Air Toxics Science Advisory Committee Meeting #3: Manganese

Cleaner Air Oregon Program

April 3, 2024
Virtual Meeting

Zoom Webinar

- Only panelists have ability to speak
- We are recording, will be available on ATSAC website
- Closed captioning available
- Chat disabled, Q&A disabled

Agenda

- Welcome and Introductions
- Updates on TRV Review
- Petitioner Presentation on Manganese
- Review Tables in Manganese Framing Document
- Break
- ATSAC Discussion of Manganese Questions
- Closing and Next Steps

TRV Review Update

Cleaner Air Oregon Program

Holly Dixon, PhD
Oregon Health Authority
Public Health Toxicologist

Authoritative Sources

Authoritative sources are listed in Oregon Administrative Rule, OAR 340-247-0030

- U.S. Agency for Toxic Substances and Disease Registry (ATSDR)
- U.S. Environmental Protection Agency (EPA)
- California Environmental Protection Agency (CalEPA)
- Oregon DEQ in consultation with the Air Toxics Science Advisory Committee (ATSAC)

TRV Update Tool

Review of Authoritative Sources

Select a TAC to review

Acetaldehyde

General Information

Seq. ID	1
CAS No.	75-07-0
Noncancer Class	HI3
187 HAP Status	Yes

Screenshots from TRV Tool

IRIS

Go To IRIS Assessment

Click to Update IRIS Values

Variable	2018 Value	Current Working Value	New Value
EPA Reference Conc (RfC) (µg/m3)	9	9	
EPA IRIS Date (Non-Cancer)	10/1/1991	10/1/1991	
Inhalation Unit Risk (IUR) (µg/m3)-1	0.0000022	0.0000022	
EPA IRIS Date (Cancer)	6/1/1988	6/1/1988	
EPA Oral Reference Dose (RfD) (mg/kg-d)			
EPA IRISDate (Non-Cancer)			
Oral Slope Factor mg/kg/day)-1			
EPA IRIS Date (Cancer)			
Assigned Staff			
Comments			

TRV Review Progress

- Reviewed ATSAC feedback and incorporated it into the TRV review process

- Revised the TRV update tool to be able to capture additional information for TRV selection and ATSAC review

- Completed a full review of existing and new TRVs
  - Reviewed at least 4 sources of TRV information for ~400 toxic air contaminants
- Contracted with a consulting firm to establish and follow a quality control process

ERG

Petition Process

- Oregon Administrative Rules give an option for members of the public to submit petitions to suggest TRV updates as part of the TRV review process
- DEQ received **one petition** to change DEQ's manganese TRV for acute exposure (24-hour)

Screenshot of the DEQ online fact sheet about the petition process

Petition for Manganese TRV Increase

0.3 µg/m³

- Current DEQ manganese TRV for acute exposure
- From OEHHA's manganese TRV for chronic exposure

5 µg/m³

- Petition proposal
- Consistent with the Texas Commission of Environmental Quality (TCEQ) manganese TRV for acute exposure

Today's Meeting

- ATSAC will listen to a presentation on the petition from ToxStrategies
- ATSAC will discuss the petition and DEQ's specific questions
- DEQ and OHA will listen and gather feedback from ATSAC on the petition

Petitioner’s Presentation

ToxStrategies on behalf of Bridgewater Group

Derivation of Manganese 24-hour Acute Inhalation Guideline

April 2024

Tox Strategies

Introductions

- Camarie Perry
  - M.S. in Toxicology and Pharmacology, University of Texas at Austin
  - B.S. in Genetics, Texas A&M University
  - Extensive experience as a state regulator (TCEQ) and consultant
    - Primary experience in human health risk assessment, evaluation of air emissions, development of remediation guidance, exposure and toxicity evaluations, endocrine disruption and metals
- Ann Holbrow Verwiel
  - MPP in Public Policy, Georgetown University
  - B.S. in Chemistry, University of California, Irvine
  - Over 20 years in environmental risk assessment consulting in California
    - Specialty areas include air toxics, metals exposure and health effects, mining sites, and consumer products exposures

General Manganese (Mn) Toxicity

- Mn is an essential element which is beneficial at low concentrations; absorption and excretion is controlled by homeostasis.
- Mn is critical for neurodevelopment and exhibits an inverted U-shaped dose response curve. During development, both Mn deficiency and excess can result in neurocognitive effects.
- Through homeostasis, systemic background levels are in the optimal range for health.
- Since Mn toxicokinetics are non-linear, derivation of toxicity criteria has been challenging as standardized uncertainty factors are not always applicable.
- Neurological effects are most sensitive endpoints for chronic exposures, but respiratory effects are evident with acute exposures.

