase in CD3-positive cells in the bronchial portion in the intermediate and high exposure groups. For the bronchoalveolar region, there was a significant increase of CD-3 positive cells in the high exposure group.

Based on these findings, the lowest dose in the 1997 study (0.4 mg/m^3) was identified as a lowest-observed-adverse-effect level (LOAEL) based on the symptom scores. This value was converted in the ATSDR calculations to 0.38 mg/m^3 measured as fluoride. ATSDR applied uncertainty factors of 3 for using a LOAEL and 10 for human variability for a total uncertainty factor of 30. The acute MRL for hydrogen fluoride measured as fluoride is 0.02 ppm or 0.016 mg/m^3.

These Lund et al. studies were conducted using hydrogen fluoride, and ATSDR lists hydrogen fluoride in the ATSDR acute MRL worksheets, regardless of the conversion to measurements of fluorine ion using atomic weight in their calculations. Indeed, ATSDR explained that "no inhalation MRLs were developed for fluoride" (ATSDR, 2003, pg. 22). Notably, ATSDR published independent MRLs for chronic oral exposure for fluoride and acute inhalation exposure for fluorine (0.01 ppm)[2] (ATSDR, 2003; Appendix A) that supports the conclusion that the hydrogen fluoride MRL is not intended to be applied to other inorganics containing fluoride. Therefore, it is not appropriate to apply the inhalation MRL for hydrogen fluoride to a broad category referencing all inorganic fluorides. ODEQ should change the proposed category name to hydrogen fluoride or withdraw the acute TRV for fluorides. This change would be more consistent with emission reporting practices, where hydrogen fluoride is distinguished from other fluoride emissions.

As indicated in the table above, ODEQ does have a note in their ATSAC Workbook 2: TRV Derivation that correctly limits the applicability of the current acute TRV for fluoride to hydrogen fluoride, modified hydrogen fluoride, and selenium hexafluoride. While changing the TAC name or withdrawing the proposed TRVs for acute noncancer effects for fluorides and inorganic compounds would be clearest, a note limiting applicability of the proposed acute TRV would also provide an appropriate clarification for this TRV.

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[2] ODEQ also published an acute TRV for fluorine but used the hydrogen fluoride MRL (0.016 mg/m^3) rather than the specific acute MRL for fluorine (0.01 ppm or 0.008 mg/m^3).

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Technical Memorandum

September 30, 2025

To:	J.R. Giska and Apollonia Goeckner, Oregon Department of Environmental Quality; Holly Dixon, PhD, Oregon Health Authority
From:	Deborah Proctor and Ann Verwiel, ToxStrategies LLC
Subject:	**Evaluation of Draft Proposed Update to Hydrogen Chloride Acute and Noncancer Chronic TRVs for Cleaner Air Oregon**

To support the current review of the proposed draft inhalation toxicity reference values (TRVs) for use in the Cleaner Air Oregon program, we have evaluated the draft proposed TRVs for acute and chronic non-cancer exposure for hydrogen chloride (HCl) that Oregon Department of Environmental Quality (ODEQ) and Oregon Health Authority (OHA) have presented to the Air Toxics Science Advisory Committee (ATSAC) for its consideration. **Table 1** briefly summarizes the proposed TRVs and the conclusions from our review, which are laid out in more detail in this memorandum.

Table 1. Summary of Recommendations for Proposed Update to Hydrogen Chloride TRV

Proposed TRV	Recommendations for Updates to Proposed TRVs
Acute TRV: 88 µg/m^3	**Acute:** We recommend maintaining the current acute TRV of **2100 µg/m^3** based on the value published by an ODEQ Authoritative Source, California's Office of Environmental Health Hazard Assessment (OEHHA). ODEQ's proposed acute TRV used OEHHA's TRV but added a time adjustment factor of 1/24 or 0.042 to calculate the proposed TRV. No other Authoritative Source has adopted the proposed acute TRV of 88 µg/m^3. Federal agencies, such as the National Institute of Occupational Health and Safety (NIOSH) and the National Research Council (NRC) and the scientific literature (Shusterman et al. 2008) do not consider it appropriate to use a time adjustment for 1-hour to 24-hour exposures for sensory irritation effects, which are considered concentration dependent, and are not expected to worsen with extended exposure time.
Chronic TRV: 9 µg/m^3	**Chronic:** We recommend that ODEQ adopt a chronic TRV of **30 µg/m^3** to address issues with uncertainty factors and animal to human adjustment factors in the current and proposed TRVs pursuant to OAR 340-247-0030(1)(a) and in consultation with ATSAC. EPA's Integrated Risk Information System's (IRIS's) reference concentration (RfC) was developed in 1991 (EPA, 1991) and last updated in 1995, and the proposed TRV based on the 1999 OEHHA chronic reference exposure level (REL) for HCl are based on the same study (Sellakuman et al., 1985). This study reported a lowest-observed-adverse effect level (LOAEL) of 15 mg/m^3,[1] which was adjusted for discontinuous exposure to 2.7 mg/m^3 for mild hyperplasia observed in rats.[2] While EPA applied a total 300-fold uncertainty factor (UF), OEHHA applied a 100-fold factor. The difference in the UFs was the LOAEL to no-observed-adverse effect level (NOAEL) UF. EPA used a factor of ten, and OEHHA used a factor of three because the effects were mild and observed at low frequency, supporting a lower UF. Both the RfC and the REL predate EPA's current guidance regarding using the Regional Gas Dose Ratio (RGDR) for extrathoracic effects, which is one (1) and assumes exposure equivalency between species (EPA, 2012).[3] Using the same point of departure (POD) (2,700 µg/m^3), OEHHA's total UF of 100, and the RGDR of 1 based on current EPA guidance—ODEQ's chronic TRV for HCl should be 30 µg/m^3.[4]

[1] The LOAEL is 10 ppm converted to 15 mg/m^3 based on HCl molecular weight of 36.46 and assuming a temperature of 25 C and pressure of 760 mmHg (36.46/24.45 = 1.5).
[2] Experimental conditions were for lifetime exposures of 6 h/day for 5 days per week.

Acute Hydrogen Chloride (HCl) TRV

HCl is a respiratory and eye irritant gas that has corrosive properties at higher concentrations (NIOSH, 2023). The current HCl acute TRV is based on the OEHHA acute reference exposure level (REL: 2,100 μg/m^3), which is for a 1-hour exposure duration. However, in the proposed TRVs, ODEQ applied a time adjustment factor to the OEHHA REL to extrapolate from a 1-hour exposure duration to a 24-hour exposure. Specifically, ODEQ applied a time-adjustment factor of 0.042, which is 1/24 hrs. This adjustment is based on Haber's Law, which states that for a constant given effect, the dose is proportionately equal to the exposure concentration and exposure duration ($c * t = k$). OEHHA, which is an Authoritative Source, did not make this adjustment. That is likely because the relationship presumed in Haber's Law between exposure concentration and duration has been disproven for many sensory irritants (Shusterman et al., 2008),[5] and, in most cases, the concentration-time relationship is modeled over a relatively narrow time parameter using a more generalized power law model ($c^n * t = k$) rather than Haber's Law *per se* (Schusterman et al., 2008; Miller et al., 2000).

Background on Study Used as the Basis for the Acute TRV

The acute REL established by OEHHA is based on the Stevens et al. (1992) study of ten asthmatics aged 18 to 25 years old. The asthmatics were exposed for 45 minutes through a half-face mask, and no effects were absorbed at either exposure concentration. Thus, the NOAEL for the study was the highest exposure of 1.8 ppm. Specific effects considered included:

- Forced expiratory volume in one second
- Forced expiratory volume
- Maximal flow at 50% and 75% of expired vital capacity
- Total respiratory resistance and peak flow
- Nasal work of breathing
- Self-reported symptoms of upper and respiratory irritation

During the study, two HCl doses were evaluated (0.8 ppm and 1.8 ppm), for a total of 45 minutes on three individual days, each one week apart. Each included 30 minutes of exercise. No adverse effects (including irritation or asthma symptoms) were observed at either dose. OEHHA adjusted the NOAEL (1.8 mg/m^3) for 45-minute exposures to account

[3] EPA applied an RGDR of 2.27, modeling both the extrathoracic (ET) and tracheal bronchial (TB) regions, and OEHHA applied an RGDR of 0.32 using EPA's 1994 guidance. Since 2012, EPA has recommended an RGDR of 1 for ET effects based on updated modeling. It is more conservative to use an RGDR of 1 for ET than to calculate an RGDR for both the ET and TB regions. We know of no more recent examples, since the 2012 guidance, where EPA combined the two regions, and as such, we recommend using the more conservative RGDR of 1 based on ET effects.

[4] POD/UF *RGDR = TRV, so 2700 μg/m^3 /100 *1 = 27 μg/m^3 rounded to 30 μg/m^3.

[5] The Schusterman et al. (2008) study—Does Haber's Law Apply to Human Sensory Irritation? *Inhalation Toxicology* 18:7: 457-471—was commissioned and co-authored by OEHHA.

for 1-hour exposures to 1.4 ppm (2.1 mg/m^3) using the modified Haber's Law formula and an exponent of one (OEHHA, 2008). Because the study was in sensitive human subjects, an uncertainty factor of one was applied.

Rationale for Retaining OEHHA's Acute REL as the Acute TRV

Application of Haber's Law to the acute REL for HCl is not appropriate because HCl is absorbed and reacts rapidly, and, consistent with other sensory irritant responses, prolonged exposures are not expected to result in enhanced effects (NRC, 2004; Shusterman et al., 2008).

OEHHA's guidance on applying Haber's Law is specific to setting 1-hour acute RELs, and the default approach for extrapolating from exposures less than one hour to one hour involves applying an exponent (n) of one, in the modified Haber Law equation $c^n * t = k$ (see OEHHA, 1999 for detailed discussion). Using an exponent of 1, the chemical's toxicity is equally dependent on time and concentration over this short exposure duration. Using an exponent of one is recognized by OEHHA as conservative, and time-period specific (OEHHA, 1999). OEHHA does not set guidelines for 24-hour exposures, so OEHHA does not discuss a general rule to follow for extrapolating from 1 to 24 hours.

In the case of HCl, it is not appropriate for ODEQ to use Haber's Law (or modified Haber's Law with an exponent of 1) when extrapolating from 1 to 24 hours. As discussed below, federal agencies have set health guidelines based on the potential for irritant effects for HCl based on the exposure concentration without accounting for increasing time of exposure. HCl does not accumulate, it is absorbed and reacts rapidly, and, as such, its irritant effects are more highly dependent on concentration than duration (or time) of exposure (NRC, 2004; NIOSH, 2023)

Further, a significant body of literature exists supporting that Haber's Law does not apply to irritant gases like HCl. For example, Shusterman et al. (2008), who evaluated chlorine, states, "The studies reviewed, with few exceptions, showed monotonic dose-response relationships for concentrations, but time-response relationships showed either asymptotic (plateauing) or frank biphasic (drop-off) behavior" (p. 468).

It should also be noted that Dr. John Budroe on the Air Toxics Science Advisory Committee (ATSAC) commented that time adjustments do not apply to chemicals that act by sensory irritation at the February 7, 2025 ATSAC meeting (approximately at 1 hour and 46 minutes of the recording for the February 7, 2025 meeting https://www.youtube.com/watch?v=FKekvexRvqQ).

National Research Council's Acute Exposure Guideline Levels (AEGLs) and NIOSH's Immediately Dangerous to Life and Health (IDLH) (External Review Draft) Support No Haber's Law Time Adjustment

In 2004, the National Research Council (NRC) of the National Academies of Sciences, Engineering, and Medicine developed Acute Exposure Guideline Levels (AEGLs) for HCl (NRC, 2004). The NRC AEGL-1 values, for 10 minutes, 30 minutes, 1-hour, 4-hour and 8-hour[6] exposures, are all based on the NOAEL of 1.8 ppm from Stevens et al. (1992), with no time adjustment. NRC states, "The no-effect level was held constant across the 10- and 30-min and 1-, 4-, and 8-h exposure time points. That approach was considered appropriate because mild irritant effects generally do not vary greatly over time, and the end point of a no-effect level in a sensitive population is inherently conservative" (NRC, 2004, p. 101). NRC provides a plot of AEGLs for HCl based on human and animal data, reproduced here as **Figure 1**. As shown in **Figure 1**, a plateau of concentration-dependent effects is expected for durations exceeding 60-minutes. Thus, although OEHHA corrected the NOAEL for respiratory effects among exercising asthmatics from 45-minutes to 60-minutes to set the 1-hour acute REL consistent with its guidance (OEHHA, 1999), a further time adjustment to extrapolate from 1-hour to 24-hour exposures is not necessary or appropriate.

Figure 1. Toxicity Data and AGELs for HCL from Animal and Human data (Figure 2-1 from NRC, 2004)

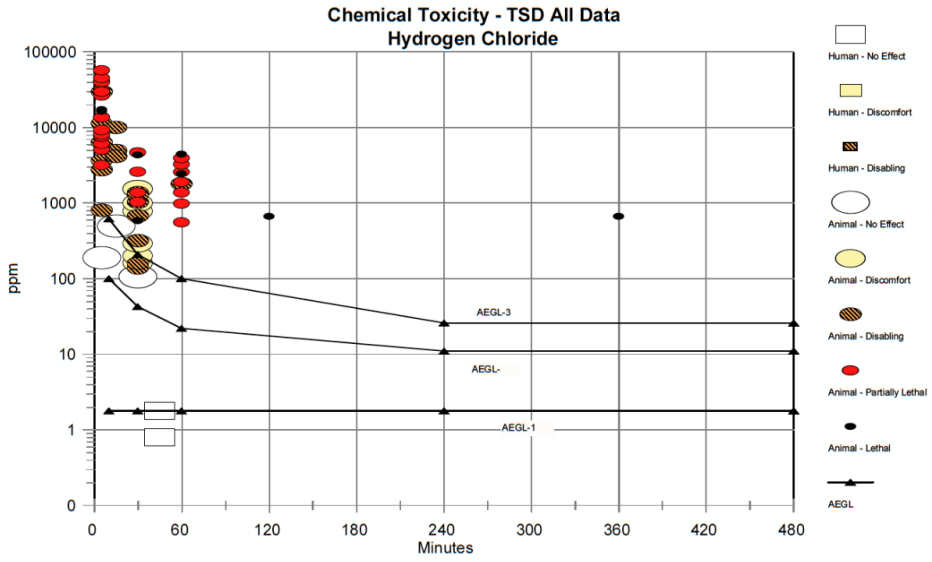

FIGURE 2-1 Toxicity data and AEGL values for hydrogen chloride. Toxicity data include both human and animal studies.

[6] AGELs are set for exposure durations up to eight hours. AGEL-1s are for non-disabling effects; AGEL-2s are for disabling effects, and AGEL-3 values are for lethal effects.

The External Review Draft Immediately Dangerous to Life and Health (IDLH) Value Profile of Hydrogen Chloride (NIOSH, 2023) also supports this position. The IDLH was based on a study indicating decreased respiration rates in mice exposed to HCl (Barrow et al., 1977). NIOSH states that "The RD_{50} value [dose at which respiration rate is decreased by 50%] of 309 ppm reported by Barrow et al. (1977) was obtained from 10-min exposures in mice, during which the maximum decrease in respiratory rates was observed very quickly, within minutes of exposure. This is consistent with other reports discussed in Section 3.4.2 that observed rapid attainment of maximal respiratory depression within minutes of exposure, after which respiration plateaus or recovers" (NIOSH 2023, p. 15). The NIOSH authors recognized that the maximum effect is achieved based on the concentration administered and that the exposure duration is not a significant factor in causing the effect. Like the NRC graph in Figure 1, the effect plateaus (i.e., does not worsen) with extended exposure duration. Accordingly, as the concentration alone is determinative of the effect and a plateau is observed despite longer exposure, Haber's law is inapplicable to the study supporting the IDLH for HCl.

In summary, the scientific literature and other regulatory guidance regarding HCl exposure do not support applying Haber's Law to the OEHHA acute REL for HCl. ODEQ should maintain the current TRV based on the OEHHA acute REL of 2100 $\mu g/m^3$.

Chronic HCl TRV

The current chronic HCl TRV is based on the EPA RfC of 20 $\mu g/m^3$, which was last updated in 1995. ODEQ is proposing to update to the OEHHA REL of 9 $\mu g/m^3$, which was set in 1999 and republished in 2008. As described in Table 1, EPA and OEHHA relied on the same study, but used different uncertainty factors and neither agency used the current approach for setting HCl RGDRs to extrapolate from animal data to human exposure. As explained below, a more appropriate chronic HCl can be developed by reviewing these two factors.

Both the current and proposed TRVs are based on the same lifetime rat exposure study (Sellakuman et al., 1985) that reported a LOAEL of 15 mg/m^3 for exposures of 6 hrs/day, 5 days per week, adjusted to continuous exposure (2.7 $\mu g/m^3$). In this study, hyperplasia of the nasal mucosa, larynx, and trachea were observed in rats. While EPA applied a total 300-fold UF, OEHHA applied a 100-fold uncertainty factor, resulting in a LOAEL to NOAEL UF of ten for EPA, and three for OEHHA. Because the effects were mild and only observed in 30% of tested animals, OEHHA used the lower UF. OEHHA and EPA applied different RGDRs to adjust for the difference in toxicokinetics between rats and humans using the EPA guidance available at the time (EPA, 1994). Specifically, the RGDR applied by OEHHA was 0.32 (extrathoracic effects), and the RGDR applied by EPA was 2.27 (for extrathoracic and tracheal bronchiole effects without providing a basis for the calculation).

However, both the RfC and the REL for HCl predate EPA's most current guidance, *Advances in Inhalation Gas Dosimetry for Derivation of a Reference Concentration (RfC) and use in Risk Assessment*, regarding using the RGDR (EPA, 2012). In 2012, EPA improved on modeling the extrathoracic region using physiologically-based pharmacokinetic (PBPK) modeling. EPA concluded, "One of the principal findings from these [PBPK models] is that internal dose equivalency in the ET [extrathoracic] region for rats and humans is achieved through similar external exposure concentrations" (EPA, 2012, p. xiv). Further, EPA stated, "A primary finding for gas deposition in the ET region is the internal target-tissue dose equivalency between humans and rats is achieved through equivalency at the level of external applied concentration, i.e., for both rats and humans, the same external air concentration, rather than one adjusted by V_E/SA [Ventilation rate/Surface Area] leads to the similar internal target-tissue dose to the URT [upper respiratory tract]" (EPA, 2012, p. xvi). As such, EPA recommends using an RGDR of one for effects to the extrathoracic region.

Finally, as evidence of this approach being applied in current risk assessments, EPA recently (2024) used the RGDR of one to evaluate RfCs for formaldehyde based on nasal metaplasia in rats (see EPA, 2024, pp. 5-39 for discussion). Similar to HCl, formaldehyde is a highly water soluble and reactive gas that causes effects in rats in the extrathoracic region. As such, the current state of the science and regulatory methods support an RGDR of one for setting a chronic HC1 TRV.

Using the same POD (2700 μg/m^3), OEHHA's total UF of 100, and EPA's current RGDR of one (EPA, 2012), the TRV should be 30 μg/m^3. Therefore, in consultation with ATSAC, we recommend that ODEQ set a TRV for chronic HCl exposure of 30 μg/m^3.

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Technical Memorandum

September 30, 2025

To:	J.R. Giska and Apollonia Goeckner, Oregon Department of Environmental Quality; Holly Dixon, PhD, Oregon Health Authority
From:	Deborah Proctor and Ann Verwiel, ToxStrategies LLC
Subject:	**Evaluation of the Acute TRV for Lead for Cleaner Air Oregon**

To support the current review of the inhalation toxicity reference values (TRVs) used in the Cleaner Air Oregon program, we have evaluated the acute TRV for lead that the Oregon Department of Environmental Quality (ODEQ) and Oregon Health Authority (OHA) have been using. We are concerned that ODEQ has not taken the opportunity, while proposing other new and revised TRVs, to develop a more appropriate acute TRV for lead; rather ODEQ has proposed to continue to use the National Ambient Air Quality Standards (NAAQS) for lead (0.15 $\mu g/m^3$) as the acute TRV. The NAAQS is intended to be applied to a 3-month average concentration and is not appropriate for the 24-hour duration of an acute TRV under Cleaner Air Oregon. The NAAQS is also used as the chronic TRV, which is a more relevant application of the NAAQS.

No authoritative source applies the NAAQS values to assess or regulate acute exposures to lead. And, the intent of Oregon's acute toxicity values is to represent toxicity resulting from short-term (24-hour) exposures, not 3-month averages. Therefore, Oregon's continued application of the 3-month average NAAQS for a 24-hour period is not appropriate. According to DEQ's Proposed TRV Update and Selection Process for ATSAC Review,[1] acute TRVs "represent air concentrations below which noncancer health effects are not expected over 24 hours or less from breathing air." While using a value for 3-month exposures to address effects from exposures lasting 24 hours or less would be conservative, that does not make it necessary or appropriate. DEQ acknowledges that "deriving acute

[1] Department of Environmental Quality. 2025. Proposed TRV Update and Selection Process for ATSAC Review. https://www.oregon.gov/deq/aq/Documents/ProposedTRVforATSAC.pdf

TRVs from chronic TRVs is not ideal and, where appropriate and possible, they would prefer to derive an acute TRV from a study with an acute exposure duration."[2]

Fortunately, as described below, a new alternative approach to setting an acute TRV for lead exists because EPA has updated its blood lead modeling software to allow for assessing single day exposures (EPA 2025). We recommend that, consistent with OAR 340-247-0030(1)(a), ODEQ revise the acute lead TRV in accordance with this new approach, in consultation with the Air Toxics Scientific Advisory Committee (ATSAC).

Lead exposure, pharmacokinetics, and toxicity have been well-studied, and the US Environmental Protection Agency (EPA), an authoritative source, has developed exposure models that predict blood lead levels (BLLs) for humans from birth through an entire lifetime, associated with various exposure routes and scenarios (EPA 2021; 2024; 2025). Using EPA's guidance, blood lead biokinetic modeling was performed to predict the concentration in air for one day of exposure that would result in an increase in blood lead of 1 micrograms per deciliter (µg/dL). The California Office of Environmental Health Hazard Assessment (OEHHA), an authoritative source, uses 1 µg/dL as the threshold for source-specific incremental increase in BLL for protection of school children and fetuses, who are more sensitive to lead exposure than adults (OEHHA, 2007).

In summary, we used the most current EPA blood lead model, the All-Ages Lead Model (AALM; v. 3.1), to predict blood lead concentrations from 24-hour exposures to lead in air.[3] As demonstrated by the model, for the most sensitive age group (0-1 year), a 24-hour lead concentrations in air of 3.9 µg/m^3 is predicted to increase BLL over background by 1 µg/dL. The AALM model also predicts that after a 24-hour exposure at 3.9 µg/m^3, BLL for the 0–1-year-old infant returns to baseline within 20 days.

We recommend that ODEQ, in consultation with the ATSAC, propose setting 3.9 µg/m^3 as the acute TRV for lead. Setting this value as the acute TRV would not change the requirement to meet the NAAQS on a 3-month average or the chronic TRV on an annual basis. Specifically, assuming average concentrations are at the upper bound of background levels (0.01 µg/m^3 is the upper bound of background levels reported in the US which range from 0.002-0.01 µg/m^3; EPA 2025) and the concentration for one day (24 hours) equals the proposed acute TRV of 3.9 µg/m^3, the three month average concentration would only be 0.05 µg/m^3, which is well below the NAAQS and chronic TRV. Further, the long-term criteria (0.15 µg/m^3 three-month rolling average NAAQS or ODEQ's chronic TRV) limit the number of days that lead concentrations could approach the acute TRV without these long-term averages being exceeded. Thus, collectively, the proposed revised acute TRV could work alongside the chronic TRV and NAAQS to be protective for lead exposure in Oregon across acute and chronic exposure conditions. Our key points are summarized in Table 1 below.

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[2] Ibid.

[3] EPA's previous lead exposure model for children, Integrated Exposure Uptake Biokinetic (IEUBK) model, is still in use for some applications, such as Superfund. https://www.epa.gov/superfund/lead-superfund-sites

Table 1. Summary of recommendations for proposed updates to lead and compounds acute TRV

ODEQ Proposed TRV (µg/m^3)	Recommendations for Updates to Proposed TRV
Acute TRV 0.15	The current lead acute TRV is based on the NAAQS, which is intended to be averaged over 3 months and does not represent acute, 24-hour exposure. EPA's most recent blood-lead model (AALM) is able to predict changes in blood lead from a single 24-hour exposure at any age. The AALM has been used to predict the airborne concentration over 24-hours that is protective of significant blood lead increase among infants (0 to 1 years old), the most sensitive age group. This value is a more appropriate TRV for acute lead exposure and is protective of public health.

All-Ages Lead Model

EPA's All-Ages Lead Model (AALM) was used to estimate blood lead levels for this evaluation (EPA 2025). The AALM provides estimates of lead levels in blood and other tissues over the entire lifespan of a hypothetical individual. Although the model can predict blood lead levels (BLLs) for all ages, we focused on children (ages 0 to 6) to be conservative because the neurological effects of lead exposure are more significant for children. The target BLL of 1 µg/dL above the model predicted baseline BLL was established for this study, based guidance issued by OEHHA (OEHHA 2007) to protect infants and school children, the most sensitive receptors, and is used widely in California.

The development of the recommended acute lead TRV was conducted in two steps:

1. BLLs were modeled, including all exposure routes in the AALM (e.g., soil, indoor dust) except for air. These are considered baseline exposures.
2. The model was run iteratively by changing the air concentration on a single day until the results corresponded to a BLL of 1 µg/dL above the baseline.

Baseline Modeling

The assumptions used in the baseline model for non-air exposures are provided in Appendix A. The baseline BLL modeling used default model inputs (EPA 2024), and where available, Oregon-specific data. The baseline modeling resulted in exposures identified in **Table *1*** for each age group. Exposures on Day 2 of each year for each age group are presented on Table 1 because Day 2 had the highest predicted BLL in the iterative modeling described below.

Table 1. Baseline and target BLL

Age (in Years)	Day	Baseline BLL (µg/dL)	Target BLL (µg/dL)
0	2	2.21	3.21
1	367	1.30	2.30
2	732	1.27	2.27
3	1097	1.25	2.25
4	1462	1.21	2.21
5	1827	1.18	2.18
6	2192	1.10	2.10

Iterative Air Concentration Modeling

EPA's AALM was used to model BLL for ages 0 through 6 (EPA 2025) simulating a single day of exposure to lead in air. The single day of exposure (i.e., acute pulse) was simulated separately for each year from 0 to 6, such that there were seven different model simulations.

Based on initial iterative modeling, the pulsed air exposures that occurred on day 0 of each year resulted in the highest BLL concentration 2 days post-exposure. Therefore, the model was run iteratively using different single day air concentrations until the target 1 µg/dL increase above baseline was estimated 2 days after the initial air exposure (**Table 1**).

Each time the AALM is run, it predicts BLL for all age groups over the simulation period (e.g., 6 years, lifetime). To simulate an acute, 24-hour exposure scenario for one age group, the air concentration was assumed to be 0 µg/m^3 except for the single day of exposure for the age group of interest. We used this value to allow for pulsed exposure in the model, but as shown in by the results of the pulsed modeling, the default ambient air concentration for lead recommended for the model (0.01 µg/m^3) is not significant. The model uses masks to set exposures for specific repeating periods. In this case, an annual mask was set to 0 µg/m^3 for days 2 through 365 of each year. Day 1 exposure was set to 0 µg/m^3 for all age groups except for the specific age group with the acute 24-hour exposure by changing the model's grouping of age groups for each simulation. The year with the acute/pulsed exposure had a non-zero air concentration. For example, for year 1 (**Figure 1**), the air concentrations on day 1 were modeled in three age groups: (1) age 0 at 0 µg/m^3, (2) age 1 at the non-zero air concentration, and (3) age 2 at 0 µg/m^3, which then continued from age 2 through the end of the simulation (6.1 years).

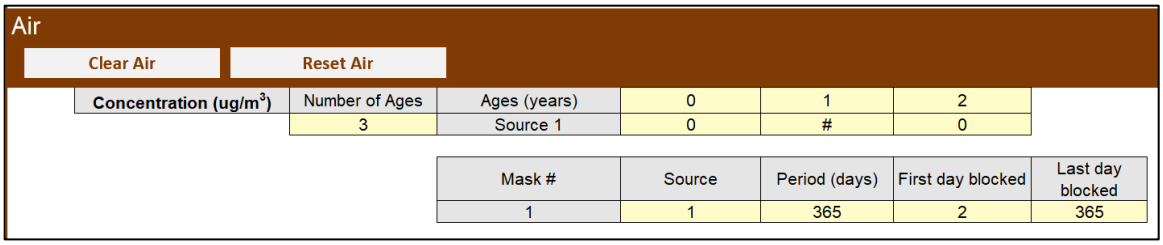

Figure 1. Pulsed air exposure model set-up example for year 1

Default lung parameters from AALM 3.0 were selected (EPA 2024, 2025). These parameters represent lung kinetics for ultra-fine (approximately 0.1 µm in diameter) combustion aerosols. Additional explanation and description of the lung parameters, as well as a sensitivity evaluation, is provided in Appendix B. The recommended conservative default inhalation rates (**Table 2**) and relative bioavailability (RBA) for inhalation exposure of 1 were used.

Table 2. Default inhalation rates used in AALM model (EPA 2024; page 240–241; abbreviated to just the years of model simulation)

Age (year)	Inhalation rate (m^3/day)
Birth < 1 yr	5.4
1 to < 2 yr	8.0
2 to < 3 yr	8.9
3 to < 6 yr	10.1
6 to < 11 yr	12.0

The day 1 air concentration (to two decimal places) that resulted in a predicted BLL closest to the target BLL was determined through an iterative series of model runs (**Table**). The air concentrations that resulted in BLLs 1 µg/dL greater than the baseline model from 1 day of exposure range from 3.86 µg/m^3 (year 0) to 7.64 µg/m^3 (year 5). These values are all well above ODEQ's acute TRV for lead of 0.15 µg/m^3.

As mentioned above, the highest BLL following the acute air exposures were on the third day of the year (i.e., two days after exposure). The BLL predicted by the model for the first month following the simulated 24-hour exposure for each age group is displayed in **Figure 2**, in which the peak BLL (i.e., target BLL) occurs on day 2. As shown on the figure, the most sensitive age group is the newborn (0-year age group). As shown in the figure, BLLs decrease essentially to long-term baseline BLLs within about 20 days.

Table 3. Iterative air concentrations and BLL

Year	Day	Baseline BLL (Day 2) (µg/dL)	Target BLL (µg/dL)	Single day air concentration[1] (µg/m^3)	Predicted BLL (µg/dL)
0	2	2.21	3.21	3.86	3.21
1	367	1.30	2.30	5.80	2.30
2	732	1.27	2.27	6.84	2.27
3	1097	1.25	2.25	6.83	2.25
4	1462	1.21	2.21	7.31	2.22[4]
5	1827	1.18	2.18	7.64	2.18
6	2192	1.10	2.10	7.01	2.10

Note:

1. U.S. EPA's default ambient air concentration for AALM (0.01 µg/m^3) is 0.3% of the pulsed air concentration and would not contribute significantly to BLL relative to the pulsed exposure.

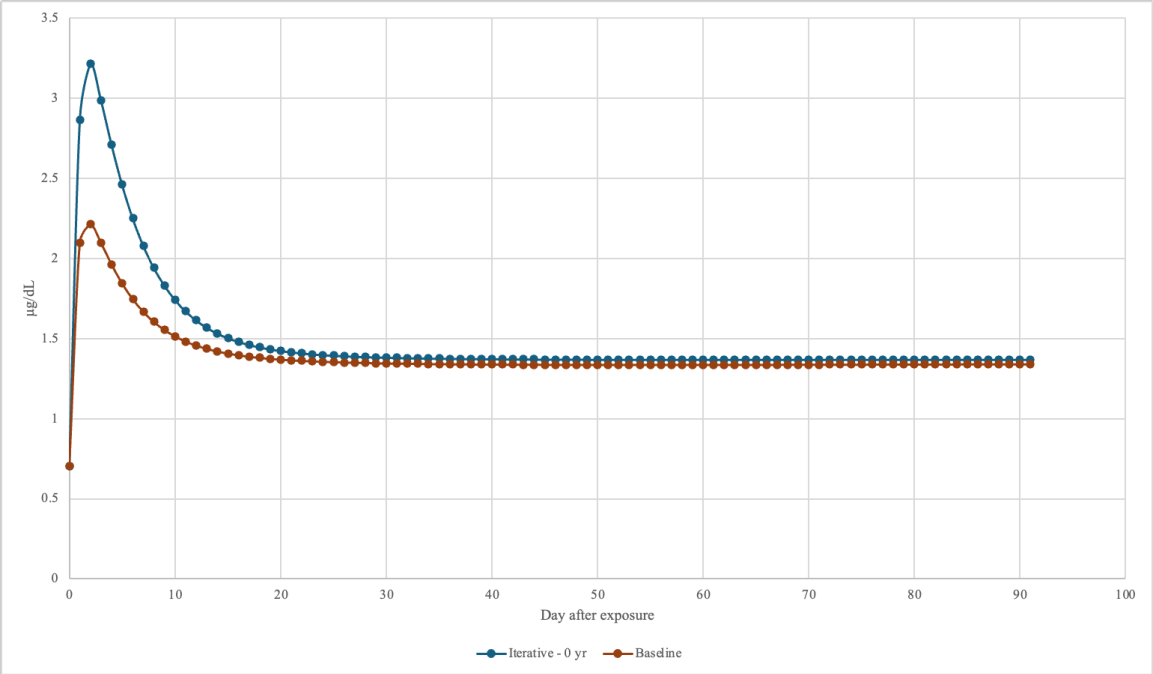

Figure 2. Baseline and pulsed iterative BLLs between year 0 to year 1

[4] Only the predicted BLL for 4-year age group was slightly higher (0.01 µg/dL) than the target BLL, but the results for the 4-year old age group were higher than (less conservative) than that for the 0-year age group.

Conclusions

Based on the modeling results, we recommend that pursuant to OAR 340-247-0030(1)(a),ODEQ, in consultation with ATSAC, propose a new acute TRV for lead of 3.9 $\mu g/m^3$, which is based on the results of the AALM modeling and would be protective of all ages including children (ages 0 to 6 years old). The AALM shows that an acute value 20 times higher than the NAAQS would still be protective and would not change the requirement to meet the NAAQS on a 3-month average or the chronic TRV on an annual basis.

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ATTACHMENT A

Baseline Assumptions for All Ages Lead Model

Appendix A: Baseline All Ages Lead Model Exposure Assumptions and Inputs

As described below, the baseline All-Ages Lead Model (AALM) modeling of blood lead levels (BLLs) used default model exposure assumptions and inputs (EPA 2024), and where available, Oregon-specific data.

Simulation Control Options

Simulation control options are the first input parameters needed for AALM, which determine how the model runs (**Table A1**). For example, the model was set to run from 0 to 6.1 years to focus on children's exposure.

Table A1. AALM baseline simulation control options

Model Compartment	Parameter	Unit	Value	Note
Base parameters	Age at end	Years	6.1	Age at beginning is always 0 years. Set to just beyond 6 years to capture BLL curve following day 1 air exposure at 6 years old
	Sex	n/a	Female	Default
Growth and Physiology	Adjust growth parameters?	n/a	No	Default
	Adjust physiology parameters?	n/a	No	Default
Set Active Media	Media	n/a	Soil: Yes	Media were assumed to be at constant concentrations levels except for air
			Dust: Yes	
			Water: Yes	
			Air: No	
			Food: Yes	
			Other: No	
	Solution type	n/a	Forward	Default
	Stepwise or interpolated?	n/a	Stepwise	Default
	Linear or non-linear red blood cell (RBC)?	n/a	Non-linear RBC	Default

Soil Media Options

The soil lead concentration was modeled as 79 µg/g based on the ODEQ Background Levels of Metals in Soils for Cleanups Fact Sheet (ODEQ 2018). The maximum regional recommendation was selected, which corresponded to the 95% upper prediction limit

(UPL) for the Portland Basin region (ODEQ 2013, 2018). This is greater than the recommended default value of 25 µg/g, which is representative of yard soil "distant from substantial current or historical emission sources" (EPA 2024). The recommended default intakes (**Table A2**) and relative bioavailability (RBA) for soil and dust of 0.6 were used.

Table A2. Default soil intake rates used in baseline model (EPA 2024; page 236)

Age (days)	Intake (g/day)
0	0.018
90	0.032
365	0.041
1825	0.036
3650	0.027
5475+	0.014

Dust Media Options

The dust lead concentration was calculated as 70% of the soil concentration (55.3 µg/g) because we assumed that the primary contribution to indoor dust was soil, which is consistent with the Integrated Exposure Uptake and Biokinetic (IEUBK) model (EPA 2024), EPA's previous model for childhood lead exposures. This differs from an AALM recommended default of 175 µg/g, which is reported as the mean concentration in indoor surfaces and referenced to the American Healthy Housing Survey from 2011, which is no longer available on line. We believe that use of 70% of the soil concentration is a more appropriate assumption because the data in the housing survey is 14 years old, and the approach is consistent with the IEUBK model. The recommended default intakes (**Table A3**) and RBA for soil and dust (0.6) were used.

Table A3. Default dust intake rates used in baseline model (EPA 2024; page 236)

Age (days)	Intake (g/day)
0	0.022
90	0.039
365	0.050
1825	0.044
3650	0.033
5475+	0.017

Water Media Options

The water lead concentration was the AALM recommended default of 0.9 µg/L, which is representative of "average U.S. exposure concentrations to tap water from public water

supplies" (EPA 2024). The recommended default intakes (**Table A4**) and RBA for water (1) were used.

Table A4. Default water intake rates used in baseline model (EPA 2024; page 238)

Age (days)	Intake (L/day)
0	0.20
90	0.30
365	0.35
1825	0.35
3650	0.45
5475	0.55
9125	0.70
18250+	1.04

Food Media Options

The food lead intakes were age-specific recommended values for our model population. These were age-scaled intake values based on the recommended default intake for adults (10 µg/day). Female intakes were modeled based on our simulation control default option of a female child; female intakes were either equal to or greater than those for males for our age population (**Table A5**). The 1-year-old intake was assumed for the 0-year-old age. The recommended RBA for food of 1 was used.

Table A5. Default dietary intakes used in baseline model (EPA 2024; page 234)

Age (year)	Intake (µg/day)
1	2.3
2	3.3
3	4.0
4	5.7
5	6.0
6	6.4
7	6.7
8	7.0
9	7.3
10	7.7
15	10.8
20+	10.0

Baseline Model Results

The AALM output includes BLLs for each day between age 0 and the end of simulation (i.e., 6.1 years). The results for the first 3 days of the year are provided in **Table A6** for each of the age groups and were the basis for development of air concentrations that resulted in a 1 µg/dL increase in BLL. As shown in this table, baseline BLL model results were relatively consistent after day 2.

Table A6. Baseline BLL model results (µg/dL)

Age (year)	Day of Year BLL (simulation day)			
	0	**1**	**2**	**3**
0	0.70 (0)	2.10 (1)	2.21 (2)	2.10 (3)
1	1.27 (365)	1.28 (366)	1.30 (367)	1.31 (368)
2	1.24 (730)	1.25 (731)	1.27 (732)	1.28 (733)
3	1.24 (1095)	1.25 (1096)	1.25 (1097)	1.26 (1098)
4	1.19 (1460)	1.20 (1461)	1.21 (1462)	1.23 (1463)
5	1.18 (1825)	1.18 (1826)	1.18 (1827)	1.18 (1828)
6	1.09 (2190)	1.09 (2191)	1.10 (2192)	1.10 (2193)

ATTACHMENT B

Sensitivity Analysis of Inhalation Exposure Lung Assumptions

Appendix B: Sensitivity Analysis of Inhalation Exposure Lung Assumptions

The default lung parameters provided in guidance for AALM v. 3.0, AALM v. 3.1, and IEUBK differ (**Table B1**), which affects uptake of lead in the lungs. The default deposition fractions in AALM v. 3.1 are zero to allow the user to define deposition and absorption properties from a variety of aerosols. In the absence of site-specific information, the v 3.0 defaults representing near-ultrafine (approx. 0.1 µm in diameter) aerosol from a human study (EPA 2025) were used. The v. 3.1 User Guide (EPA 2025) notes that the v. 3.0 model defaults may still be used to represent near-ultrafine aerosols. Therefore, to model inhalation exposures, the AALM v. 3.0 defaults were selected for the iterative model.

Table B1. Default lung parameters for AALM and IEUBK

Variable	Unit	Description	AALM v. 3.0[a]	AALM v. 3.1[a]	IEUBK[b]
DepFracLET	f	Fraction of inhaled aerosol deposited in Extrathoracic region.	0.200	0	0
DepFracLTB	f	Fraction of inhaled aerosol deposited in Tracheobronchial region.	0.159	0	0
DepFracLalv	f	Fraction of inhaled aerosol deposited in Alveolar region.	0.040	0	0.32
RLETplas	1/day	Loss rate from Extrathoracic region to plasma.	7.680	0	0
RLETstom	1/day	Loss rate from Extrathoracic region to GI tract (stomach).	0	100	0
RLTBplas	1/day	Loss rate from Tracheobronchial region to plasma.	1.940	0	0
RLTBLET	1/day	Loss rate from Tracheobronchial region to Extrathoracic region.	0	2.77	0
RLalvPlas	1/day	Loss rate from Alveolar region to plasma.	0.347	0	1
RLalvLTB	1/day	Loss rate from Alveolar region to Tracheobronchial region.	0	0.002	0
RLalvLint	1/day	Loss rate from Alveolar region to Interstitial region.	0	0.001	0
RLintPlas	1/day	Loss rate from Interstitial region to plasma.	0	0	0

[a] EPA 2025
[b] Day 2 of Training Slides: https://www.clu-in.org/conf/tio/TRW-LeadRisk/

To understand the sensitivity of using the AALM v. 3.0 lung parameter defaults, the year 5 iterative model was re-run[5] using the IEUBK model lung parameter defaults (**Table B1**) and an air concentration of 7.64 µg/m^3. The predicted BLL on the second day of year 5 using the IEUBK model was 1.86 µg/dL, which was less than the BLL using the AALM v. 3.0 iterative run (2.18 µg/dL). Therefore, the use of the AALM v. 3.0 is more conservative (predicts higher BLL concentrations for the same air concentration).

[5] Selected in this sensitivity analysis because it had the highest iterative air concentration.

ToxStrategies

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Technical Memorandum

September 30, 2025

To:	J.R. Giska and Apollonia Goeckner, Oregon Department of Environmental Quality; Holly Dixon, PhD, Oregon Health Authority
From:	Deborah Proctor and Ann Verwiel
Subject:	**Evaluation of the Draft Proposed Acute TRV for Naphthalene for Cleaner Air Oregon**

To support the current review of the inhalation toxicity reference values (TRVs) used in the Cleaner Air Oregon program, we have evaluated the draft proposed acute TRV for naphthalene published by Oregon Department of Environmental Quality (ODEQ) and Oregon Health Authority (OHA) and presented to the Air Toxics Science Advisory Committee (ATSAC) for its consideration. **Table 1** briefly summarizes our conclusions, which are laid out in more detail in this memorandum.

Table 1. Summary of Recommendations for Proposed Update to the Acute TRV for Naphthalene.