Example Inverted U-shaped Dose Response Curve for Mn

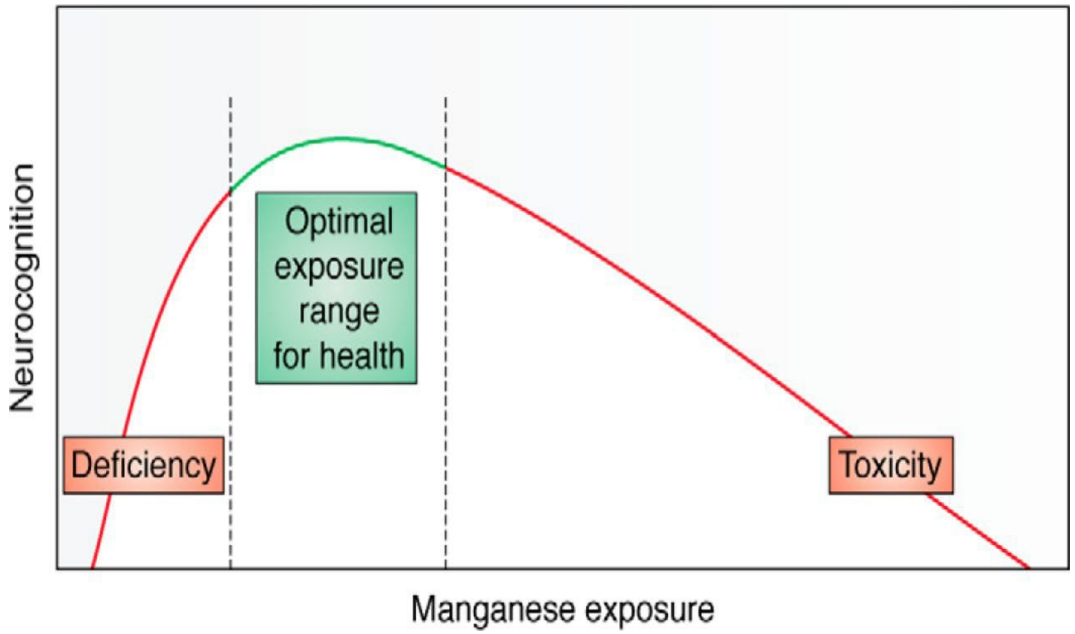


Figure from Balachandran et al. (2020) based on Vollet et al.(2016); data from pediatric populations.

Proposed Manganese Acute TRV

- Objective: Develop a 24-hour acute health guideline value protective of respiratory and neurological effects and use current physiologically-based pharmacokinetic (PBPK) models to address potential Mn accumulation in critical brain compartments during sensitive developmental life stages.
- Derived acute, 24-hour guideline for Mn inhalation exposure of 5 $\mu g/m^3$ based on 3-week (90-hour) monkey studies evaluating respiratory effects (Dorman et al. 2005) as well as oxidative stress markers in the brain (Erikson et al. 2008). We will discuss uncertainty factors in more detail later.
- PBPK modeling used to confirm that 5 $\mu g/m^3$ acute exposures do not significantly increase Mn in brain tissues (e.g., globus pallidus – primary target tissue for Mn accumulation & CNS toxicity).