Recommendations for Updates to Proposed TRV for Naphthalene
• The proposed acute naphthalene TRV (0.3 µg/m^3) is based on the Agency for Toxic Substance Disease Registry (ATSDR) acute inhalation minimum risk level (MRL) derived from a study reporting irritation effects of the olfactory epithelium in rats following 6 hours of exposure. However for calculation of the MRL, ATSDR used EPA's outdated guidance from 1994 to calculate a dosimetric adjustment factor (DAF) for extrathoracic (ET) effects of 0.4. The correct DAF for ET effects for naphthalene is 1 based on EPA's most current guidance released in 2012. Use of the correct DAF results in a TRV that is 2.5-fold higher than the proposed TRV. The proposed TRV should be modified using the correct DAF.
• ATSDR used EPA's Benchmark Dose Modeling Software (BMDS) to calculate the 95% lower confidence interval on the 10% Benchmark Concentration ($BMCL_{10}$) and selected the lowest $BMCL_{10}$ predicted by BMDS.[1] However, the model selected by

[1] BMDS provides results from 12 models that fit dichotomous data, such as that from Dodd et al. (2010).

Recommendations for Updates to Proposed TRV for Naphthalene

ATSDR was not the best fitting model in the BMDS results, and was flagged by BMDS for indicators of high model uncertainty.[2] BMDS identified five better fitting models for the naphthalene dose-response data, and all five resulted in a $BMCL_{10}$ that are more than 2-times higher (0.037 ppm) than the value selected by ATSDR (0.017 ppm). These models were not flagged for high model uncertainty. It is more reasonable to base the proposed TRV on the $BMCL_{10}$ from the best fitting models, resulting in a higher TRV.

- In addition, to verify that the $BMCL_{10}$ from the best fitting models (0.037 ppm) is conservatively health-protective, we calculated the statistical NOAEC from the rat bioassay data. The statistically-based NOAEC is 0.3 ppm, which is almost 10-fold higher than the $BMCL_{10}$ from the best fitting models, indicating that the $BMCL_{10}$ from the best fitting models is health protective.
- In consultation with ATSAC, ODEQ should propose an acute TRV correcting ATSDR's DAF and BMDS model selection decisions. Correcting these decisions, but following other assumptions made by ATSDR regarding application of uncertainty factors and time adjustment, results in an acute TRV of 1.6 µg/m^3 (0.00031 ppm).[3]

A more detailed summary of our conclusions is provided below:

Background on ATSDR's Acute Minimal Risk Level

The ATSDR finalized its Toxicological Profile for naphthalene in 2025 (ATSDR 2025), which included an acute inhalation MRL. The acute MRL was developed based on a rat inhalation toxicity bioassay in which Sprague-Dawley (S-D) and Fischer 344 (F344) exposed male and female rats (5 per dose group) to naphthalene for 6 hours at 0, 0.1, 0.3, 1, 10, and 30 ppm (Dodd et al. 2010). Minimally severe necrosis of the olfactory epithelium was reported at 0.1 ppm (520 µg/m^3) in S-D rats and 1 ppm (5,200 µg/m^3) in F344s. ATSDR modeled the dose-response using the combined sex data for S-D rats, which were the more sensitive strain, and calculated the lower confidence interval on the 10% extra risk ($BMCL_{10}$) using the EPA's BMDS Version 3.2.0.1, which provides several models for developing benchmark concentrations.

[2] Specifically, the log-logistic predicted a $BMCL_{10}$ more than three times lower than the lowest dose in the study, and a BMC_{10} to $BMCL_{10}$ ratio greater than 3. The two ratios are presented as warnings in BMDS output but were not reproduced in the ATSDR Toxicological Profile (Table A-3).
[3] ToxStrategies has also contacted ATSDR regarding the issues outlined herein.

Table 2. Summary of BMDS results

Models	BMC_{10}[4] (ppm)	$BMCL_{10}$[5] (ppm)	p-value	AIC[6]
Log-logistic	0.062	0.017	0.96	49.00
Gamma	0.064	0.037	0.99	46.85
Multistage Degree 3				
Multistage Degree 2				
Multistage Degree 1				
Weibull				

ATSDR selected the results from the log-logistic model to define the point of departure (POD) (**Table 2**). The $BMCL_{10}$ from the log-logistic model was then adjusted for 24-hour exposures (6/24 = 0.25), and a dosimetric adjustment factor (DAF) based on the Regional Deposited Gas Ratio (RDGR) for extrathoracic effects (ET) of 0.4 was used to calculate the acute MRL. The RDGR was derived based on EPA's outdated 1994 guidance. Use of the exposure adjustment factor and the DAF of 0.4 with the $BMCL_{10}$ results in a human equivalent concentration (HEC) ($BMCL_{10\text{-}HEC}$) of 0.0017 ppm (8.9 µg/m^3).

$$BMCL_{10\text{-}HEC} = BMCL_{10} \times 0.25 \times 0.4 = 0.017 \times 0.25 \times 0.4 = 0.0017 \text{ ppm}$$

A 30-fold uncertainty factor was applied, consisting of a 10-fold intraspecies factor (human variability) and 3-fold interspecies factor (animal to human after dosimetric adjustment).

$$MRL = BMCL_{10\text{-}HEC} \div 30 = 0.0017 \div 30 = 0.00006 \text{ ppm}$$

ODEQ has proposed to use the MRL of 0.00006 ppm (0.3 µg/m^3) as the acute TRV.

Outdated EPA guidance used to set the RDGR for the extrathoracic region $RGDR_{ET}$

It is unclear why ATSDR (2025) did not use EPA's most current guidance, *Advances in Inhalation Gas Dosimetry for Derivation of a Reference Concentration (RfC) and use in Risk Assessment*, to derive the $RGDR_{ET}$ (EPA, 2012). In 2012, EPA improved the understanding of conditions in the extrathoracic region using pharmacokinetic and computation fluid dynamic models. EPA concluded, "One of the principal findings from these reviews is that internal dose equivalency in the ET [extrathoracic] region for rats and

[4] BMC10 – Maximum likelihood estimate for the exposure concentration corresponding to a 10 percent extra risk.
[5] BMCL10 – 95% lower confidence limit on the BMC10.
[6] AIC - Akaike Information Criteria. Lower values indicate better model fit to the data.

humans is achieved through similar external exposure concentrations" (EPA, 2012, p. xiv). Further, EPA stated, "A primary finding for gas deposition in the ET region is the internal target-tissue dose equivalency between humans and rats is achieved through equivalency at the level of external applied concentration, i.e., for both rats and humans, the same external air concentration, rather than one adjusted by V_E/SA [Ventilation rate/Surface Area] leads to the similar internal target-tissue dose to the URT [upper respiratory tract]" (EPA, 2012, p. xvi). Therefore, the $RGDR_{ET}$ based on the current EPA guidance is one (1). As evidence that the $RGDR_{ET}$ is in use at EPA, EPA (2024) applied this approach in its current risk assessments to evaluate the RfC for formaldehyde based on nasal metaplasia in rats (see EPA, 2024, pp. 5-39 for discussion). As such, the current state of the science and EPA regulatory methods support an $RGDR_{ET}$ of one (1) for setting an acute TRV for naphthalene. Correcting this factor would result in a TRV that is 2.5-fold higher than that proposed by ODEQ. In addition to this correction, the POD should also be revised to account for ATSDR's use of the incorrect benchmark dose model (see following section).

ATSDR Used the Wrong Benchmark Dose Model

EPA's BMDS fits the animal data to several models, and the best fitting models are often judged based on the lowest AIC score. For each model in BMDS, a BMC_{10} and $BMCL_{10}$ is predicted. The BMC_{10} is the most likely result (also called the maximal likelihood estimate or MLE), and the $BMCL_{10}$ is the 95% lower confidence limit on the BMC_{10}.

For ATSDR's BMD modeling of the acute naphthalene data, twelve models were run, which are all the models that fit dichotomous data, in BMDS. Five of the 12 produced the same results and had the lowest AIC (46.85); results for these models and the log-logistic model selected by ATSDR are presented in Table 2. The BMC_{10} (MLE) values for the Log-Logistic model (0.062 ppm) and the best fitting models (0.064 ppm) are nearly identical—meaning that at the MLE, the models converge producing essentially the same result. Although the model results converge at a similar BMC_{10}, the best fitting models all resulted in a $BMCL_{10}$ of 0.037 ppm, as compared to a $BMCL_{10}$ of 0.017 ppm using the log-logistic model. ATSDR used the results of the log-logistic model because it predicted the lowest $BMCL_{10}$, even though model fit was not as good (AIC of 49.00 vs 46.85). In fact, the log-logistic model predicted a $BMCL_{10}$ more than three-times lower than the lowest dose, and the ratio of the BMC_{10} to $BMCL_{10}$ was greater than 3; both of these metrics are used in BMDS as indicators of model uncertainty.[7] The 2.2-fold variance in $BMCL_{10}$ values between these models is due to wider confidence intervals for the log-logistic model as compared to the other better fitting models. As such, the $BMCL_{10}$ of the best-fitting models should be used to estimate the MRL and TRV (0.037 ppm) rather than selecting the lowest value.

ATSDR (2025) identifies a LOAEC of 0.1 ppm (ATSDR did not identify a NOAEC) based on "minimal severity necrosis of the nasal olfactory epithelium" in SD rats (sex

[7] This information appears as a warning message in the BMDS software output, but was not reproduced by ATSDR in their summary Table A-3.

unspecified) from Dodd et al. (2010). However, this LOAEC is not statistically significant for either sex or both sexes combined considering the small sample size (N=5) and that one of five female rats in the control group also had these effects (**Table 3**). A statistical analysis of the two sexes combined results in a statistically significant LOAEC and NOAEC of 1 ppm and 0.3 ppm, respectively (**Table 3**). ATSDR (2025) combined the male and female data for BMD modeling to help mitigate the lack of statistical power of each sex alone. Models providing the lowest AIC provide a BMC_{10} of 0.064 ppm which is lower than the statistical NOAEC of 0.3 ppm in the combined data and is lower than the 0.1 ppm concentration where lesions were observed in male rats (**Table 3**). The $BMCL_{10}$ of 0.037 ppm is almost 10-times lower than the statistical NOAEC, indicating that this value is health protective.

Table 3. Statistical Evaluation of Olfactory Epithelial Necrosis in S-D Rats*

Concentration (ppm)	Male	Female	Combined
0	0/5	1/5	1/10
0.1	2/5	1/5	3/10
0.3	3/5	2/5	5/10
1.0	4/5[a,b]	4/5	8/10[a,b]
10	5/5[a,b]	5/5[a,b]	10/10[a,b]
30	5/5[a,b]	5/5[a,b]	10/10[a,b]

* adapted from Table 2 in Dodd et al. (2010)
[a] Statistically significant ($p< 0.05$ Fischer's exact test (two-tail))
[b] Statistically significant ($p< 0.05$ Fischer's exact test (one-tail))

Revised acute TRV for Naphthalene

Using the exposure adjustment factor (6/24 hours or 0.25), the DAF based on the EPA's current guidance, and the $BMCL_{10}$ from the best-fit model results (Table 2), the $BMCL_{10\text{-}HEC}$ is calculated as:

$$BMCL_{10\text{-}HEC} = BMCL_{10} \times 0.25 \times 1 = 0.037 \times 0.25 \times 1 = 0.00925 \text{ ppm}$$

After applying a 30-fold uncertainty factor]10-fold intraspecies (human variability) and 3-fold interspecies (animal to human after dosimetric adjustment)], the resulting TRV is 0.0003 ppm (1.6 µg/m^3).

$$TRV_{update} = BMCL_{10\text{-}HEC} \div 30 = 0.00925 \div 30 = 0.00031 \text{ ppm } (1.6 \text{ µg/m}^3)$$

Conclusion

In consultation with the ATSAC, ODEQ should use the $RDGR_{ET}$ from EPA's most recent guidance and set an acute TRV for naphthalene based on the $BMCL_{10}$ from the best fitting models, resulting in a proposed acute TRV for naphthalene of 1.6 µg/m^3 (0.00031 ppm). The statistical evaluation of the original rat bioassay data (Dodd et al., 2010) indicates this is a health-protective value that is well below levels at which effects were statistically significant (5,240 µg/m^3 or 1 ppm).

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ToxStrategies

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Technical Memorandum

September 30, 2025

To:	J.R. Giska and Apollonia Goeckner, Oregon Department of Environmental Quality; Holly Dixon, PhD, Oregon Health Authority
From:	Deborah Proctor and Ann Verwiel, ToxStrategies LLC
Subject:	**Evaluation of Draft Proposed Update of the Acute TRVs for Nickel Oxide and Nickel and Nickel Compounds for Cleaner Air Oregon**

To support the current review of the inhalation toxicity reference values (TRVs) used in the Cleaner Air Oregon (CAO) program, we have evaluated the draft proposed acute nickel[1] TRV that Oregon Department of Environmental Quality (ODEQ) and Oregon Health Authority (OHA) have presented to the Air Toxics Science Advisory Committee (ATSAC). This memorandum discusses in more detail the proposed nickel acute health effects TRV, and **Table 1** briefly summarizes our conclusions and recommendations.

Table 1. Summary of Recommendations for Proposed Updates to Nickel Acute TRV

Recommendations for Updates to Proposed Acute Nickel TRV

• Do not proceed with revising the acute nickel TRV because the proposed update is based on the Agency for Toxic Substances Disease Registry (ATSDR) Nickel Toxicological Profile, which has been removed by ATSDR from its website while the Agency "evaluate[s] some calculations."[2]
  ○ The removed ATSDR acute MRL for nickel was not appropriate for a 24-hour TRV because the total exposure duration of the underlying supporting study was for 30 hours over five days.
  ○ A 24-hour acute TRV for nickel should be based on immunological effects, which are more sensitive than irritation for 24-hour exposure durations.

[1]The acute TRVs for nickel oxide, nickel, and nickel compounds are the same value, and referred to herein as "nickel."

[2] See: https://wwwn.cdc.gov/TSP/ToxProfiles/ToxProfiles.aspx?id=245&tid=44. ToxStrategies has sent comments to ATSDR for its consideration regarding the nickel acute minimum risk level (MRL).

Recommendations for Updates to Proposed Acute Nickel TRV

- Because no authoritative source offers a relevant health value consistent with the TRV acute exposure duration of 24-hours, in consultation with ATSAC, ODEQ should revise the proposed nickel acute TRV to be based on a more appropriate study that matches ODEQ's 24-hour exposure time frame or at a minimum wait until ATSDR finishes their revisions to the MRL.
- Buxton et al. (2021) provides a no observed adverse effect level (NOAEL) for 24-hour exposures to nickel chloride for the sensitive endpoint of immunological suppression, which may be used to set an acute TRV for nickel.[3] ToxStrategies calculates a suggested value of 11 $\mu g/m^3$ based on this study using standard methods for consideration by ATSAC and ODEQ/OHA.[4]
- Additionally, there are less reliable alternatives to the recommendation above that are more relevant to 24-hour acute exposures:
  - Retain, for the time being, the current acute TRV for nickel, based on California's Office of Environmental Health Hazard Assessment (OEHHA) acute reference exposure level (REL) (0.2 $\mu g/m^3$).
  - Use the acute Reference Value (ReV) from the Texas Commission on Environmental Quality (TCEQ) (1.1 $\mu g/m^3$).

  Note that both the OEHHA REL and TCEQ ReV values are for 1-hour exposures, but are lower than the suggested value calculated based on the new high quality study by Buxton et al. (2021) for 24-hour exposures.

Do Not Base Proposed Acute Nickel TRV on Withdrawn ATSDR Value

ToxStrategies has become aware that ATSDR received significant public comments regarding the derivation of minimal risk levels (MRLs) for nickel after the final document was released in 2024. As a result, ATSDR has removed the 2024 Nickel Toxicological Profile from its website while the Agency "evaluate[s] some calculations."

In addition, and importantly, the ATSDR acute MRL is for exposures of up to 14 days. The ODEQ TRV, however, is for exposures of 24 hours. The adjustments ATSDR made to derive the MRL are not required for a 24-hour value. Considering that the ATSDR acute MRL is for up to 14 days of exposure, and the OEHHA REL is for only one hour of exposure, neither of these authoritative sources offers a value consistent with ODEQ's definition of an acute TRV, which is 24 hours.

[3] The Buxton et al. (2021) study was conducted according to Good Laboratory Practice (GLP) using United States Environmental Protection Agency (EPA) Office of Prevention, Pesticides and Toxic Substances (OPPTS) 870.7800 immunotoxicity test guideline. Hence, it is a GLP-compliant guideline study, considered the gold standard for immunotoxicity studies.

[4] See **Attachment A** for a detailed description of the derivation.

The proposed acute inhalation TRV for nickel was updated from an earlier REL published by OEHHA (OEHHA, 2012) (0.2 μgNi/m^3), which is based on immune suppression, the most appropriate and sensitive endpoint for acute effects. The value published by ATSDR in its Toxicological Profile for Nickel (ATSDR, 2024) (0.1 μgNi/m^3) is based on respiratory effects following subacute exposure (up to 14 days) compared to ODEQ's definition of acute (24 hours).

The details of ATSDR's acute MRL development for nickel are provided below:

> The ATSDR (2024) acute MRL for nickel inhalation was based on respiratory effects of nickel (bronchiole epithelial degenerations/hyperplasia) in rats exposed to 0.2244 mgNi/m^3 as nickel sulfate for six hours per day for five days [30 hours total]. Adjusting the lowest-observed-adverse effect level (LOAEL) (0.2244 mgNi/m^3) to continuous acute exposure (6 hours/24 hours) resulted in an adjusted LOAEL of 0.0561 mgNi/m^3. A human equivalent concentration (HEC) was developed using the multiple-path particle dosimetry (MPPD) model with a dose adjustment factor (DAF) of 0.718, resulting in a $LOAEL_{HEC}$ of 0.0403 mgNi/m^3. A total uncertainty factor of 300 was applied based on a factor of ten for using a LOAEL, three for extrapolating from rats to humans after dosimetric adjustments, and ten for human variability. These uncertainty factors resulted in an acute MRL of 0.1 μgNi/m^3.

The ATSDR acute MRL is based on a study of appropriate duration for ATSDR's definition of acute exposures, which is up to14 days, but ODEQ's acute TRV is intended for a 24-hour exposure period. Using a time adjustment factor of 6 hours/24 hours when the total study exposure time of 30 hours is already greater than 24 hours is too conservative. However, as authoritative sources have not set a toxicity criteria specific to the 24-hour acute TRV for nickel, and nickel inhalation toxicity is highly studied, ODEQ and OHA should consider proposing a TRV based on an alternative study.

Immune Effects are a More Appropriate Endpoint for Proposing Acute TRV

The ATSDR acute MRL is based on respiratory irritation effects; however both respiratory and immune effects are identified as the most sensitive endpoints for ATSDR's acute exposure definition (exposures up to 14 days).

Importantly, in addition to investigating lung histopathology in the highest dose group, which is the basis of the LOAEL, Efremenko et al. (2017) also evaluated transcriptomics (genetic markers) of response and found that the lowest benchmark doses (BMDs)—the most sensitive effects—were observed for immune responses at both one and four weeks of exposure. The transcriptomic BMD at one week of exposure for immune effects (0.047 mgNi/m^3) is considerably lower than the LOAEL for respiratory effects (0.22 mg/m^3). In summary, the endpoint that ATSDR selected for acute effects (respiratory) is relatively

arbitrary in that it was the only dose group in the Efremenko et al. (2017) study for which histopathology was performed.

Transcriptomics data support that immune effects are more sensitive. Immunotoxicity is the critical endpoint for the acute OEHHA REL and TCEQ ReV. The ATSDR acute MRL is slightly lower than the REL, but the acute MRL is based on a free-standing LOAEL, meaning that a no-observed-adverse effect level (NOAEL) was not defined for this endpoint. As a result it includes a 300-fold uncertainty factor (10-fold for using a LOAEL) and, in addition, a time adjustment factor.

OEHHA (2012) relied on Graham et al. (1978), which exposed mice for an exposure duration of two hours to nickel chloride at 0.1-0.49 mg/m^3. OEHHA calculated the 95% lower confidence limit on the benchmark dose (BMDL) of 0.165 mg/m^3. To this BMDL, OEHHA applied a 1,000-fold uncertainty factor, and did not use a dosimetry adjustment model to calculate an HEC because Graham et al. (1978) did not include sufficient data to perform the dosimetric modeling. Although OEHHA's work predates the more recent studies of Efremenko et al. (2017), as well as other newer studies, the study selected is more applicable to OEHHA's definition of an acute REL, which is for 1-hour exposures. In contrast, and as noted above, the Efremenko et al. (2017) study exposed rats for six hours per day for five days, which is more consistent with ATSDR's definition of acute (<14 days). In summary, neither the OEHHA REL nor the ATSDR acute TRV uses ODEQ's definition of acute, which is a 24-hour exposure. The OEHHA REL is very conservative, considering the application of a 1,000-fold uncertainty factor instead of developing a human equivalent concentration (HEC) (10-fold is for the extrapolation of animal to human exposures). As discussed in more detail below, the study by Buxton et al. (2021) demonstrated a NOAEL for 24-hour exposures in mice (0.08 mg/m^3) that is somewhat lower than the LOAEL reported by Graham et al. (1978) for 2-hour exposures (0.25 mg/m^3), suggesting that time-weighting these immune effects that are concentration dependent is not necessary.

Regarding immune effects, ATSDR's (2024) review states:

> "Several studies have examined the relationship between nickel exposures and acquired immune function. A concentration-related increase in susceptibility to *Streptococci* infection was seen in mice exposed to nickel chloride (0.5 mgNi/m^3) for 2 hours and then infected either immediately or after a 24-hour recovery period (Adkins et al. 1979). Increased susceptibility was indicated by an exposure-related increase in mortality and decrease in relative mean survival time in exposure groups when compared to simultaneously infected non-nickel-exposed controls (Adkins et al. 1979). Increased mortality and reduced survival time were also observed following a 2-hour exposure to 0.46 mg Ni/m^3 as nickel sulfate (Adkins et al. 1979). An additional group of mice, exposed to 0.66 mg Ni/m^3 as nickel chloride, developed septicemia from the *Streptococci* infection and had a reduced ability to clear the inhaled bacteria 96 hours after infection (Adkins et al. 1979). Other studies have found an impaired response to sRBCs in mice exposed to 0.25 mg Ni/m^3 as nickel chloride for 2 hours (Graham et al. 1978) or rats continuously exposed to 0.2 mg Ni/m^3 as nickel oxide for 4 weeks or 0.15 mg Ni/m^3 for 4 months (Spiegelberg et al. 1984). At lower concentrations, no

> immunosuppressive response to sRBCs was observed in mice exposed to 0.081 mg Ni/m^3 as nickel chloride for 24 hours (Buxton et al. 2021). A decreased resistance to a tumor challenge was also observed in mice exposed to 0.45 mg Ni/m^3 as nickel sulfate 6 hours/day, 5 days/week for 65 days (Haley et al. 1990)" (ATSDR, 2024, pp. 114-115).

The ATSDR (2024) Toxicological Profile provides a summary of all inhalation toxicity data. As reported by ATSDR, one study (Buxton et al. 2021) reports a NOAEL of 0.081 mg/m^3 among mice exposed for 24-hours to nickel chloride heptahydrate. This study follows the OPPTS guideline 870.7800 for immunotoxicity and was GLP-compliant. Further, this study was specifically conducted for the purpose of setting a 24-hour standard for nickel. The study provides a preferrable point of departure (POD) as compared to the ATSDR MRL because: 1) the exposure duration is consistent with ODEQ's definition of an acute TRV (24-hours); 2) the study protocol is the gold standard for investigating immune toxicity, the most sensitive endpoint for acute exposures; 3) the study addresses many of the uncertainties in the older Graham et al. (1978) study relied upon by OEHHA; and 4) it provides a NOAEL, reducing the need to add uncertainty factors.

Propose an Acute TRV for Nickel Based on Immune Effects

ToxStrategies used the MPPD dosimetry adjustment model as described in **Attachment A** to calculate a DAF. The MPPD model is the same model that ATSDR used to calculate MRLs. Using the NOAEL from the Buxton et al. (2021) study of 0.081 mg/m^3, the calculated Human Equivalent Concentrations (HECs) ranged from 0.29 to 0.439 mg/m^3, with a median of 0.318 mg/m^3. Applying a 30-fold uncertainty factor (standard factors of ten for intraspecies sensitivity and three for interspecies sensitivity) to the median HEC results in an acute TRV for nickel of 0.0106 mg/m^3, or 11 μg/m^3. The derivation is described in in detail in **Attachment A**.

Importantly, a TRV based on Buxton et al. (2021) is more certain (less need for application of uncertainty factors) than the ATSDR MRL and OEHHA REL, and is based on immunotoxicity, the most sensitive endpoint for acute exposure. ODEQ should reevaluate its basis of the proposed TRV and consider basing a value on the mouse NOAEL by Buxton et al. (2021).

Alternately at the very least, ToxStrategies recommends that ODEQ continue to rely on the current acute TRV, based on the OEHHA acute REL (0.2 μg/m^3), until an authoritative source develops a more appropriate value.

A final option would be to adopt the TCEQ acute ReV of 1.1 μg/m^3 (TCEQ, 2017) until an authoritative source develops a more appropriate value. This ReV also was based on immunological effects (asthma) observed among occupational asthmatics from a metal plating facility who were exposed to 67 μg/m^3 for 30 minutes (Cirla, Bernabeo, and Ottoboni, 1985), and includes a 30-fold uncertainty factor. This value is not as well-suited for deriving the TRV as a value based on Buxton et al. (2021), but it is based on human

data for a sensitive subpopulation, and it supports a TRV that is 5- to 10-fold higher than the OEHHA REL or ATSDR MRL.

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ATTACHMENT A

MPPD Modeling to Derive a Suggested acute TRV for nickel based on Buxton et al. (2021)

To calculate a non-cancer toxicity criteria for inhalation exposures, a point of departure (POD) is multiplied by a dose adjustment factor (DAF) to calculate a Human Equivalent Concentration (HEC) due to physiological differences between species. The HEC is divided by appropriate uncertainty factors to result in the toxicity criteria, which, in this example, is an acute TRV.

To calculate the DAF, the multiple-path particle dosimetry (MPPD) model was run for the mouse and the human to estimate an HEC for the highest dose and no-observed-adverse effect level (NOAEL) of (80.9 μg/Ni/m^3 – target dose of 100 μg/Ni/m^3) in the Buxton et al. (2021) study. Most input parameters are automatically calculated in MPPD model. A list of values used is provided below in **Table A-1**.

The body weight used for the mouse is the average of the Group 4 body weights for Days 1 thru 6 reported in Buxton et al. (2012); MPPD assumes a human body weight, and does not allow a user to input an alternative value. MPPD only has two options for a mouse model species (BALB/c and B6C3F1); however CD-1 mice were used in the Buxton et al. (2021) study. Thus, model runs were made with assumptions for each mouse species for comparison.

The mass median aerodynamic diameter (MMAD) and corresponding geometric standard deviation (GSD) were taken from Buxton et al. (2021). The aerosol concentration is the dose of nickel from Buxton et al. (2021) in units of mg/m^3. Initially, the mouse value automatically calculated for tidal volume was used, but that value seemed too large for a mouse. After contacting ARA, the developers of MPPD, about this parameter, we learned that, for the mouse, there is an error in MPPD, and the calculated tidal volume is off by a factor of ten. Rather than dividing the automatically calculated value by ten, a value from Guyton (1947)[1] was used for the mouse, along with a corresponding breathing frequency rate from Guyton (1947).

Several models available are available for humans in MPPD. Three of those were run here for comparison (Yeh/Schum Symmetric, Yeh/Schum 5 Lobe, and Stochastic (60^{th} percentile)). The human values for tidal volume and breathing frequency were the EPA values from its 2017 Integrated Risk Information System (IRIS) review for benzo[a]pyrene. The breathing scenario for the mouse and human was also used in EPA's 2017 IRIS review of benzo[a]pyrene for rat and human. Note that even though "Whole Body Exposure" was chosen for the breathing scenario, the output files show the breathing route as "Nasal." Also, total fractional deposition for human was the same whether the breathing scenario was "Nasal" or "Oro-Nasal Augmenter."

The output from each of the MPPD models runs (two for mouse and three for human) was used to calculate the DAF. The DAF is calculated as

[1] See: https://www.informatics.jax.org/greenbook/tables/table16-6.shtml

$$DAF = \left(\frac{Human\ BW}{Mouse\ BW}\right) \times \left(\frac{Mouse\ Ventilation\ Rate}{Human\ Ventilation\ Rate}\right) \times (Total\ Fractional\ Deposition).$$

For comparison, the DAF was calculated using ventilation rates from the MPPD model runs and from the EPA 1986 Reference Values for Risk Assessment for the mouse and from the EPA's 2017 IRIS review of benzo[a]pyrene for humans. The resulting DAFs ranged from 3.45 to 5.43 (**Attachment A-1**). The DAFs were then multiplied by the dose at which the MPPD models were run (The NOAEL of 0.0809 mg/m^3) to estimate the HEC. The resulting HECs ranged from 0.279 to 0.439 mg/m^3, with a median value of 0.318 mg/m^3. Using the median value (0.318 mg/m^3) as the POD_{HEC} and a 30-fold uncertainty factor (ten for intraspecies sensitivity and three for interspecies kinetic variability) results in a suggested acute TRV value of 0.0106 mg/m^3, or 11 µg/m^3.

Table A-1: Input Values Used for MPPD Simulations

	Parameter	Units	Value	
AIRWAY MORPHOMETRY				
	Species		Mouse	Human
	Body weight (BW)	G	30.455	Default
	Model		BALB/c or B6C3F1	Yeh/Schum Symmetric, Yeh/Schum 5 Lobe, or Stochastic (60th percentile)
	FRC Default for human; automatically calculated for mouse	mL	0.219 for BALB/c or 0.3 for B6C3F1	3300
	URT Volume Default for human; automatically calculated for mouse	mL	0.0322	50
INHALANT PROPERTIES				
	Select "Aerosol"			
	Density	g/cm^3	1 – Default value	

	Parameter	Units	Value	
	Aspect Ratio	--	1 – Default value	
	Diameter	µm	1.1	
	"Single", "Multiple" or "Multimodal"	--	Single	
	CMD, MMD or MMAD	--	MMAD	
	Inhalability Adjustment box	--	Checked	
	GSD (diam.)	µm	2.26	
	GSD (length)	µm	1 – Default value	
	Correlation	--	0 – Default value	
	Equiv. Diam. Model	--	not checked	
	Diff. Diameter	µm	1 – Default value	
	Sed. Diameter	µm	1 – Default value	
	Imp. Diameter	µm	1 – Default value	
	Int. Diameter	µm	1 – Default value	
EXPOSURE CONDITION				
	Constant or Variable Exposure		Constant	
	Acceleration of Gravity	cm/s^2	981 – Default value	
	Body Orientation	--	Upright – Default value	
	Aerosol Concentration	mg/m^3	0.0809	
	Breathing Frequency	/minute	163	16
	Tidal Volume	mL	0.15	860
	Inspiratory Fraction	--	0.5 – Default value	
	Pause Fraction	--	0 – Default value	
	Breathing Scenario	--	Whole body (output file says "Nasal")	Nasal or Oro-nasal augmenter
DEPOSITION CLEARANCE				

	Parameter	Units	Value
	Deposition Only or Dep. + Clearance		Deposition Only

Link for table with values from Guyton (1947):
https://www.informatics.jax.org/greenbook/tables/table16-6.shtml

Link for book with table: https://www.informatics.jax.org/greenbook/

References

Guyton AC. 1947. Measurement of respiratory volumes of laboratory animals. Amer J Physiol 150(1):70-77.

ATTACHMENT A-1

MPPD Modeling Results

Attachment A-1A. Calculations -- using deposition in TB region only

	Mouse			Human		
	BALB/c Model	**B6C3F1 Model**	**Yeh/Schum Symmetric**	**Yeh/Schum 5 Lobe**	**Stochastic (60th percentile)**	
POD (mg/m3)	0.0809					
BW (kg)	0.030455			70		
VE (L/min) -- from MPPD output	0.0489			27.52		
VE (L/min) -- human value from 2017 IRIS	0.036111111					
Benzo[a]pyrene review -- mouse values from 1986 EPA				13.88888889		human value of 13.8 used in EPA IRIS Review of Benzo[a]pyrene
Reference Values for Risk Assessment - Table 1-2	0.027083333					
Ftot (fractional deposition in **TB region only**) at 0.0809 mg/cm3	0.0496	0.0274	0.0487	0.0408	0.0505	

Mouse model used:	**BALB/c Model**			**B6C3F1 Model**			**Range**	
Human model used:	**Yeh/Schum Symmetric**	**Yeh/Schum 5 Lobe**	**Stochastic (60th percentile)**	**Yeh/Schum Symmetric**	**Yeh/Schum 5 Lobe**	**Stochastic (60th percentile)**	**Min**	**Max**
BW ratio				2298.473157				
VE ratio -- using values from MPPD output				0.00177689				
VE ratio -- using EPA values -- mouse 0.052 m3/day				0.0026				
VE ratio -- using EPA values -- mouse 0.039 m3/day				0.00195				
FTot ratio (head, TB and pulmonary)	1.018480493	1.215686275	0.982178218	0.562628337	0.671568627	0.542574257		
RDDR / DAF								
HEC -- using VE ratio from MPPD output	4.16	4.97	4.01	2.30	2.74	2.22		
VE ratio -- using EPA values -- mouse 0.052 m3/day	6.09	7.26	5.87	3.36	4.01	3.24		
VE ratio -- using EPA values -- mouse 0.039 m3/day	4.56	5.45	4.40	2.52	3.01	2.43		
HEC (mg/m3)								
HEC -- using VE ratio from MPPD output	0.337	0.402	0.325	0.186	0.222	0.179	0.179	0.402
HEC -- using EPA VE values -- mouse 0.052 m3/day	0.492	0.588	0.475	0.272	0.325	0.262	0.262	0.588
HEC -- using EPA VE values -- mouse 0.039 m3/day	0.369	0.441	0.356	0.204	0.244	0.197	0.197	0.441
						Overall	0.179	0.588
						with UF of 30	0.005976	0.019591

Attachment A-1B. MPPD Calculations -- using total deposition in head, TB and pulmonary regions

Input Parameters	Mouse		Human			
	BALB/c Model	B6C3F1 Model	Yeh/Schum Symmetric	Yeh/Schum 5 Lobe	Stochastic (60th percentile)	
POD (mg/m3)	0.0809					
BW (kg)	0.030455			70		
VE (L/min) -- from MPPD output	0.0489			27.52		
VE (L/min) -- human values from 2017 IRIS	0.036111111					human value of 13.8
Benzo[a]pyrene review -- mouse values from 1986 EPA				13.88888889		used in EPA IRIS
Reference Values for Risk Assessment - Table 1-2	0.027083333					Review of
Ftot (fractional deposition in **head, TB and pulmonary**) at 0.0809 mg/cm3	0.4683	0.4416	0.5231	0.5159	0.5153	

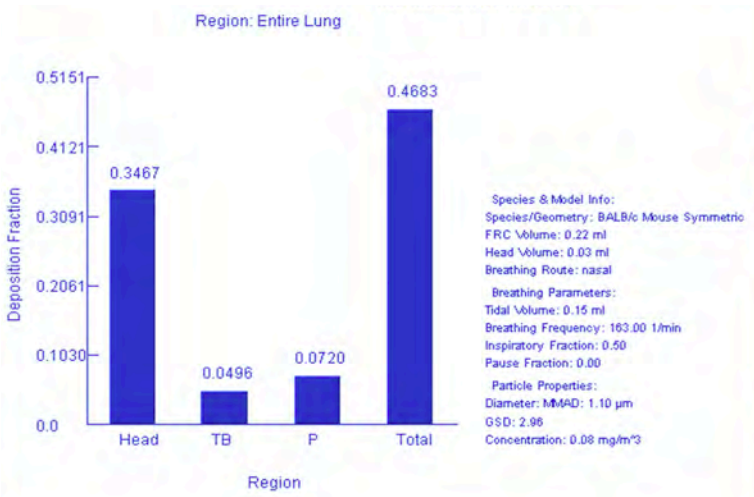
	Mouse model used:	BALB/c Model			B6C3F1 Model			Range		
	Human model used:	Yeh/Schum Symmetric		Yeh/Schum Symmetric	Yeh/Schum 5 Lobe	Stochastic (60th percentile)		Min	Max	Median
	BW ratio			2298.473157						
	VE ratio -- using values from MPPD output			0.00177689						
	VE ratio -- using EPA values -- mouse 0.052 m3/day			0.0026						
	VE ratio -- using EPA values -- mouse 0.039 m3/day			0.00195						
	FTot ratio (head, TB and pulmonary)	0.895239916	0.907734057	0.908790996	0.84419805	0.855979841	0.856976519			
DAF										
	VE ratio -- using VE ratio from MPPD output	3.66	3.71	3.71	3.45	3.50	3.50			
	VE ratio -- using EPA values -- mouse 0.052 m3/day	5.35	5.42	5.43	5.04	5.12	5.12			
	VE ratio -- using EPA values -- mouse 0.039 m3/day	4.01	4.07	4.07	3.78	3.84	3.84			
HEC (mg/m3)										
	HEC -- using VE ratio from MPPD output	0.296	0.300	0.300	0.279	0.283	0.283	0.279	0.300	0.289
	HEC -- using EPA VE values -- mouse 0.052 m3/day	0.433	0.439	0.439	0.408	0.414	0.414	0.408	0.439	0.424
	HEC -- using EPA VE values -- mouse 0.039 m3/day	0.325	0.329	0.330	0.306	0.310	0.311	0.306	0.330	0.318
Final HEC								0.279	0.439	0.318
Suggested Acute TRV Based on Median (mg/m3)							Applying a 30-fold UF 30	0.009298	0.014645	**0.010589**
Suggested Acute TRV Range (ug/m3)										**11**

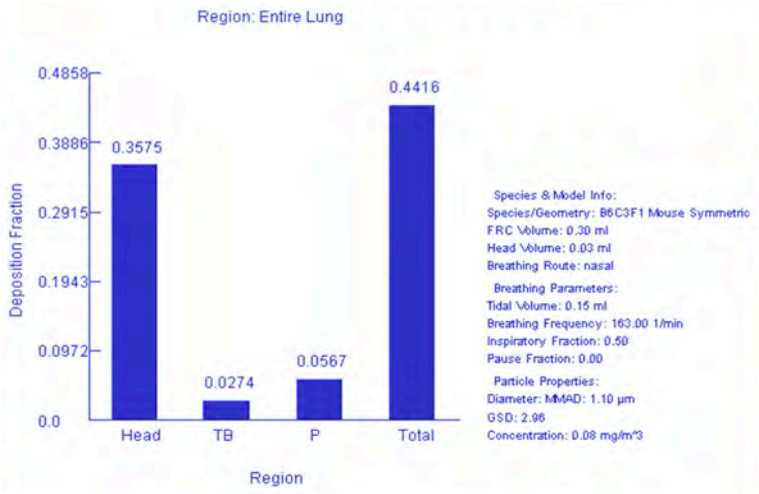
Attachment A-1C. Mouse Settings and Output

Based on Buxton et al. (2021) study (Buxton S, Taylor MD, Weinberg JT, Randazzo JM, Peachee VL, Oller A. 2021. A T-dependent antibody response evaluation in CD-1 mice after acute whole-body inhalation exposure to nickel (II) chloride hexahydrate. Journal of Immunotoxicology, 18(1):144-153.

MPPD output file	Mouse_BALBc_Standard_Report.txt	Mouse_B6C3F1_Standard_Report.txt
AIRWAY MORPHOMETRY		
Species	Mouse	Mouse
BW (g)	30.455	30.455
Model	BALB/c	B6C3F1
FRC (mL) -- AUTOMATICALLY CALCULATED	0.219	0.3
URT Volume (mL) -- AUTOMATICALLY CALCULATED	0.0322	0.0322
INHALANT PROPERTIES		
Select "Aerosol"		
Density (g/cm3) -- DEFAULT	1	1
Aspect Ratio -- DEFAULT	1	1
Diameter (um)	1.1	1.1
"Single", "Multiple" or "Multimodal"	Single	Single
CMD, MMD or MMAD	MMAD	MMAD
Inhalability Adjustment	checked	checked
GSD (diam.)	2.26	2.26
GSD (length) -- DEFAULT	1	1
Correlation -- DEFAULT	0	0
Equiv. Diam. Model -- DEFAULT	not checked	not checked
Diff. Diameter (um) -- DEFAULT	1	1
Sed. Diameter (um) -- DEFAULT	1	1
Imp. Diameter (um) -- DEFAULT	1	1
Int. Diameter (um) -- DEFAULT	1	1
EXPOSURE CONDITION -- Constant or Variable Exposure	Constant	Constant
Acceleration of Gravity (cm/s2) -- DEFAULT	981	981
Body Orientation -- DEFAULT	Upright	Upright
Aerosol Concentration (mg/m3)	0.0809	0.0809
Breathing Frequency (per minute) -- value from Guyton (1947)	163	163
Tidal Volume (mL) -- value from Guyton (1947)	0.15	0.15
Inspiratory Fraction -- DEFAULT	0.5	0.5
Pause Fraction -- DEFAULT	0	0
Breathing Scenario	Whole body (output file says "Nasal")	Whole body (output file says "Nasal")
DEPOSITION CLEARANCE -- Deposition Only or Dep. + Clearance	Deposition Only	Deposition Only

Output		
Total head deposition fraction	0.3467	0.3575
Total TB deposition fraction	0.0496	0.0274
Total pulmonary deposition fraction	0.072	0.0567
Total deposition fraction	0.4683	0.4416
Volumetric inhalation/exhalation flow rate at trachea (mL/sec)	0.815	0.815
Volumetric inhalation/exhalation flow rate at trachea (L/min)	0.0489	0.0489


Region: Entire Lung
Deposition Fraction
0.5151
0.4121
0.3091
0.2061
0.1030
0.0
0.3467
0.0496
0.0720
0.4683
Head
TB
P
Total
Region
Species & Model Info:
Species/Geometry: BALB/c Mouse Symmetric
FRC Volume: 0.22 ml
Head Volume: 0.03 ml
Breathing Route: nasal
Breathing Parameters:
Tidal Volume: 0.15 ml
Breathing Frequency: 163.00 1/min
Inspiratory Fraction: 0.50
Pause Fraction: 0.00
Particle Properties:
Diameter: MMAD: 1.10 µm
GSD: 2.96
Concentration: 0.08 mg/m^3

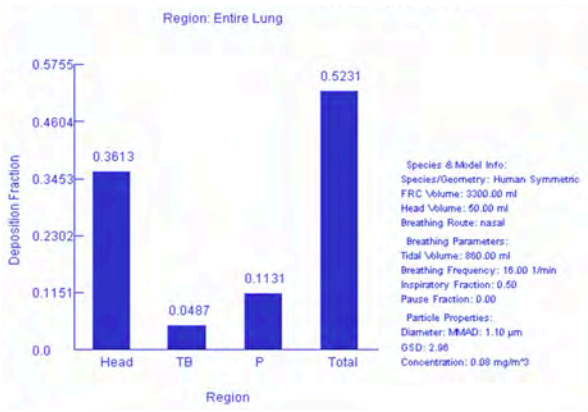

Region: Entire Lung
Deposition Fraction
0.4858
0.3886
0.2915
0.1943
0.0972
0.0
0.3575
0.0274
0.0567
0.4416
Head
TB
P
Total
Region
Species & Model Info:
Species/Geometry: B6C3F1 Mouse Symmetric
FRC Volume: 0.30 ml
Head Volume: 0.03 ml
Breathing Route: nasal
Breathing Parameters:
Tidal Volume: 0.15 ml
Breathing Frequency: 163.00 1/min
Inspiratory Fraction: 0.50
Pause Fraction: 0.00
Particle Properties:
Diameter: MMAD: 1.10 µm
GSD: 2.96
Concentration: 0.08 mg/m^3