PBPK Modeling

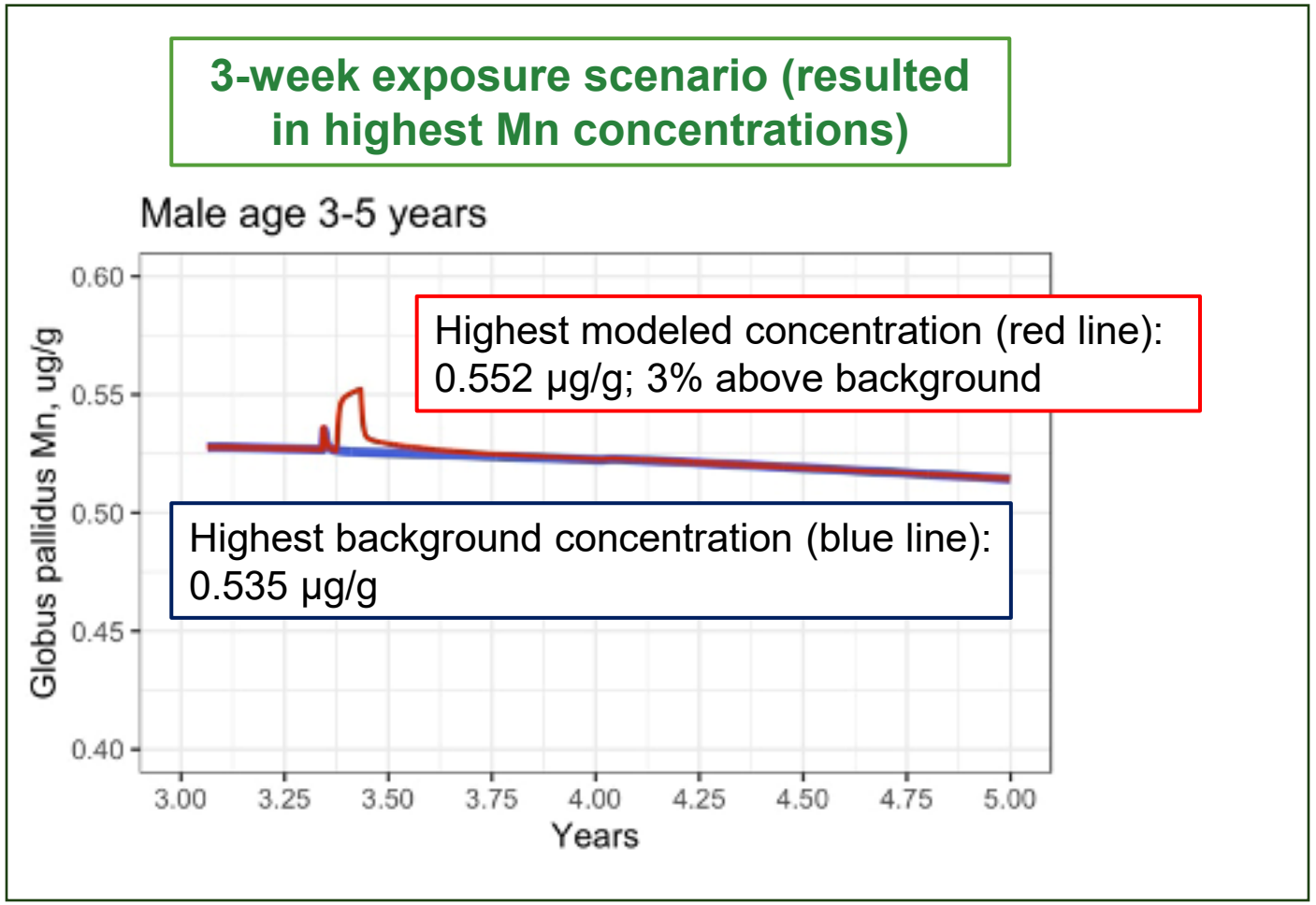
- PBPK models predict Mn accumulation in sensitive brain compartments, including the globus pallidus, from oral and inhalation exposures, and for multiple life-stages.
- PBPK models are particularly useful for Mn to address the challenges of assessing Mn accumulation considering homeostasis and potential neurotoxicity (Yoon et al. 2019; Campbell et al. 2023).
- From Yoon et al. (2011 and 2019), we used the "lactation/infant" and the "child/adolescent/adult" model codes, respectively. (*Child/adolescent/adult model code predicted higher globus pallidus concentrations.)*
- Evaluated potential outcomes for two short-term exposure scenarios at 5 μg/m^3 Mn.

  1.) Monthly exposure scenario: A 24-hour inhalation exposure one time per month, from birth throughout life, with diet and ambient air exposures set to background levels.

  2.) 3-Week exposure scenario: A single, 3-week period of constant inhalation exposure at age 3, since the model predicts the highest Mn levels in globus pallidus at ~3 years of age, with diet and ambient air exposures set to background levels. (*Scenario with highest tissue Mn accumulation.)*