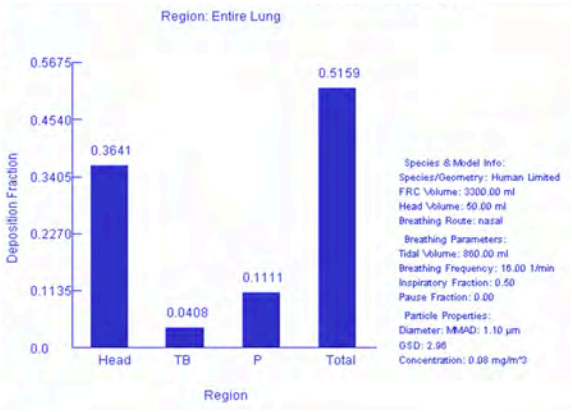
Attachment A-1D. Mouse Settings and Output

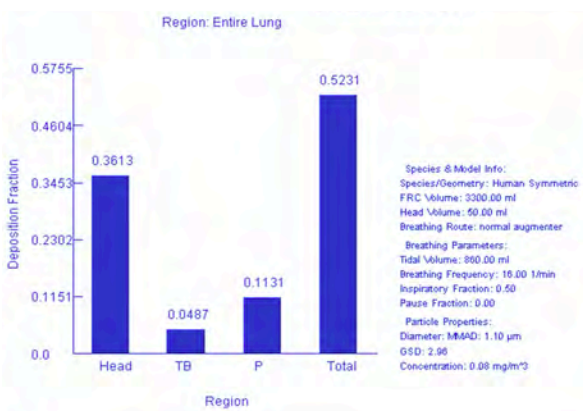
Human Settings and Output

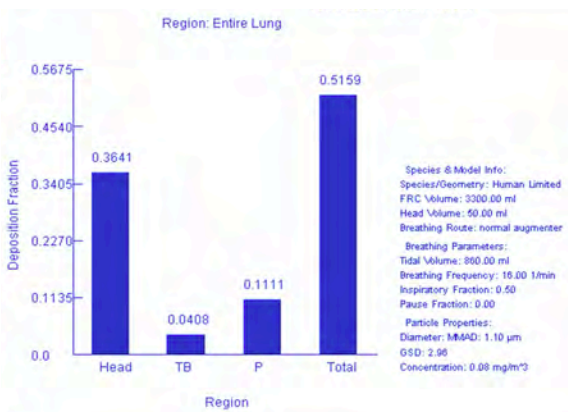
Used same particle description and inhaled concentration as for mouse

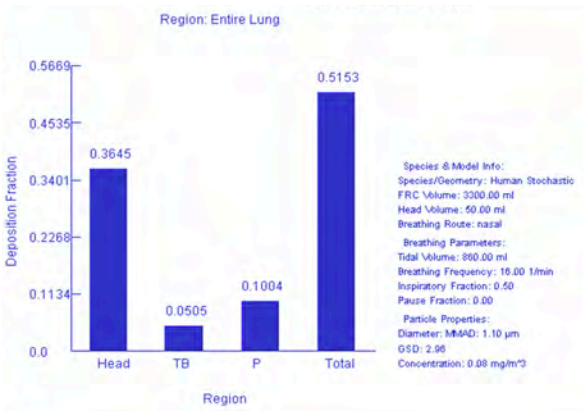
	MPPD output file	Human_Yeh-Schum-Symmetric_Nasal_Standard_Report.txt	Human_Yeh-Schum-Symmetric_Oronasal_Standard_Report.txt	Human_Yeh-Schum-5Lobe_Nasal_Standard_Report.txt	Human_Yeh-Schum-5Lobe_Oronasal_Standard_Report.txt	Human_Stochastic_Nasal_Standard_Report.txt	Human_Stochastic_Oronasal_Standard_Report.txt
AIRWAY MORPHOMETRY							
	Species	Human		Human		Human	
	BW			No option to enter for Human			
	Model	Yeh/Schum Symmetric		Yeh/Schum 5 Lobe		Stochastic (60th percentile)	
	FRC (mL) -- DEFAULT	3300		3300		3300	
	URT Volume (mL) -- DEFAULT	50		50		50	
INHALANT PROPERTIES							
	Select "Aerosol"						
	Density (g/cm3) -- DEFAULT	1		1		1	
	Aspect Ratio -- DEFAULT	1		1		1	
	Diameter (um)	1.1		1.1		1.1	
	"Single", "Multiple" or "Multimodal"	Single		Single		Single	
	CMD, MMD or MMAD	MMAD		MMAD		MMAD	
	Inhalability Adjustment	checked		checked		checked	
	GSD (diam.)	2.26		2.26		2.26	
	GSD (length) -- DEFAULT	1		1		1	
	Correlation -- DEFAULT	0		0		0	
	Equiv. Diam. Model -- DEFAULT	not checked		not checked		not checked	
	Diff. Diameter (um) -- DEFAULT	1		1		1	
	Sed. Diameter (um) -- DEFAULT	1		1		1	
	Imp. Diameter (um) -- DEFAULT	1		1		1	
	Int. Diameter (um) -- DEFAULT	1		1		1	
EXPOSURE CONDITION -- Constant or Variable Exposure		Constant		Constant		Constant	
	Acceleration of Gravity (cm/s2) -- DEFAULT	981		981		981	
	Body Orientation -- DEFAULT	Upright		Upright		Upright	
	Aerosol Concentration (mg/m3)	0.0809		0.0809		0.0809	
	Breathing Frequency (per minute) -- from 2017 IRIS Benzo[a]pyrene review	16		16		16	
	Tidal Volume (mL) -- from 2017 IRIS Benzo[a]pyrene review	860		860		860	
	Inspiratory Fraction -- DEFAULT	0.5		0.5		0.5	
	Pause Fraction -- DEFAULT	0		0		0	
	Breathing Scenario -- 2017 IRIS Benzo[a]pyrene review used "Nasal"	Nasal	Oro-nasal augmenter	Nasal	Oro-nasal augmenter	Nasal	Oro-nasal augmenter
DEPOSITION CLEARANCE -- Deposition Only or Dep. + Clearance		Deposition Only		Deposition Only		Deposition Only	
Output							
	Total head deposition fraction	0.3613		0.3641		0.3645	
	Total TB deposition fraction	0.0487		0.0408		0.0505	
	Total pulmonary deposition fraction	0.1131		0.1111		0.1004	
	Total deposition fraction	0.5231		0.5159		0.5153	
	Volumetric inhalation/exhalation flow rate at trachea (mL/sec)	458.6666667		458.6666667		458.6666667	
	Volumetric inhalation/exhalation flow rate at trachea (L/min)	27.52		27.52		27.52	EPA used 13.8 L/min

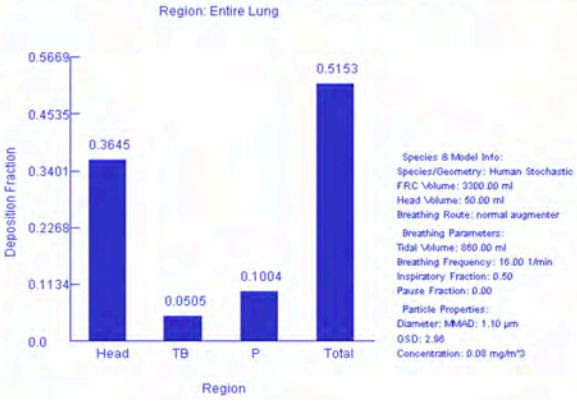

Region: Entire Lung
Deposition Fraction
0.5755
0.4604
0.3453
0.2302
0.1151
0.0
0.3613
0.0487
0.1131
0.5231
Head
TB
P
Total
Region
Species & Model Info:
Species/Geometry: Human Symmetric
FRC Volume: 3300.00 ml
Head Volume: 50.00 ml
Breathing Route: nasal
Breathing Parameters:
Tidal Volume: 860.00 ml
Breathing Frequency: 16.00 1/min
Inspiratory Fraction: 0.50
Pause Fraction: 0.00
Particle Properties:
Diameter: MMAD: 1.10 µm
GSD: 2.96
Concentration: 0.08 mg/m^3


Region: Entire Lung
Deposition Fraction
0.5675
0.4540
0.3405
0.2270
0.1135
0.0
0.3641
0.0408
0.1111
0.5159
Head
TB
P
Total
Region
Species & Model Info:
Species/Geometry: Human Limited
FRC Volume: 3300.00 ml
Head Volume: 50.00 ml
Breathing Route: nasal
Breathing Parameters:
Tidal Volume: 860.00 ml
Breathing Frequency: 16.00 1/min
Inspiratory Fraction: 0.50
Pause Fraction: 0.00
Particle Properties:
Diameter: MMAD: 1.10 µm
GSD: 2.96
Concentration: 0.08 mg/m^3


Region: Entire Lung
Deposition Fraction
0.5755
0.4604
0.3453
0.2302
0.1151
0.0
0.3613
0.0487
0.1131
0.5231
Head
TB
P
Total
Region
Species & Model Info:
Species/Geometry: Human Symmetric
FRC Volume: 3300.00 ml
Head Volume: 50.00 ml
Breathing Route: normal augmenter
Breathing Parameters:
Tidal Volume: 860.00 ml
Breathing Frequency: 16.00 1/min
Inspiratory Fraction: 0.50
Pause Fraction: 0.00
Particle Properties:
Diameter: MMAD: 1.10 µm
GSD: 2.96
Concentration: 0.08 mg/m^3


Region: Entire Lung
Deposition Fraction
0.5675
0.4540
0.3405
0.2270
0.1135
0.0
0.3641
0.0408
0.1111
0.5159
Head
TB
P
Total
Region
Species & Model Info:
Species/Geometry: Human Limited
FRC Volume: 3300.00 ml
Head Volume: 50.00 ml
Breathing Route: normal augmenter
Breathing Parameters:
Tidal Volume: 860.00 ml
Breathing Frequency: 16.00 1/min
Inspiratory Fraction: 0.50
Pause Fraction: 0.00
Particle Properties:
Diameter: MMAD: 1.10 µm
GSD: 2.96
Concentration: 0.08 mg/m^3


Region: Entire Lung
Deposition Fraction
0.5669
0.4535
0.3401
0.2268
0.1134
0.0
0.3645
0.0505
0.1004
0.5153
Head
TB
P
Total
Region
Species & Model Info:
Species/Geometry: Human Stochastic
FRC Volume: 3300.00 ml
Head Volume: 50.00 ml
Breathing Route: nasal
Breathing Parameters:
Tidal Volume: 860.00 ml
Breathing Frequency: 16.00 1/min
Inspiratory Fraction: 0.50
Pause Fraction: 0.00
Particle Properties:
Diameter: MMAD: 1.10 µm
GSD: 2.96
Concentration: 0.08 mg/m^3


Region: Entire Lung
Deposition Fraction
0.5669
0.4535
0.3401
0.2268
0.1134
0.0
0.3645
0.0505
0.1004
0.5153
Head
TB
P
Total
Region
Species & Model Info:
Species/Geometry: Human Stochastic
FRC Volume: 3300.00 ml
Head Volume: 50.00 ml
Breathing Route: normal augmenter
Breathing Parameters:
Tidal Volume: 860.00 ml
Breathing Frequency: 16.00 1/min
Inspiratory Fraction: 0.50
Pause Fraction: 0.00
Particle Properties:
Diameter: MMAD: 1.10 µm
GSD: 2.96
Concentration: 0.08 mg/m^3

ToxStrategies

Innovative solutions
Sound science

Technical Memorandum

September 30, 2025

To:	J.R. Giska and Apollonia Goeckner, Oregon Department of Environmental Quality; Holly Dixon, PhD, Oregon Health Authority
From:	Deborah Proctor, Chad Thompson and Ann Verwiel, ToxStrategies LLC
Subject:	**Evaluation of Draft Proposed TRVs for PFAS Compounds**

ODEQ has proposed chronic and acute inhalation toxicity reference values (TRVs) for several PFAS compounds that did not previously have TRVs. The proposed inhalation TRVs are based on inhalation toxicity values published by non-authoritative sources as defined in Cleaner Air Oregon regulations. Given the issues presented below, it is not appropriate to adopt these acute and chronic inhalation TRVs for PFAS compounds at this time; additional evaluation is necessary before ODEQ should set TRVs for these PFAS compounds. There is general consensus that exposures to PFAS compounds via inhalation of ambient air are far less significant than food, water, and soil exposures (ATSDR, 2021, page 713), such that regulation of exposures in air at this time will not significantly change overall exposures to PFAS compounds. In other words, regulating exposures to PFAS compounds in air will not reduce overall exposures to PFAS in the population under current conditions.

Overarching issues with the proposed PFAS inhalation TRVs are provided in the table below and discussed further in the text.

Issue	Description
1. Limited Inhalation Toxicity Studies and the Absence of Inhalation Toxicity Values Published by Authoritative Sources	• There is an absence of inhalation toxicity studies that can be used to derive inhalation reference concentrations for the PFAS compounds. Inhalation studies are preferred over the use of route-to-route extrapolation of oral toxicity data to develop inhalation TRVs. Only the proposed TRV for perfluorononanoic acid (PFNA) is based on an inhalation study, but even that TRV is technically flawed as discussed in Attachment A.

Issue	Description
	• Sources deemed authoritative by Cleaner Air Oregon (i.e., the Environmental Protection Agency [EPA], the Agency for Toxic Substances Disease Registry [ATSDR], and California's Office of Environmental Health Hazard Assessment [OEHHA]) have not published inhalation reference criteria for PFAS compounds. For example, EPA has Reference Doses (RfDs) for many of the PFAS compounds, but has not developed inhalation toxicity values for any of them. ODEQ should rely on and wait for Authoritative Sources to develop inhalation toxicity values before ODEQ proceeds to set TRVs for the PFAS compounds.
2. Oral Toxicity Values are Uncertain and Evolving Rapidly and are Not Appropriate for TRVs Intended to be Used for a Long Period of Time	• Toxicity criteria for PFAS compounds *by the oral route* are rapidly changing (e.g., EPA published RfDs for PFOA (final) and PFNA (draft) in 2024 [EPA, 2024a,b] to replace values previously published in 2009 and/or 2016. • Additionally, some recently proposed toxicity values are increasingly being scrutinized and concluded to be highly uncertain. For example, recent reviews of EPA's 2024 RfD for PFOA have raised serious concerns about the scientific merits of the RfD, which could lead to scientific and legal challenges and additional revisions.
3. Derivation of inhalation TRVs requires consideration of the toxicity of individual PFAS compounds and relevant endpoints	• Development of TRVs should not be taken on without considered evaluation of the underlying toxicity data, points of departure (PODs), toxicokinetics by route, and compound-specific data. • For example, derivation of acute TRVs based on acute inhalation studies does not require interspecies adjustments that are typically applied in chronic TRVs because steady state pharmacokinetics are unlikely to play a role in acute toxicity. An example of this point is included in Attachment A for PFNA.

Additional discussion of these concepts is presented below. ODEQ should not set TRVs for any PFAS compounds based on oral toxicity data alone and for which inhalation studies are not yet available. The only proposed TRV based on an inhalation study is an acute TRV for PFNA. Attachment A highlights deficiencies in ODEQ's acute TRV for PFNA and

proposes an alternative acute TRV using the same toxicity endpoint, but using derivation methods which are consistent with EPA risk assessment guidance.

1.0 Limited Inhalation Toxicity Studies and the Absence of Inhalation Toxicity Values Published by Authoritative Sources

All but one of the PFAS inhalation TRVs proposed by ODEQ are based on oral toxicity data. There are currently insufficient PFAS inhalation toxicity data available to inform whether PFAS inhalation poses a health risk in experimental animals, and there are insufficient data to confidently estimate safe PFAS inhalation exposure levels.

While EPA has proposed several RfD values for PFAS compounds in the last 15 years, EPA has no Reference Concentration (RfC) values for any of the PFAS compounds for which ODEQ has derived inhalation TRV values. Critically, EPA did not conduct route-to-route extrapolation from these RfD values (or oral toxicity data) to derive RfC values. For example, EPA explicitly declined to develop an inhalation RfC for perfluorohexanesulfonic acid (PFHxS) stating: "No studies that examine toxicity in humans or experimental animals following inhalation exposure are available and no acceptable physiologically based pharmacokinetic (PBPK) models are available to support route-to-route extrapolation; therefore, no RfC was derived." (EPA, 2025, p.5). EPA's unwillingness to use route extrapolation from oral toxicity studies highlights the extreme uncertainty in conducting such extrapolation as ODEQ has done. Similarly, ATSDR, another Authoritative Source, has not developed inhalation minimum risk levels (MRLs) for PFAS compounds while they have published oral MRLs (ATSDR, 2021).

2.0 Oral Toxicity Values are Uncertain and Evolving Rapidly and are Not Appropriate for TRVs Intended to be Used for a Long Period of Time

In addition to the uncertainty associated with route extrapolation, there are uncertainties around several of EPA's oral RfD values. This has been demonstrated most clearly for one of the most well-studied PFAS compounds, PFOA. Over a relatively short period of time, EPA has proposed several RfD values for PFOA starting with 2E-4 mg/kg-day in 2009, then 2E-5 mg/kg-day in 2016, and now 3E-8 mg/kg-day in 2024.

Also, the most recent RfD for PFOA is based on human observational data, which has received significant scrutiny by experts in human health risk assessment. A recently published uncertainty analysis concluded that some of the purported associations between PFOA and adverse effects in humans were so unreliable as to warrant preclusion from even considering dose-response analysis (Wikoff et al., 2025). A panel of experts in Burgoon et al. (2023) concluded that "existing human observational studies cannot be used reliably for [selection of critical effect for RfD]." Notably, the ultra-low PFOA 2024 RfD value suggests that PFOA is a highly toxic chemical. However, as discussed in Burgoon et al. (2023), PFOA has been used in a phase I chemotherapy treatment clinical trial without

signs of overt toxicity (Convertino et al., 2018). These studies indicate that the EPA (2024) RfD is overly conservative (if not flawed), and it is, therefore, not responsible to use this highly uncertain RfD value to derive TRV values for PFOA. These issues with uncertainty also apply to other PFAS compounds (Burgoon et al. 2023).

Given the state of the science and uncertain nature of guidelines for these compounds, there is a high likelihood that the proposed TRVs will be outdated—even if it is scientifically credible to conduct route-to-route extrapolation for some of the compounds—before the TRVs are even approved. Under the Cleaner Air Oregon program, these highly uncertain TRVs would remain as the basis for regulation in Oregon for three or more years while the science and new guideline values continue to be developed within agencies including those deemed Authoritative Sources. This is very different from EPA's application of RfDs to regional screening levels for soil and water, for example, which are guidance values and updated every six months.

3. Derivation of inhalation TRVs requires detailed understanding of toxicity of PFAS compounds and relevant endpoints

Several of the proposed TRVs are based on data that requires a more detailed evaluation of the underlying toxicity before being used as a basis for a TRV.

For example, ODEQ's proposed acute TRV for perfluorononanoic acid (PFNA) is based on inhalation data, where adjustment factors were misapplied. Acute toxicity values based on acute exposure studies do not require pharmacokinetic adjustments because steady state pharmacokinetics are unlikely to play a major role in acute toxicity. This is evidenced by the fact that regulatory agencies do not typically apply allometric scaling for acute toxicity. However, ODEQ applied an 81-fold PK adjustment to the acute 4-hour exposure study used as the basis for the acute TRV. In addition, ODEQ applied a 10-fold acute-to-subchronic uncertainty factor for the use of an acute study for an *acute* TRV, which is unnecessary and counterintuitive. Any uncertainty in the use of a 4-hour study for a 24-hour toxicity value was already accounted for when ODEQ applied a 6-fold duration adjustment factor (i.e., 1 ÷ 4/24 h). Attachment A shows how toxicity assumptions were misinterpreted in the ODEQ derivation of the acute TRV for PFNA.

In another example, ODEQ has proposed an acute TRV for perfluorobutanesulfonic acid (PFBS) based on a subchronic oral RfD derived by Minnesota Department of Health. However, EPA, which is an Authoritative Source, proposed a different subchronic oral RfD (EPA, 2021). No justification for excluding EPA's RfD was provided.

Also, as shown in Table 1, the duration of the studies used to develop proposed acute TRVs vary. However, only the study of PFNA exposures considered a time-frame within a 24-hour exposure period, which is the time period applicable to acute TRVs.

Conclusion

We recommend that ODEQ pause the effort to develop inhalation TRVs for PFAS compounds now and only resume if and when Authoritative Sources develop inhalation toxicity values. Without values from Authoritative Sources, ODEQ, in collaboration with the ATSAC, would need to identify and analyze the availability of inhalation toxicity data, evaluate the appropriateness of the exposure durations studied for the TRV, assess the relevance of route-to-route extrapolation, and consider the level of uncertainty in the resulting values. Simply adopting criteria published by other state regulatory agencies that are not Authoritative Sources does not meet the intent in the Cleaner Air Oregon regulations, which specifically lists these Authoritative Sources in recognition of the level of effort and consideration given to developing toxicity criteria by EPA, ATSDR, and OEHHA. ODEQ should wait until at least one of these Authoritative Sources acts to set acute or chronic inhalation values before proposing values under Cleaner Air Oregon.

Table 1 provides a list of the acute and chronic TRVs proposed by ODEQ for ten of the 13 PFAS compounds and various sources of uncertainty related to the discussion herein that provides further support for waiting to propose acute and chronic TRVs for PFAS compounds.

Table 1. Basis for Proposed ODEQ Toxicity Reference Values for 10 of 13 PFAS Compounds

CAS No.	TAC	TRV Type	Number of Carbons in Chain	Proposed TRV (ug/m3)	Proposed DEQ TRV Source	Detailed TRV Source	Time Frame Derivation
375-73-5	Perfluorobutanesulfonic acid (PFBS)	Acute	4	0.3	DEQ	MN DOH	MN DOH used 28-day oral study for acute TRV
375-22-4	Perfluorobutanoic acid (PFBA)	Chronic	4	3.5	DEQ	TCEQ	EPA used 90-day oral study; TCEQ adapted EPA's chronic RfD
375-22-4	Perfluorobutanoic acid (PFBA)	Acute	4	10	DEQ	MN DOH	MN DOH used 28-day oral study for acute TRV and 90-day oral study for subchronic/chronic values. All 3 values were the same in the end.
335-76-2	Perfluorodecanoic acid (PFDA)	Chronic	10	0.053	DEQ	TCEQ	TCEQ used 1-week oral study for chronic TRV
307-55-1	Perfluorododecanoic acid (PFDoA)	Chronic	12	0.042	DEQ	TCEQ	TCEQ used 14-day oral study for chronic TRV
355-46-4	Perfluorohexanesulfonic acid (PFHxS)	Acute	6	0.034	DEQ	MN DOH	MN DOH used 28-day oral study for acute TRV
307-24-4	Perfluorohexanoic acid (PFHxA)	Chronic	6	0.5	DEQ	MN DOH	MN DOH used 90-day oral study for subchronic/chronic TRV
307-24-4	Perfluorohexanoic acid (PFHxA)	Acute	6	1	DEQ	MN DOH	MN DOH used 28-day oral study for acute TRV
375-95-1	Perfluorononanoic acid (PFNA)	Acute	9	0.047	DEQ	TCEQ	TCEQ used 4-hour inhalation study for chronic TRV, which was adjusted to acute by ODEQ.
1763-23-1	Perfluorooctanesulfonic acid (PFOS)	Chronic	8	0.0004	DEQ	MI EGLE	MI EGLE adopted EPA chronic oral RfD
1763-23-1	Perfluorooctanesulfonic acid (PFOS)	Acute	8	0.011	DEQ	MN DOH	MN DOH used 60-day oral study for acute TRV
335-67-1	Perfluorooctanoic acid (PFOA)	Chronic	8	0.0001	DEQ	MI EGLE	MI EGLE adopted EPA chronic oral RfD
335-67-1	Perfluorooctanoic acid (PFOA)	Acute	8	0.063	DEQ	MN DOH	MN DOH used developmental mouse ingestion study (GD 1-17)
754-91-6	Perfluorooctane sulfonamide (PFOSA)	Chronic	8	0.0001	DEQ	MI EGLE	See PFOA
754-91-6	Perfluorooctane sulfonamide (PFOSA)	Acute	8	0.063	DEQ	MN DOH	See PFOA

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ATTACHMENT A

Example Derivations for PFNA

Attachment A. Example Derivation for PFNA

ODEQ's proposed acute TRV for PFNA has two errors that result in an overly conservative TRV. ODEQ relied on the Texas Commission on Environmental Quality's (TCEQ's) chronic RfC for PFNA based on labored breathing in rats exposed to PFNA for 4 hours in an inhalation study (Kinney, 1989). Labored breathing was observed at 596 mg/m^3 PFNA thereby making the lowest concentration, 67 mg/m^3, the no-observable-adverse-effect-concentration (NOAEC). Because TCEQ was developing a chronic RfC from an acute study, TCEQ applied two 10-fold uncertainty factors to account for the use of an acute study (Table A-1). ODEQ eliminated one of these adjustments (subchronic-to-chronic) but left in the acute-to-subchronic adjustment when doing their calculations, and then also added a duration adjustment factor of 6 to convert the 4-hour exposure to a 24-hour daily exposure. However, using both the duration adjustment and the 10-fold factor is essentially double counting the adjustment (Table A-1).

A second error in the ODEQ acute TRV calculation is the application of an 81-fold pharmacokinetic uncertainty factor (UFA-PK). While this factor might have been appropriate for the chronic RfC TCEQ developed, it is not appropriate for an acute TRV because acute single-exposure toxicity effects are more direct effects that are less likely to be a consequence of pharmacokinetic factors (e.g., steady-state clearance). This is why regulators such as the EPA and TCEQ do not conduct allometric scaling (a form of pharmacokinetic adjustment) for acute toxicity criteria (EPA, 2012; TCEQ, 2015). Under a single acute exposure scenario, pharmacokinetic differences in PFNA clearance are not likely relevant—especially for an endpoint based on labored breathing, which is likely a result of the extremely high exposure concentrations administered in the study and unrelated to any systemic effects. As such, this factor should be removed and replaced with the default 10-fold UFA (UFA-PK = 3; UFA-PD = 3), which results in an alternative proposed acute TRV of 11 μg/m^3 (**Table A-1**).

Table A-1. Comparison of derivation of PFNA inhalation toxicity values

	TCEQ (chronic)	ODEQ (acute)	Proposed (acute)
NOAEC (mg/m3)	67	67	67
UFA-PK	81	81	3
UFA-PD	3	3	3
UFH	10	10	10
UFD	10	10	10
UFsubchron-to-chronic	10	Not applied	Not applied
UFacute-to-subchron [1]	10	10	Not applied
Duration Adjustment	Not applied	6	6
Composite Adj	2,430,000	1,458,000	6,000
RfC/TRV ($\mu g/m^3$)	2.8E-2 (chronic)	4.6E-2 (acute)	11 (acute)

Notes:

1. The acute to subchronic uncertainty factor applied by TCEQ is not present in the ERG summary of the TCEQ RfC for PFNA.

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Technical Memorandum

September 30, 2025

To:	J.R. Giska and Apollonia Goeckner, Oregon Department of Environmental Quality; Holly Dixon, PhD, Oregon Health Authority
From:	Deborah Proctor and Ann Verwiel, ToxStrategies LLC
Subject:	**Evaluation of Draft Proposed Updates to Vanadium TRVs for Cleaner Air Oregon**

To support the current review of the inhalation toxicity reference values (TRVs) used in the Cleaner Air Oregon program, we have evaluated the draft proposed TRVs that Oregon Department of Environmental Quality (ODEQ) and Oregon Health Authority (OHA) have presented to the Air Toxics Science Advisory Committee (ATSAC) for its consideration for vanadium. This memorandum discusses in more detail the proposed vanadium TRV, and **Table 1** below briefly summarizes our conclusions.

Table 1. Summary of Recommendations for Proposed Updates to Vanadium TRVs

ODEQ Proposed TRV (µg/m^3)	Recommendations for Updates to Proposed TRV
Acute TRV 0.8 **Chronic TRV** 0.1 **Cancer TRV** 0.00012	• Revise the TRVs to specify vanadium pentoxide or withdraw the proposed TRVs for acute and chronic noncancer effects because the underlying key studies are based on vanadium pentoxide, and not generally applicable to all forms of vanadium or the predominant forms of vanadium expected to exist in Oregon ambient air. • Withdraw the existing TRV for carcinogenic effects because the U.S. Environmental Protection Agency (EPA) only applies this value to vanadium pentoxide, and clearly states it is only applicable to vanadium pentoxide in its regional screening level documentation. As such, use of the vanadium pentoxide inhalation unit risk is inconsistent with the authoritative source. • Postpone setting TRVs until EPA or another authoritative source completes an evaluation specific to vanadium and compounds before using vanadium pentoxide to represent all forms of vanadium.

Vanadium in the Pentoxide Valence is Unlikely to be Emitted by the Vast Majority of Sources in Oregon

As a transition metal, vanadium exists in several valence states and toxicity varies depending on valence. ATSDR (2012) states that "vanadium has oxidation states of +2, +3, +4 and +5". It also exists in elemental form (zero valence). Applying toxicity criteria for the most highly oxidized from of vanadium (pentoxide) to all forms of vanadium will overestimate risk and hazard associated with vanadium in the Cleaner Air Oregon (CAO) program.

It is not likely that emissions of vanadium from industrial operations in Oregon are in the pentoxide form. ATSDR states that "vanadium is used in producing rust-resistant, spring and high-speed tool steels. It is an important carbide stabilizer in making steels. About 80% of the vanadium produced is used as ferrovanadium as a steel additive. Vanadium foil is used as a bonding agent in cladding titanium to steel. Vanadium pentoxide is used in ceramics and as a catalyst as well as in producing superconductive magnet with a field. Metallurgical use as an alloying agent for iron and steel accounted for approximately 95% of domestic vanadium consumption in 2008."[1] As such, although sources of vanadium

[1] ATSDR 2012, page 119

pentoxide may exist in a few industries, the predominant source of vanadium emissions in Oregon ambient air are likely related to titanium and steel production and metal fabrication. Vanadium from these industries is expected to exist as elemental vanadium and bound in an alloy matrix. And, similar to other metals in alloys, vanadium in alloy form is not likely to be bioaccessible or remotely relevant to exposure to pure vanadium pentoxide. As indicated in ATSDR's toxicological profile, other entities that propose health-based values have focused on vanadium pentoxide rather than extending the applicability to vanadium and compounds [e.g., the American Conference of Governmental Hygienists (ACGIH)], or have made an exception for vanadium metal [e.g., the National Institute of Occupational Health (NIOSH)]. For example, EPA explicitly excludes "vanadium when contained in an alloy" from the emergency planning and community right-to-know reporting requirements (ATSDR, 2012, p.169, Table 8-1).

ATSDR states "the most important anthropogenic sources of vanadium include the combustion of fossil fuels, particularly residual fuel oils, which constitute the single largest overall release of vanadium to the atmosphere…Natural gas and distillate fuel oils contain very low or undetectable levels of vanadium."[2] Further ATSDR (2012) states that, "Higher vanadium levels have been measured in the eastern United States due to the high density of oil fired power plants using vanadium-rich residual fuel oil."[3] As there are no active residual oil or fossil fuel fired power plants in Oregon, the potential for significant vanadium pentoxide emissions are very low.

The studies used as the basis for all three of the "vanadium and compounds" TRVs are for research based on vanadium pentoxide and not for vanadium metal or other vanadium forms. ATSDR provides detailed discussion of the difference in toxicity of tetravalent (vanadyl or V^{+4}) and pentavalent (vanadate or V^{+5}). ATSDR states, "Vanadate is considered more toxic than vanadyl because vanadate is reactive with a number of enzymes and is a potential inhibitor of the Na+K+APTase of plasma membranes…There is slower update of vanadyl into erythrocytes compared to the vanadate form."[4] Vanadium metal and vanadium pentoxide are distinct in form and potential toxicity. The inhalation toxicity data available from animal studies provided in the Toxicological Profile is limited to studies of vanadium pentoxide. However, by oral exposure in a subchronic rat and mouse drinking water study, Roberts et al. (2016) also reported that vanadyl was less toxic than vanadate in both species. No data on exposure to vanadium in alloy or elemental form exist to our knowledge.

As such, it would be prudent for ODEQ to specify that the vanadium TRVs are specific to vanadium in the pentoxide form, or withdraw the proposed values until authoritative sources set vanadium guidelines that are relevant to vanadium emissions in Oregon.

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[2] ATSDR 2012, page 141
[3] ATSDR 2012, page 31
[4] ATSDR 2012, page 105

Withdraw or Change Proposed Acute and Chronic TRVs for Vanadium

The proposed vanadium TRVs for acute and chronic health effects should be withdrawn, or be made specific to vanadium pentoxide, because the Agency for Toxic Substances and Disease Registry (ATSDR) minimal risk levels (MRLs) are based on vanadium pentoxide, and neither ATSDR nor EPA provide a justification for applying vanadium pentoxide-based values to regulate all forms of vanadium and vanadium compounds. In fact, in ATSDR's public health statements in its Toxicological Profile, exposure to vanadium pentoxide, not vanadium compounds, was highlighted. In the main portion of its Toxicological Profile, ATSDR's summary of health effects is based on vanadium pentoxide, but when calculating the MRL, ATSDR broadens its discussion to vanadium. ATSDR simply uses the molecular weights of vanadium and oxygen to convert the study results from vanadium pentoxide (X mgV_2O_5/m^3) to vanadium, using a factor of 0.56 (X*0.56 V/m^3). While converting the amount of vanadium pentoxide to vanadium using molecular weight is mathematically valid, ATSDR offers no discussion in the document about why the toxicity of vanadium pentoxide and other forms of vanadium would be directly related. The ATSDR document presents insufficient evidence to show that the adverse health effects are interchangeable. EPA has used the ATSDR MRL as the toxicity criteria for vanadium for developing its Regional Screening Levels (RSLs) simply because the CAS numbers were made to match. EPA's RSL website states that in 2013, "Vanadium and compounds was given the CAS number 7440-62-2. Previously, it did not have a CAS number. This results in the database matching a reference concentration (RfC) from ATSDR" (EPA, 2013, heading: May 2013, bullet: 7).

Withdraw or Change Proposed Cancer TRVs for Vanadium

Although ODEQ's cancer TRV for vanadium and compounds was not proposed to be changed, it should at least be made more specific. The current TRV is based on EPA's PPRTV published in 2008. PPRTVs are "developed by EPA for use in the Superfund Program when such a value is not available in EPA's Integrated Risk Information System (IRIS)" (EPA, 2008, p. 1). The PPRTV document clearly identifies in the title that it applies to vanadium pentoxide and not "vanadium and compounds." The PPRTV for carcinogenic health effects is based on a National Toxicology Program (NTP) study of mice exposed to vanadium pentoxide (NTP, 2002), and the endpoint was alveolar/bronchiolar neoplasms (adenoma and carcinoma). However, EPA cautions "there is only suggestive evidence of human carcinogenicity from vanadium pentoxide exposure so there is uncertainty associated with quantitation of the database" (EPA, 2008, p. 51).

In the RSLs developed for the Superfund program, EPA only uses the vanadium pentoxide PPRTV (0.00012 $\mu g/m^3$) to develop RSLs for carcinogenic health effects for vanadium pentoxide. Consistent with the PPRTV documentation, EPA explicitly has not developed RSLs for "vanadium and compounds" for carcinogenic health effects via inhalation exposure (EPA, 2024). RSLs for vanadium and compounds were added to EPA's RSLs in 2013 based on ATSDR's update to the chronic MRL in 2012 (previous discussion), but no

change was made at that point or since to apply the PPRTV for carcinogenic health effects to vanadium and compounds in general. The potential toxicity of other vanadium forms, especially vanadium in an alloy matrix, is not addressed by the PPRTV, and is likely negligible because metals in an alloy matrix are generally not bioaccessible, and are elemental and not in the pentoxide form. To be consistent with the authoritative source and the available science, ODEQ should propose to withdraw the TRV for carcinogenic health effects for vanadium and compounds that uses toxicity data from vanadium pentoxide, or alternatively, the value should specify applicability to vanadium pentoxide.

ODEQ should consider that although authoritative sources such as EPA and ATSDR have developed *screening levels* using the vanadium pentoxide toxicity data and used it to screen for potential hazards for all forms of vanadium, it is more problematic to use vanadium pentoxide data to represent all forms of vanadium in the CAO enforcement program. ATSDR states "MRLs are intended to serve as a screening tool to help public health professionals decide where to look more closely. MRLs are **not** intended to define cleanup or action levels for ATSDR or other agencies" [Emphasis not added].[5] Vanadium pentoxide-based toxicity criteria used as TRVs in CAO, should be only applied to emissions of vanadium in the pentoxide form.

It is recommended that ODEQ develop TRVs specific to vanadium pentoxide, and wait for evaluations by other authoritative sources to set any TRVs for other forms of vanadium. Also, any proposed vanadium TRV should exempt vanadium in alloy forms because of the negligible solubility of vanadium in alloy forms.

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PROFESSIONAL PROFILE

Ms. Deborah Proctor has more than 30 years of experience in environmental and occupational health risk assessment, specializing in applied toxicology, mode-of-action evaluations for chemical carcinogens, air toxics and air pollution risk assessment, exposure reconstruction, and quantitative dose-response analysis for the purpose of developing toxicity criteria.

Ms. Proctor has technical expertise for assessing the potential human health risk associated with contaminated air, soil, sediments, groundwater, biota, and consumer products; evaluating failure-to-warn litigation claims pursuant to California Proposition 65, including determination of Safe Harbor Levels; designing risk-based site investigations; assessing the environmental fate and toxicity of metals in the environment; determining the bioavailability of metals in soil and solid media; and risk/hazard communications. Ms. Proctor has conducted studies of oral and inhalation bioaccessibility for metals in alloys, slags, and affected soil, dust, and baghouse dust, and has designed and conducted relative bioavailability studies for cobalt, nickel, and manganese. Ms. Proctor uses state-of-the-art scientific approaches to evaluate potential hazards and develop health-protective and science-driven remediation goals. She provides technical comments to regulatory agencies on policy and guidance documents, and technical support for public communication. Ms. Proctor has designed studies involving human volunteers and is experienced with the use of Internal Review Boards (IRBs) and the ethical requirements and considerations associated with research involving humans.

Ms. Proctor is a nationally recognized expert regarding the potential health risks associated with occupational and environmental exposure to chromium. She has published extensively in this field and managed research projects that have been used to develop federal and state regulatory health criteria. Additionally, she has extensive experience in metals risk assessment and specific expertise for evaluating nickel, cobalt, titanium, manganese, lead, vanadium, beryllium, and arsenic.

Ms. Proctor is a subject matter expert regarding human health and environmental applications of steel slag and heavy metals in the environment. She has experience using physiologically based pharmacokinetic (PBPK) modeling in risk assessment for chromium, lead, manganese, and perchlorate.

Ms. Proctor's research has been applied to support regulatory decisions and inform health-based criteria. Specific examples include the US Environmental Protection Agency (EPA) Inhalation Reference Concentration for hexavalent chromium using Malsh et al. (1994), the OSHA risk assessment for the 2006 Hexavalent Chromium Rule and revised Permissible Exposure Limit using Luippold et al. (2003); Crump et al. (2003), and Proctor et al. (2003; 2004), EPA Office of Prevention, Pesticides and Toxic Substances 2008 Reregistration Eligibility Decision (RED) for Chromated Arsenicals using Technical Study Reports FPRL #012506 and FPRL #012406; and the New Jersey Department of Environmental Protection Soil Cleanup Criteria for dermal contact with hexavalent chromium using Fowler et al. (1999). She has published an adverse outcome pathway (AOP) analysis for rodent forestomach tumors by nongenotoxic initiating events (Proctor et al., 2018), and an AOP framework for small intestinal tumors in mice (Bhat et al. 2020).

Ms. Proctor is a regular science peer reviewer for the *Journal of Applied Toxicology*, *Toxicology*, *Regulatory Toxicology and Pharmacology*, *Chemico-Biological Interactions*, *Journal of Occupational and Environmental Medicine,* and *PLOS One,*

ACADEMIC CREDENTIALS

1988	B.S., Environmental Toxicology, University of California, Davis
1996-1998	Graduate Studies, Epidemiology, University of Pittsburgh

PROFESSIONAL AFFILIATIONS

Society for Risk Analysis (member)

Association for Environmental Health Sciences (Scientific Review Board member)

International Society of Exposure Assessment (member)

International Society of Environmental Epidemiology (member)

Society of Toxicology (Councilor, Risk Assessment Specialty Section [RASS])

PUBLICATION AND PRESENTATION AWARDS

Society of Toxicology (SOT) 2025
Awarded Second Place for Best Risk Assessment Abstract at the Society of Toxicology Annual Meeting (Proctor DM, Thompson C) by the Risk Assessment Specialty Section (RASS), Orlando, FL.

SOT 2014
Awarded Top 10 Risk Assessment Presentations at the Society of Toxicology Annual Meeting (Proctor DM, Suh M, Tachovsky JA, Abraham L, Hixon JG, Brorby GP, Campleman SL) by the RASS, Phoenix, AZ.

SOT 2013
Awarded for three of the Top Ten Risk Assessment Presentations at the Society of Toxicology Annual Meeting (Kirman et al., Thompson et al., Kopec et al.) by the RASS, San Antonio, TX.

SOT 2012
Awarded Top Nine Published Papers Advancing the Science of Risk Assessment (Thompson CM, Haws LC, Harris MA, Gatto NM, Proctor DM) by the RASS, San Francisco, CA.

SOT 2004
Awarded Top Five Risk Assessment Presentations at the Society of Toxicology Annual Meeting (Leung H, Madl A, Proctor D, Hays S, Cohen E) by the RASS, Baltimore, MD.

SOT 2002
Awarded Top Five Risk Assessment Presentations at the Society of Toxicology Annual Meeting (Crump K and Proctor D) by the RASS, Nashville, TN.

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CONFERENCE SYMPOSIA SESSION CHAIR

2018 ASSOCIATION OF ENVIRONMENTAL HEALTH SCIENCES: Session 5b: The Evolving Risk Assessment Landscape in California.

2017 AMERICAN INDUSTRIAL HYGIENE ASSOCIATION CONFERENCE: Challenges in Protecting Worker Health and Achieving Compliance in the World of Low Submicrogram Concentrations: A Case Study of Beryllium.

2016 SOCIETY OF TOXCIOLOGY: The Cancer Risk Assessment for Ingested Hexavalent Chromium: Challenges and Controversies

2015 SOCIETY OF TOXICOLOGY: Advanced Approaches for Quantitative Risk Assessment Using Human Data with Applications Across Disciplines

2014 TOXICOLOGY AND RISK ASSESSMENT: Using New Data and Methods to Improve the Risk Assessment of Environmental Perchlorate Exposure

2011 SOCIETY OF TOXICOLOGY: Using Mode of Action Data to Guide Quantitative Cancer Risk Assessment: A Case Study of Hexavalent Chromium in Drinking Water

2003 SOCIETY OF TOXICOLOGY: Health Risk Assessment of Hexavalent Chromium in Drinking Water: Carcinogenicity, Research and Regulation.

1996 ASSOCIATION FOR THE ENVIROMENTAL HEALTH OF SOIL: Chromium in Soil: Perspectives in Chemistry, Health and Environmental Regulation.

ABSTRACTS AND PRESENTATIONS

Proctor D, Thompson C. Why oral cavity tumors should not be the basis of the hexavalent chromium oral cancer slope factor-weight of evidence review. Abstract 3136, Society of Toxicology 64th Annual Meeting, Orlando, FL, March 2025.

Suh M, Mittal L, Brorby G, Pastula S, Vincent M, **Proctor D**. Epidemiology is critical in advancing cumulative impact assessment (CIA) research: A pilot study in San Antonio, Texas. International Society of Exposure Science Annual Meeting, Montreal, Canada, October 2024.

Allen B, Vincent M, Lipword L, Panko J, Suh M, Jiang X, Mumma, **Proctor D**. Lung cancer risk and exposure to hexavalent chromium: Results of extended mortality study of workers with low level exposures and quantitative risk assessment using pooled analysis of three cohorts. Society of Toxicology 63rd Annual Meeting, Salt Lake City, UT, March 2024.

Perry CS, Vivanco SN, Verwiel AH, **Proctor DM**. Derivation of manganese 24-hour acute inhalation guideline protective of respiratory and neurological effects. Abstract 4751, Society of Toxicology 63rd Annual Meeting, Salt Lake City, UT, March 2024.

Racz L, Mittal L, Perry CS, Blanchette A, **Proctor D**. Assessing sustainable applications of electric arc furnace steel slag as construction aggregate: Applications of probabilistic risk assessment and physiologically-based pharmacokinetic modeling. Poster presented at Society of Environmental Toxicology and Chemistry North America 44th Annual Meeting, Louisville, KY, November 2023.

Proctor DM, Vivanco S, Blanchette A. Relative oral bioavailability of manganese in electric arc furnace steel slag is influenced by high iron content and low bioaccessibility. Poster presented at Society of Toxicology 62nd Annual Meeting, Nashville, TN, March 2023.

Thompson CM, Wikoff DS, **Proctor DM**, Harris MA. An evaluation of risk assessments on hexavalent chromium [Cr(VI)]: The past, present, and future of mode of action research. Poster presented at Society of Toxicology 62nd Annual Meeting, Nashville, TN, March 2023.

Perry C, **Proctor D**. Short-term environmental inhalation toxicity criteria for airborne manganese protective of neurological and respiratory effects for use in air toxics risk assessment. Presentation 5-15.t-04 to Society of Environmental Toxicology and Chemistry, Pittsburgh PA, November 2022.

Proctor D, Mittal L, Vivanco S, Perry C, Blanchette A. Probabilistic health risk assessment for residential exposures to metals in electric arc furnace (EAF) steel slag. Presentation 5.15.P-Th123 to Society of Environmental Toxicology and Chemistry, Pittsburgh PA, November 2022.

Proctor DM, Mittal L, Vivanco S, Antonijevic T. Probabilistic health risk assessment for residential exposures to metals in electric arc furnace (EAF) steel slag. Poster at Society of Environmental Toxicology and Chemistry (SETAC), Philadelphia, PA, November 2022.

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Thompson CM, Chappell GA, Mittal L, Gorman B, **Proctor DM**, Haws LC, Harris MA. Use of targeted mode-of-action research to inform human health risk assessment of hexavalent chromium. Poster presented at Society of Toxicology 61st Annual Meeting, San Diego, CA, March 2022.

Suh M, Verwiel A, **Proctor D**. Oral and inhalation bioaccessibility of cobalt and nickel in metal alloys: A critical consideration for site-specific human health risk assessments and read across. Poster for Society of Toxicology 59th Annual Meeting, Virtual, 2020, https://eventpilotadmin.com/web/page.php?page=Session&project=SOT20&id=P3190.

Proctor D. Use of the latest science in cancer risk assessment for hexavalent chromium: Is it time to step away from the default regulatory approaches? Invited presentation to the International Union of Toxicology (IUTOX) / International Congress of Toxicology (ICT) meeting, Honolulu, HI, June 17, 2019.

Ring CL, Suh M, Casteel S, Dunsmore M, Verwiel A, **Proctor D**. Relative oral bioavailability of cobalt and nickel in residential soil and dust affected by metal grinding operations. Presented at Joint Annual Meeting of International Society of Exposure Science and International Society for Environmental Epidemiology (ISES-ISEE 2018), Ottawa, Canada, August 2018.

Suh M, Wikoff D, Harvey S, Mittal L, Lipworth L, Goodman M, Goodmanson A, Ring C, Rohr A, **Proctor D**. Hexavalent chromium and stomach cancer: A systematic review and meta-analysis. Presented at Joint Annual Meeting of International Society of Exposure Science and International Society for Environmental Epidemiology (ISES-ISEE 2018), Ottawa, Canada, August 2018.

Proctor, DM. Hexavalent chromium in drinking water: When is the science sufficient to deviate from defaults? Invited Speaker, Genetic and Environmental Toxicology Association (GETA). Thresholds in Toxicology and Risk Assessment Fall Symposium, Oakland, CA, November 14, 2018.

Proctor, DM. Updating the regulatory risk assessment for hexavalent chromium in California: Implications for regulatory standards. Association of Environmental Health Sciences, San Diego, CA, March 20, 2018.

Thompson CM, Suh M, **Proctor DM**, Harris MA. Ten factors for considering the mode of action of Cr(VI)-induced intestinal tumors in rodents. Society of Toxicology 57th Annual Meeting, San Antonio, TX, March 11-15, 2018.

Thompson CM, Wolf JC, Suh M, **Proctor DM**, HJaws LC, Harris MA. Toxicity and recovery in the duodenum of B6C3F1mice following treatment with intestinal carcinogens; captan, folpet, and hexavalent chromium: Evidence for an adverse outcome pathway. Society of Toxicology 57th Annual Meeting, San Antonio, TX, March 11-15, 2018.

Proctor DM, Corbett ME. The world of low submicrogram beryllium concentrations. Session F5, American Industrial Hygiene Conference and Exhibition (AIHce), Seattle, WA, June 6, 2017.

Thompson C, Rager J, Suh M, **Proctor D**, Haws L, Harris M. Mechanistic support for nonlinear risk assessment of rat oral cavity tumors induced by exposure to Cr(VI) in drinking water. Poster presented at Society of Toxicology 56th Annual Meeting, Baltimore, MD, March 15, 2017.

Proctor DM, Suh M, Dunsmore D, Verwiel A, Casteel S. Bioaccessibility and relative oral bioavailability of cobalt and nickel from metal alloys in soil and dust. Poster presented at Society of Toxicology 56th Annual Meeting, Baltimore, MD, March 15, 2017.

Kirman CR, **Proctor D**, Suh M, Haws L, Harris M, Thompson C, Hays S. Using physiologically-based pharmacokinetic modeling to address potentially sensitive subpopulations exposure to hexavalent chromium. Poster presented at Society of Toxicology 5^{6th} Annual Meeting. Baltimore, MD, March 15, 2017.

Thompson C, Kirman C, Suh M, **Proctor D**, Haws L, Harris M, Hays S. Risk assessment of oral exposure to Cr(VI): Integration of mode of action, pharmacokinetics, and dose-response modeling. Poster presented at Society of Toxicology Annual Meeting, Baltimore, MD, March 14, 2017.

Suh M, Harvey S, Wikoff D, Mittal L, Ring C, Goodmanson A, **Proctor D**. Meta-analysis of hexavalent chromium and stomach cancer. Poster presented at Society of Toxicology 56th Annual Meeting, Baltimore, MD, March 13, 2017.

Verwiel A, **Proctor D**, Tachovsky A. Principal component analysis of metals in soil and dust to distinguish background and anthropogenic sources in an urban area. Association for Environmental Health and Sciences Foundation Annual Meeting, San Diego, CA, March 14, 2016.

Verwiel A, **Proctor DM**. Oral bioaccessibility of nickel and cobalt from metal alloy emissions in soil and dust. Society for Risk Analysis Annual Meeting, Arlington, VA, December 7, 2015.

Proctor, DM. Overview of hexavalent chromium mode of action (MOA) and implications for determining safe drinking water concentrations. Naturally occurring compounds of regulatory concern. Groundwater Resources Association Symposium, Garden Grove, CA, November 18, 2015.

Brorby G, Suh M, Bichteler A, **Proctor D**. Use of cluster analysis and homogeneity testing to characterize distributions of exposures among beryllium workers: Tools for developing occupational exposure limits from quantitative risk assessment. 2015 International Society for Exposure Science Annual Meeting, Henderson, NV, October 22, 2015.

Kirman CR, **Proctor DM**, Suh M, Hays S. Reduction of hexavalent chromium by gastric fluids from fed and fasted individuals with applications to toxicokinetic modeling. Presented at Society of Toxicology 54th Annual Meeting, San Diego, CA, March 22-26, 2015.

Suh M, Mittal L, Hirsch S, Valdes R, Bartlett C, Rohr A, **Proctor D**. Lung cancer risk in chromate production workers exposed to hexavalent chromium. Presented at Society of Toxicology 54th Annual Meeting, San Diego, CA, March 22-26, 2015.

Proctor D, Suh M, Thompson C, Hixon G. Inhalation Cancer Risk Assessment of Titanium Dioxide. Presented at the Society of Toxicology 54th Annual Meeting, San Diego, CA, March 22-26, 2015.

Harris MA, Thompson CM, **Proctor DM**, Suh M, Wolf JC, Seiter JM, Chappell MA, Haws LC. Analysis of duodenal crypt health following exposure to Cr(VI) in drinking water. Presented at Society of Toxicology 54th Annual Meeting, San Diego, CA, March 22-26, 2015.

Thompson CM, Young RR, Suh M, Dinesdurage H, Elbekai R, Harris, MA, Rohr AC, **Proctor DM**. Hexavalent chromium does not induce mutations in the oral mucosa of transgenic Big Blue® rats following drinking water exposures at a carcinogenic dose. Presented at Society of Toxicology 54th Annual Meeting, San Diego, CA, March 22-26, 2015.

Crump KS, Suh M, Bichteler A, Brorby GP, Hixon JG, and **Proctor DM**. Chronic beryllium disease risk assessment for occupational beryllium exposure. Presented at Society of Toxicology 53rd Annual Meeting, Phoenix, AZ, March 23-27, 2014.

Proctor DM, Suh M, Tachovsky JA, Abraham L, Hixon JG, Brorby GP, Campleman SL. Cumulative risk assessment of urban air toxics: A pilot study in San Antonio, TX. Presented at the Society of Toxicology 53rd Annual Meeting, Phoenix, AZ, March 23-27, 2014.

Suh M, Yzenas JJ, **Proctor DM**. Evaluation of electric arc furnace-processed steel slag for dermal corrosion, irritation, and sensitization. Presented at Society of Toxicology 53rd Annual Meeting, Phoenix, AZ, March 23-27, 2014.

Hays SM, Kirman CR, Suh M, **Proctor DM**. Gastric reduction of hexavalent chromium [Cr(VI)] in fed and fasted human stomach samples. Presented at Society of Toxicology 53rd Annual Meeting, Phoenix, AZ, March 23-27, 2014.

Thompson CM, **Proctor DM**, Suh M, Wolf JC, Haws LC, Seiter JM, Chappell MA, Harris MA. X-ray Fluorescence microspectroscopic analysis of duodenal mucosae following Cr(VI) exposure in drinking water. Presented at Society of Toxicology 53rd Annual Meeting, Phoenix, AZ, March 23-27, 2014.

Suh M, Thompson CM, Hixon JG, Harris MA, Kirman C, Hays S, Haws L, **Proctor D**. Potential involvement in the development of oral cavity tumors in rats exposed to hexavalent chromium. Presented at Society of Toxicology 52nd Annual Meeting, San Antonio, TX, March 10-14, 2013.

Kirman C, Thompson C, **Proctor D**, Suh M, Haws L, Harris MA, Hays S. Using PBPK modeling to address diurnal variation and age differences in hexavalent chromium toxicokinetics in humans. Presented at Society of Toxicology 52nd Annual Meeting, San Antonio, TX March 10-14, 2013.

Thompson C, Kirman C, **Proctor D**, Suh M, Hays S, Haws L, Harris MA. A chronic oral reference dose for hexavalent chromium. Presented at Society of Toxicology 52nd Annual Meeting, San Antonio, TX, March 10-14, 2013.

Proctor D, Suh M, Thompson, C., Harris, M.A. Mode of action evaluation for hexavalent-induced lung cancer. A chronic oral reference dose for hexavalent chromium. Presented at Society of Toxicology 52nd Annual Meeting, San Antonio, TX, March 10-14, 2013.

Brorby G, **Proctor D**, Perry C, Fitzgerald L, Tachovsky A. Probabilistic risk assessment of human exposure to iron and steel slag. Presented at Society of Toxicology 51st Annual Meeting, San Francisco, CA, March 11-15, 2012.

Harris MA, Thompson CM, Wolf JC, Fedorov Y, Hixon JG, **Proctor DM**, Suh M, Haws LC. Assessment of genotoxic potential of Cr(VI) in the intestine via in vivo intestinal micronucleus assay and in vitro high content analysis in differentiated and undifferentiated caco-2. Presented at Society of Toxicology 51st Annual Meeting, San Francisco, CA, March 11-15, 2012.

Hays SM, Kirman C, Aylward L, Suh M, **Proctor D**. Gastric reduction of Cr(VI) in mice, rats and humans. Presented at Society of Toxicology 51st Annual Meeting, San Francisco, CA, March 11-15, 2012.

Hixon JG, **Proctor D**. Use of constrained logistic regression models for the dose-response analysis of beryllium sensitization and chronic beryllium disease with mean exposure. Presented at Society of Toxicology 51st Annual Meeting, San Francisco, CA, March 11-15, 2012.

Kirman CR, Hays SM, Aylward LL, Suh M, **Proctor D**. Physiologically-based pharmacokinetic model for mice, rats and humans orally exposed to chromium. Presented at Society of Toxicology 51st Annual Meeting, San Francisco, CA, March 11-15, 2012.

O'Brien TJ, Hao D, Suh M, **Proctor D**, Thompson CM, Harris MA, Parsons BL, Meyers MB. K-ras codon 12 GGT to GAT mutation is not elevated in the duodenum of mice subchronically exposed to hexavalent chromium in drinking water. Presented at Society of Toxicology 51st Annual Meeting, San Francisco, CA, March 11-15, 2012.

Proctor DM, Thompson CM, Suh M, Haws LC, Harris MA. Mode of action for intestinal carcinogenesis of ingested hexavalent chromium in mice. Presented at Society of Toxicology 51st Annual Meeting, San Francisco, CA. March 11-15, 2012.

Thompson CM, Hixon JG, Kopec AK, Harris MA, **Proctor DM**, Haws LC. Assessment of genotoxic potential of Cr(VI) in the mouse duodenum via toxicogenomic profiling. Presented at Society of Toxicology 51st Annual Meeting, San Francisco, CA, March 11-15, 2012.

Haws L, **Proctor D**, Thompson C, Harris M. Research plan to fill data gaps in the mode of action for cancer risk assessment of hexavalent chromium in drinking water. Presented at Society of Toxicology 50th Annual Meeting, Washington, DC, March 6-10, 2011.

Proctor D, Thompson C, Haws L, Harris M. Use of mode of action and pharmacokinetic findings to inform the cancer risk assessment of ingested Cr(VI): A case study. Presented at Society of Toxicology 50th Annual Meeting, Washington, DC, March 6-10, 2011.

Proctor D, Meek B. Using mode of action data to guide quantitative cancer risk assessment: A case study of hexavalent chromium in drinking water. Presented at Society of Toxicology 50th Annual Meeting, Washington, DC, March 6-10, 2011.

Thompson C, **Proctor D**, Haws L,Harris M. Mode-of-action for the cancer risk assessment of ingested hexavalent chromium: Identifying and resolving data gaps. Abstract 1937, Society of Toxicology 49th Annual Meeting, Salt Lake City, UT, March 2010.

Proctor D, Haws L, Tachovsky A, Harris M. Critical Evaluation of the data underlying the USA Today rankings of air quality at schools. Toxicologist. Abstract 1909. Presented at Society of Toxicology 49th Annual Meeting, Salt Lake City, UT, March 2010.

Gatto N, Kelsh M, HaMa D, Shu M, **Proctor D**. A meta-analysis of the relationship between occupational exposure to hexavalent chromium and cancers of the gastrointestinal tract. Abstract, Society of Toxicology 48th Annual Meeting, Baltimore, MD, March 2009.

Proctor D, HaMai D. Human health risk assessment for environmental applications of steel slag: Differences between material-specific and default approaches. Poster Presentation, Society of Toxicology 48th Annual Meeting, Baltimore, MD, March 2009.

Gujral JS, **Proctor DM**, Su SH, Fedoruk MJ. Water adherence factors for human skin. Poster, International Society for Exposure Analysis and International Society for Environmental Epidemiology, Pasadena, CA, October 13–16, 2008.

Gujral JS, Fowler JF Jr, Su SH, Morgan D, **Proctor DM**. Repeated open application tests for allergic contact dermatitis due to hexavalent chromium [Cr(VI)]: Risk assessment for dermal contact with Cr(VI). 3rd Conference of Occupational and Environmental Exposure of Skin to Chemicals, Golden, CO, June 17–20, 2007.

Hong S, **Proctor D**, Finley B. Assessment of LA sewage spills on Santa Monica Bay beaches. Society of Toxicology 45th Annual Meeting, San Diego, CA, March 2006.

Hong SJ, **Proctor DM**, Finley BL. Exposure to sewage spill-related pathogens at Santa Monica Bay beaches. 4th Society of Environmental Toxicology and Chemistry World Congress and 25th Annual Meeting, Portland, OR, November 2004.

Proctor D. Exposure assessment for perchlorate in milk. Abstract 421, Society of Toxicology 45th Annual Meeting, New Orleans, LA, 2005.

Proctor D, Hong S. Relevance of rodent forestomach tumors in cancer risk assessment. Abstract 382, Society of Toxicology 45th Annual Meeting, New Orleans, LA, 2005.

Proctor D, Cohen E, Leung H, Hays S, Barraj L, Madl A. Exposure assessment for perchlorate in drinking water. Abstract 1754, Society of Toxicology 44th Annual Meeting, Baltimore, MD, 2004.

Madl A, **Proctor D**, Leung H, Goswami E, Hays S, Cohen E. Derivation of an RfD for perchlorate: Identifying a Critical Health Endpoint and Most Sensitive Subpopulation. Abstract 1755, Society of Toxicology 44th Annual Meeting, Baltimore, MD, 2004.

Leung H Madl A, **Proctor D**, Hays S, Cohen E. Scientific rational for the derivation of an RfD for perchlorate. Abstract 1756, Society of Toxicology 44th Annual Meeting, Baltimore, MD, 2004.

Proctor D, Ohanian E. Health risk assessment of hexavalent chromium in drinking water: Carcinogenicity, research and regulation. Symposium Chairman. Abstract 277, Society of Toxicology 42nd Annual Meeting, Salt Lake City, UT, 2003.

Proctor D, Lau E, Cahill J, Kelsh M. Alternative reference population sensitivity analysis for the morality assessment of a hexavalent chromium exposed worker cohort. Abstract 2008, International Society of Environmental Epidemiology, 2002.

Proctor D, Hays S, et al. Rate of hexavalent chromium reduction by human gastric fluid. Abstract 1700, Society of Toxicology 41st Annual Meeting, Nashville, TN, March 2002.

Proctor D, Williams P. Costs and benefits of compliance with alternative remediation standards at hexavalent chromium-contaminated sites. Abstract 1073, Society of Toxicology 41st Annual Meeting, Nashville, TN, March 2002.

Proctor D, Luippold R, et al. Lung cancer mortality among workers exposed to airborne hexavalent chromium. Abstract 773, Society of Toxicology 41st Annual Meeting, Nashville, TN, March 2002.

Crump C, **Proctor D**, et al. Dose-response assessment for lung cancer mortality of an occupational cohort exposed to airborne hexavalent chromium. Abstract 774, Society of Toxicology 41st Annual Meeting, Nashville, TN, March 2002. *Awarded top five Risk Assessment Presentations at the conference*.

Proctor D, Kelsh M, Lau E, Exuzides A, Cahill J. Analysis beyond publication: Further evaluation of an occupational study of chromium workers. Abstract 318, Society of Epidemiological Research, 2003.

Proctor DM, Su S, Finley BL. Multi-media exposure scenario survey for defining the conceptual site model of a human health risk assessment for a highly urbanized area. Society of Risk Analysis Conference, December 8, 2002.

Shay E, **Proctor D**, Long T. Community response and health risk assessment of a PCB release from a natural gas pipeline rupture. Association for the Environmental Health of Soils, San Diego, CA, March 2000.

Proctor DM. Use of bench top laboratory studies to quantify potential health risks due to mercury vapors: A case study. Society for Risk Analysis, 1998.

Proctor DM, et al. Methods for refining health-based remediation goals for PAHs in soil. Association for the Environmental Health of Soil, March 12, 1998.

Proctor DM, et al. Prevalence of chromium allergy in the United States and it implications for setting soil cleanup levels: A cost-benefit case study. Society of Risk Analysis, December 1997.

Proctor D, Nethercott J, Fredrick M, Finley B, Paustenbach D. Assessing the potential for elicitation of allergic contact dermatitis in Cr(VI)-sensitized subjects following prolonged contact with Cr(VI) in solution. Society of Toxicology 36th Annual Meeting, Cincinnati, OH, March 1997.

Scott P, **Proctor D**, Paustenbach D. Evaluating the 10% elicitation threshold for Cr(VI) in terms of mass per surface area using benchmark dose methods. Society of Toxicology 36th Annual Meeting, Cincinnati, OH, March 1997.

Proctor DM. Strategies for approaching liability using risk based corrective action (RBCA). Industrial Site Recycling Conference (ISRC), Pittsburgh, PA, April 8, 1997.

Proctor D, Shay E, Scott P. Health-based soil action levels for trivalent and hexavalent chromium: A comparison to state and federal standards. Association for the Environmental Health of Soils (AEHS), Newport Beach, CA, March 13, 1996.

Proctor D, Fehling KA, Scott PK. Use of health risk assessment to facilitate redevelopment of a former steel production site. Society for Risk Analysis Annual Conference and Exposition, December 7, 1995.

Proctor DM, Scott PK, Finley BL. Approach for determining generic health based soil action levels for trivalent and hexavalent chromium at residential and industrial sites. Abstract F4.16, Society for Risk Analysis Annual Conference and Exposition, December 6, 1994.

Proctor DM, Malsch PA, Gargas ML. Considerations for determining appropriate reference doses for soluble and insoluble trivalent chromium compounds. Abstract P1.26, Society for Risk Analysis Annual Conference and Exposition, December 5, 1994.

Proctor DM. Chromium speciation and risk assessment issues. Ohio Chapter Society for Risk Analysis, June 29, 1994.

Malsch PA, **Proctor DM**, Finley BL. Estimation of chromium inhalation RfC by the benchmark dose method. Society of Toxicology 33rd Annual Meeting, Dallas, TX, March 1994.

Gargas ML, Finley BL, Norton RL, **Proctor DM**, Paustenbach DJ. Biomonitoring of chromium (Cr) exposure by urinary excretion: Bioavailability and sampling design. Society of Toxicology 33rd Annual Meeting, Dallas, TX, March 1994.

Proctor DM, Finley BL. A methodology for setting soil cleanup goals based on protection of allergic contact dermatitis. Society for Risk Analysis Annual Meeting, December 5–8, 1993.

Proctor DM, Finley BL. Using real human sweat to extract chromium from chromite ore processing residue: Implications for setting standards based on allergic contact dermatitis. Society for Risk Analysis Annual Meeting, December 5–8, 1993.

Proctor DM, Scott PK, Fehling KA. Comparison of exposure estimates obtained using conservative state-mandated methodology, refined point estimate approach, and Monte Carlo analyses. Society for Risk Analysis Annual Meeting, December 5–8, 1993.

Proctor DM, Ulrich GA, Agnew WW. Application of human health risk assessment in oil and gas production. No 26362, Society of Petroleum Engineers International Annual Technical Conference and Exhibition, October 3–6, 1993.

Proctor DM, Finley BL, Paustenbach DJ. An alternative to the USEPA's proposed inhalation reference concentration for hexavalent and trivalent chromium. Society of Toxicology 32nd Annual Meeting, New Orleans, LA, March 1993.

Proctor DM, Trowbridge KR. An analysis of risk driven site investigation and remediation. Abstract 9970, Society of Environmental Toxicology and Chemistry 13th Annual Meeting, October 8-12, 1992.

PUBLISHED TECHNICAL STUDY REPORTS

Proctor DM, Gujral J, Su S, Fowler Jr. JF. Repeated open application test for allergic contact dermatitis due to hexavalent chromium [Cr(VI)] as CopperShield®: Risk assessment for dermal contact with Cr(VI). FPRL #012506. Environmental Protection Agency. Washington, DC, July 2006.

Proctor DM, Gujral J, Su S, Fowler Jr. JF. Repeated open application test for allergic contact dermatitis due to hexavalent chromium [Cr(VI)] as potassium dichromate: Risk assessment for dermal contact with Cr(VI). FPRL #012406. Environmental Protection Agency Washington, DC, September 2006.

Ann Holbrow Verwiel, M.P.P.

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PROFESSIONAL PROFILE

Ann Verwiel is Director of ToxStrategies' Exposure Sciences Practice and a Senior Managing Scientist. Ms. Verwiel has more than 20 years of experience in environmental consulting in the areas of human health risk assessment, site assessment, and environmental regulation. Over her career, she has focused on integrating risk assessment into an overall risk management approach to problem definition, investigation, and mitigation. She has successfully applied this approach in negotiations with regulatory agencies and public groups to develop cost-effective investigations, assessments, and mitigation strategies. She has also studied the science behind using cumulative impact assessments to assess health conditions in vulnerable communities. She has published and presented papers on a wide variety of topics, including probabilistic risk assessment (Monte Carlo analysis), environmental fate and transport of contaminants, and environmental auditing.

Ms. Verwiel has managed and conducted numerous human health risk assessments that addressed a wide variety of chemicals in soil, soil vapor, air, and groundwater. Petroleum, aerospace, electronics, mining, and MGP sites are among some of the most common sites for which she has performed these risk assessments. She has evaluated the chemical signatures, transport mechanisms and ultimate fate, and likely current and future human exposures as key first steps in the health risk evaluation. She has worked to develop investigation strategies and assess exposure to indoor and ambient air, which included evaluating air emission sources, modeling, soil vapor measurements, and indoor/ambient air measurements. At sites where volatile organic compounds (VOCs) are present in the subsurface, she has addressed the potential existence of a vapor intrusion exposure pathway using modeling and measurement approaches.

Ms. Verwiel has a detailed understanding of a broad cross section of environmental regulations, which she has applied to regulatory impact analyses, environmental compliance, and training programs. She has evaluated potential impacts of new regulations on operating facilities and new developments, assessed compliance at operating facilities with a wide variety of environmental regulations, and developed training materials to help regulatory agencies establish their requirements clearly and help regulated entities comply. She has conducted air toxics analysis to meet the requirements of California Proposition 65, the AB2588 Toxic "Hot Spots" Act, and the California Environmental Quality Act (CEQA).

Ms. Verwiel also has communicated risk to formal public groups, such as Restoration Advisory Boards, as well as the general public, in open meetings and direct written communications. She has worked with regulatory public participation specialists, public affairs officers, and others to develop written summaries and presentation materials to convey complex technical issues to the public. She has provided litigation support for several projects involving disputes between owners and operators, alleged air emissions exposures, and Proposition 65 litigation.

EDUCATION AND DEGREES EARNED

1996 Master of Public Policy (M.P.P.)
Georgetown University, Washington, DC

1987 Bachelor of Science (B.S.)
Chemistry
University of California, Irvine

CERTIFICATIONS

OSHA 40-hour training (updated annually since 1987)

OSHA Supervisor training

PROFESSIONAL ASSOCIATIONS

American Chemical Society (ACS; member)

Society of Environmental Toxicology and Chemistry (SETAC; member)

Society of Risk Analysis (SRA; member)

SELECTED PROJECT EXPERIENCE

Air Toxics Health Risk Assessments

Prepared a modeling and risk assessment protocol and completed an air toxics human health risk assessment for a metals recycling facility in Ohio to support a RCRA Part B permit. As part of their permit conditions, Ohio EPA required that the operator complete a risk assessment. Results of community air monitoring had previously resulted in evaluation of the facilities' air emission sources. A protocol was developed to achieve concurrence on the plan for emission estimates, modeling, and risk assessment. Going forward, comments on the protocol from Ohio EPA will be incorporated, and then emissions from various handling, storage, and treatment operations will be characterized and used in an air dispersion model (AERMOD) to estimate off-site concentrations in air and potential risk.

Managed a California AB2588 health risk assessment (AB2588 HRA) for a metal forge operation in southern California. This facility was the focus of public interest related to odors being observed in the neighborhood, and air emission sources were discussed in a series of public meetings. A community air monitoring program was also in place in the neighborhood. Mitigation strategies were developed, and as a result of source controls and operating procedure changes, the potential exposures from air emissions were below significance levels.

Managed a California AB2588 health risk assessment (AB2588 HRA) to evaluate emissions from a metal-finishing facility in the South Coast Air Quality Management District (SCAQMD). The SCAQMD also instituted a community air monitoring program to assess off-site impacts from this facility and others in the area that identified localized

increases in air concentrations of some metals. An air toxics risk assessment was performed that required generating emission estimates for unique sources, characterizing source operations for a facility that operated 24 hours per day, conducting air dispersion modeling, and completing risk evaluation and comparisons to local monitoring data. All work was performed on an expedited schedule to meet agency enforcement deadlines, and the results were reported during a community meeting.

Developed a risk assessment protocol and emission estimates for an explosives manufacturing facility to support a risk assessment prior to renewal of the RCRA Part B permit application for storage and open burning of explosive wastes. Evaluated various waste materials and combustion by-products to identify emission estimates and toxicity criteria. Used air dispersion modeling to estimate off-site concentrations and estimated potential human health risks for off-site residents, ranchers, and recreators.

Managed evaluation of source material testing for metals (including hexavalent chromium) at various emission sources at a cement manufacturing plant in northern California.

Performed a California AB2588 HRA for a manufacturing facility in northern California, and obtained regulatory approval from the Bay Area Air Quality Management District (BAAQMD), receiving only minimal comments.

Prepared a California AB2588 HRA for a film-processing facility with emissions of PCE and other solvents used in film developing and cleaning processes.

Evaluated chemical emissions from multiple air emission sources at an urban medical center, in support of an Environmental Impact Report (EIR) under CEQA.

Evaluated chemical emissions from multiple emission sources at the University of California – Riverside campus, to support preparation of an EIR for the long-range development plan for the university.

Project manager responsible for evaluating potential worker exposure to vehicle emissions in a proposed subterranean parking garage for a convention center that managed large volumes of material transport requiring diesel-emitting trucks. Findings were used to revise the building design to mitigate potential exposures incurred by workers in the garage.

Led a study to evaluate emissions from neighboring industrial sources and a highway prior to construction of a child-care facility at a food production facility, for the convenience of their employees. Conducted air monitoring to understand concentrations and looked at industrial sources in the vicinity of the food production facility.

Project manager responsible for evaluating potential health effects associated with emissions from an oil drilling operation in a highly urban area of Los Angeles.

Prepared an HHRA for remedial action activities, including dust generation and diesel exhaust, in support of a permit application for a remedial action at a former burn dump and shooting range. Managed development and implementation of an air monitoring plan to document concentrations of particulates and lead during remediation activities for comparison to acceptable levels established in the monitoring plan. Monitoring data were made available to the public electronically, which required rapid assessment of the results and adjustments to remedial activities as necessary.

Vapor Intrusion Risk Assessments

Evaluated PCE in groundwater for potential vapor intrusion to off-site residents. Considered the unique geologic setting of a thick, competent clay layer between groundwater and the surface, which likely serves to mitigate vapor intrusion from groundwater to off-site residences. However, soil gas measurements near a sanitary sewer line detected concentrations of VOCs that complicated the interpretation and required additional evaluation.

Evaluated potential vapor intrusion of petroleum hydrocarbons into a building adjacent to a former gas station planned for use as a daycare center. Soil at the gas station was remediated, but a groundwater plume appeared to extend beneath the building, and because excavation would have affected the integrity of the building, residual

petroleum hydrocarbons remained in soil near and potentially under the building. Multiple rounds of indoor air samples were collected to demonstrate that vapor intrusion was not an issue for this building.

Evaluated vapor intrusion of TCE at two industrial buildings adjacent to a shallow soil vapor source. The buildings were monitored over a period of 2 years, and results demonstrated minimal impacts, with indoor air concentrations below health-based screening levels.

Evaluated potential vapor intrusion of TCE and six other VOCs at 100+ homes in the vicinity of a shallow groundwater plume. Developed an indoor air sampling protocol, health-based screening levels, and letters reporting results to residents. We developed presentations for the lead agency and other regulators to define the scope of the evaluation, results, and conclusions. Continued monitoring at fewer than 10 homes after 5 years, when the extent of TCE in groundwater was formally assessed.

Provided third-party review for a vapor intrusion assessment at a future residential development. Worked with landowner to design a development plan that minimizes potential impacts to new homes. Open spaces and parks were used for areas where vapor intrusion may have been an issue. Homes were located at least 100 feet from these areas.

Lead risk assessor for a vapor intrusion HHRA at a former manufacturing facility redeveloped as a business park in southern California. VOCs, primarily trichloroethylene (TCE), were detected in subsurface soil, groundwater, and soil vapor. Developed an indoor air sampling program, calculated site-specific screening levels, and evaluated off-site migration using soil vapor measurements under regulatory oversight.

Lead risk assessor for a vapor intrusion evaluation at an operating hazardous waste treatment facility with chlorinated solvents present in soil and groundwater both on and off site. Evaluated potential human health risks at nearby residences for on-site workers.

Conducted an indoor air evaluation using multiple lines of evidence to evaluate conditions at a surgical hospital prior to a property transaction. Soil gas, sub-slab soil gas, and indoor air samples were collected simultaneously to provide information for decision making within the time frame of the property transaction.

Conducted an indoor air evaluation at a public building to address potential vapor intrusion issues related to a tetrachloroethene (PCE) plume from a former dry-cleaning operation at the site.

Lead risk assessor responsible for evaluating potential human health risks associated with free product on the groundwater table approximately 200 feet below ground surface at a former refinery, and for assessing potential impacts to off-site residents.

Lead risk assessor for an HHRA for a former (UST) site where potential indoor air impacts were the key issue following soil remediation because of residual concentrations of petroleum constituents and 1,2-dichloroethane in groundwater at the site and off-site.

Cumulative Impact Assessments and Environmental Justice

Co-author of "Comprehensive Review of Frameworks, Methods, and Metrics for Cumulative Impact Assessment of Vulnerable Communities: A Science Perspective," which presents the results of a multidisciplinary review of the various components of cumulative impact assessment from a scientific perspective. The overall objective of the study was to clarify the current underlying science and identify research needs to improve the quality and usefulness of cumulative impact assessments for communities with environmental justice concerns.

Prepared an evaluation of screening tools used by federal, state, and local entities to identify vulnerable communities with environmental justice concerns. Evaluated parameters in screening tools to compare source data sets, frequency of parameters, indexes, and other information. The report also provided examples of cumulative impact assessments from the literature to contrast with the approach using screening tools.

California Proposition 65 Evaluations

Evaluated concentrations of chemical ingredients in lubricant products such as gear oils, greases, and other oils and lubricants, that would require a warning label pursuant to California's Safe Drinking Water and Toxic Enforcement Act of 1986 (commonly referred to as Proposition 65). Developed exposure scenarios relevant to each product group, such as chemical-specific dermal absorption factors, potential incidental ingestion, product-specific density, and product-specific exposure frequencies. Using these exposure parameters, estimated potential exposures to the listed chemicals in the product, to assess whether Proposition 65 notifications were required.

Provided support to legal counsel and their client in the evaluation of potential off-site exposure to diesel exhaust from ski resort operations.

Performed a Proposition 65 evaluation for a metal forge operation in southern California; results demonstrated that notification was not required for off-site residents.

Evaluated potential exposures to lead in a dietary supplement and in a skin product, based on daily use suggested by the product label. Recommended additional analysis to assess bioavailability to more accurately assess exposure.

Sixty-day notices were sent by plaintiffs' attorneys to numerous industrial facilities in California based on the simple listing of a Proposition 65 chemical in their emission inventory reported to local air districts and made publicly available. Assisted several clients by conducting simple evaluations of their emissions, which showed that, under conservative assumptions, specific regulatory levels for the Proposition 65-listed chemicals had not been exceeded.

Evaluated requirement to notify off-site persons potentially exposed to emissions from an industrial facility in southern California. Developed specific regulatory levels when such levels had not been published by the state.

Provided technical support in negotiations with the California Attorney General's office on behalf of a manufacturing facility that was issued a 60-day notice based on erroneous interpretations of a public air toxics risk assessment report.

Developed a Proposition 65 emission calculator for diesel exhaust from construction activities for a client that conducts numerous construction projects every year, to assess whether notification may be required,

Evaluated building materials, furniture, and chemical products at a large child-care facility, to identify Proposition 65-listed chemicals and assess whether Proposition 65 notification may be required.

Estimated potential exposure to cadmium and lead in a food product, including evaluating laboratory data and researching typical consumption patterns.

Multi-Media Environmental Human Health Risk Assessments

Managed the risk assessment planning process for the soil operating unit of a former airport, aircraft maintenance facility, and military manufacturing site. Worked with EPA to attain concurrence on a scoping document for the risk assessment that addressed the major questions regarding the approach to the risk assessment. This allowed the risk assessment to proceed quickly and streamlined EPA's review.

Managed a site-wide HHRA for an active chemical manufacturing facility subject to RCRA under EPA oversight. Chemicals at the site included VOCs, semi-volatile organic compounds (SVOCs), polychlorinated biphenyls (PCBs), pesticides, dioxin/furans, and inorganics. Key factors included an upgradient contribution of VOCs from an adjacent Superfund site, shallow groundwater (~5 feet below ground surface), redevelopment of a portion of the former site as a regional park, off-site residences 350 feet from the site boundary, a nearby creek, and a variety of source areas.

Managed human health risk assessment activities at a confidential Superfund mining site. Over the last 10 years, participated in the project management team that developed work plans, performed site characterization activities,

evaluated nature and extent of affected areas, developed a baseline human health risk assessment work plan, and completed a draft baseline human health risk assessment. Unique features of this project included:

- Developed a site conceptual model that incorporated unique receptors, including Native American tribal members and foragers
- Evaluated incremental sampling methods for mine-waste piles
- Conducted bioaccessibility testing for key metals
- Prepared a work plan and collected data to develop site-specific plant uptake factors
- Collected site-specific background data sets for multiple media and calculated statistically based benchmarks for comparison to site data
- Predicted a risk and hazard index for seven receptors at up to 16 study areas and seven reference areas
- Presented results in a 6-hour meeting with EPA, other federal agencies, and state and tribal representatives.

Provided technical expertise to Nevada Department of Environmental Protection (NDEP) to review documents related to redevelopment of a former manganese mine. ToxStrategies' responsibility was to review documents related to the assessment of potential human health risk, such as the baseline human health risk assessment work plan, the baseline human health risk assessment, the Remedial Investigation report, and other documents. ToxStrategies provided comments to NDEP, which were forwarded to the responsible party and incorporated into their documents.

Developed cleanup goals for future redevelopment of a former Department of Energy facility that was being decommissioned. ToxStrategies was hired by the developer to assist in evaluating the implications of hundreds of due diligence samples collected in support of the property transaction. Developed site-specific cleanup goals for more than 50 chemicals in soil, soil gas, and/or groundwater and evaluated these data with respect to the cleanup goals. The cleanup goals were also used by the developer to estimate remediation costs and strategies. The project team worked with regulators—including Missouri's Department of Natural Resources and Department of Health and Senior Services—to achieve regulatory concurrence on the cleanup goals and enable the project to move forward.

Managed a human health and ecological risk assessment for an operating lumber mill for impacts of dioxins and other chemicals, both on-site in operational areas and off-site in a slough. Developed a baseline human health risk assessment (HHRA) and cleanup levels for upland soil and performed the scoping ecological and off-site human health risk assessment to evaluate ecological and human health risks associated with chemicals present in the slough, both of which received regulatory approval. Developed a sediment management strategy to document that conditions in the slough remained protective of aquatic organisms.

Developed a risk assessment approach for the investigation of former ponds believed to have been affected by mine drainage from a nearby mine. Developed a risk-based investigation and risk assessment work plan to evaluate the residual material and assess the effort necessary to mitigate the impacts at the site.

Project Manager responsible for evaluating environmental issues associated with an approximately 1100-acre ranch where wastewater from a nearby pulp and paper mill was used to irrigate specific agricultural fields, resulting in dioxin in the soil. Developed presentation materials for a public meeting and supported various parts of the California Environmental Quality Act (CEQA) process related to future use of the site as a gravel mine, including preparing public information sheets on dioxins.

Performed an HHRA in support of a Remedial Action Workplan (RAW) for two parcels that were formerly part of a larger manufactured gas plant where PAHs and benzene were key chemicals of potential concern (COPCs) in soil, groundwater, and/or indoor air. The HHRA was approved by the California Department of Toxic Substances Control (DTSC), and the RAW was implemented.

Performed an HHRA and developed risk-based remediation goals for future residential or commercial/industrial land use at a former manufacturing site with metals in soil and VOCs in soil vapor, which were approved by DTSC.

Managed a multi-disciplinary project to provide consulting services to the operators of a former fuel storage terminal (the terminal) in the Port of Los Angeles. Performed the HHRA, obtained regulatory concurrence, developed remediation goals, negotiated with the regulatory agency, and provided support to the client's negotiations with the landowner.

Used a risk-based approach to evaluate off-site risk resulting from a groundwater plume that had migrated from a bulk petroleum storage facility beneath an adjacent residential neighborhood. Worked with members of the public in a formal Restoration Advisory Board (RAB) to refine the existing HHRA Work Plan, perform the risk assessment, and achieve regulatory concurrence.

Managed a multi-phase investigation of petroleum hydrocarbons in soil at a residential development that was discovered after redevelopment. Worked with the City, developer, and numerous regulatory agencies to prioritize investigation needs, conduct a comprehensive investigation, and perform a screening risk assessment. Work was completed in an expedited time frame, and the development was able to move forward.

Managed preparation of an HHRA Work Plan for a jet-fuel plume at a major U.S. airport that focused on current and potential future receptors. Negotiated acceptance of the work plan with property owner, and completed the risk assessment.

Lead risk assessor for a residential development planned adjacent to a former agricultural chemical manufacturing facility (the site) where groundwater had been affected by agricultural chemicals and VOCs. Completed the risk assessment, which was approved by the regulators, within strict time constraints required to obtain approval of development financing by lending agencies.

Lead risk assessor for site characterization activities and subsequent remediation measures related to VOCs in soil gas, VOCs, and hexavalent and total chromium in soil and groundwater at a former metal-plating facility pursuant to a Cleanup and Abatement Order with the Los Angeles Regional Water Quality Control Board (RWQCB).

Managed the health risk assessment components of the evaluation of waste piles at a former mine site. Performed a background comparison and a risk assessment to evaluate site conditions.

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Continuing Education

1989 UC Irvine, Hazardous Waste Certification Program