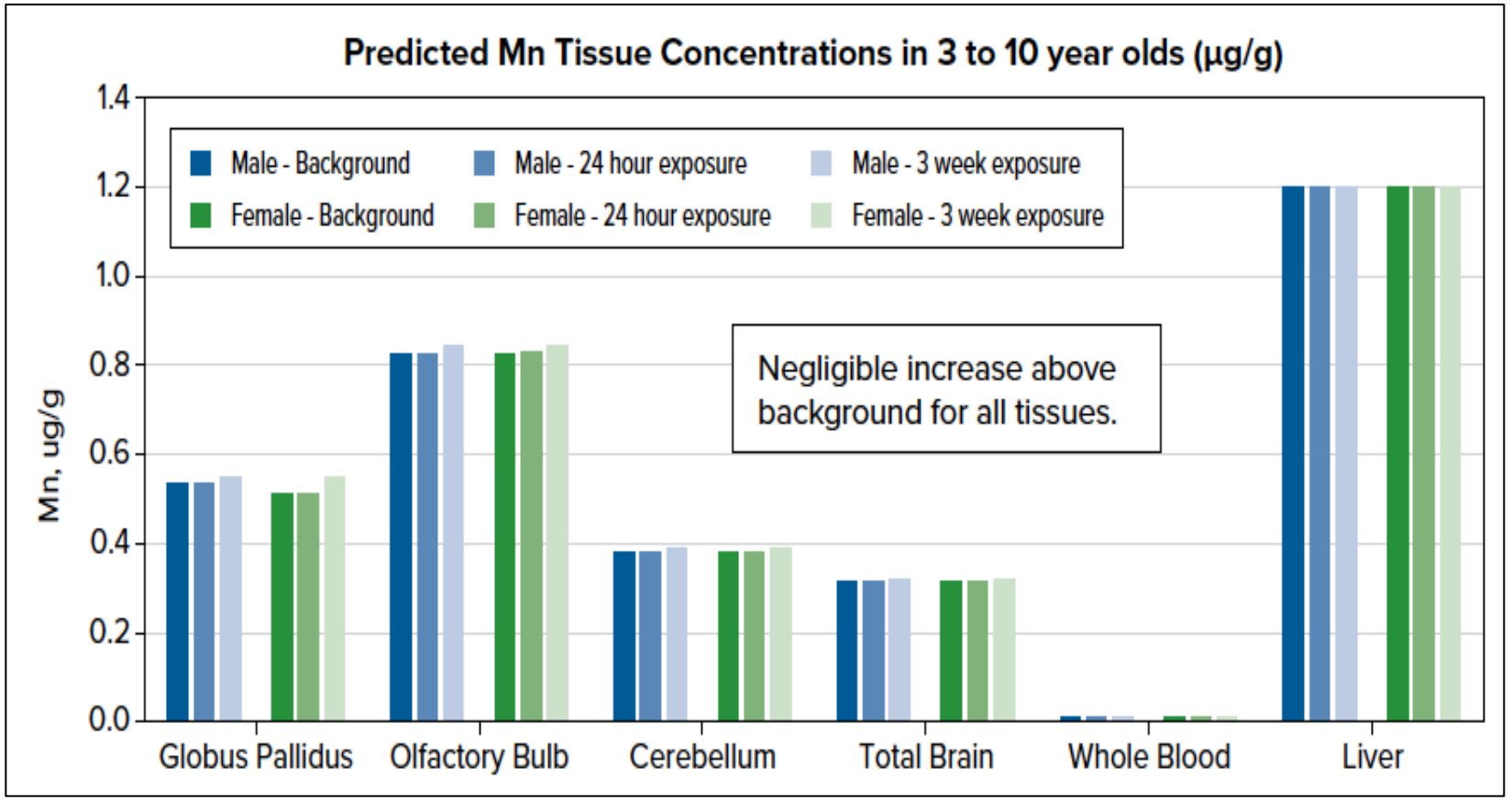
PBPK Modeling Results

- Neither exposure duration (24-hour exposure monthly or 3-week continuous exposure) results in Mn concentrations significantly above background exposures.
- **Predicted Mn levels in the globus pallidus are lower than the tissue-based NOAELs for neurotoxic effects in humans and monkeys which range from 0.7-0.9 µg/g (Gentry et al. 2017, Schroeter et al. 2012).**
- **An acute TRV of 5 µg/m^3 even with 3-weeks of continuous exposure would not result in significant exposures above background or NOAELs in humans and monkeys.**



Based on Figure 1 from Perry et al. 2023

PBPK Modeling Results (cont.)



Based on Figure 2; Perry et al., 2024

Multiple brain tissues and whole blood and liver tissue concentrations were not above background under either exposure scenario.

Note: Children 3-10 years had the highest model-predicted Mn tissue concentrations of any age group in the PBPK models.

ODEQ Framing Document

- Framing document summarizes information relevant to the proposed Mn acute TRV.
  - "DEQ acknowledges that deriving **acute TRVs from chronic TRVs is not ideal** and, where appropriate and possible, DEQ would prefer to derive an acute TRV from a study with an acute exposure duration."
  - "DEQ agrees that TCEQ's manganese acute TRV is a good resource because
    1) TCEQ's acute TRVs match DEQ's acute exposure time (24 hours),
    2) TCEQ's manganese acute TRV is based on short-term toxicity study data, and
    3) TCEQ provides comprehensive developmental support documentation."
  - Provides a detailed discussion of uncertainty that we will discuss in the next slides.

Addressing Uncertainty

- Individual UFs are not completely independent of each other, and this is especially true for essential nutrients which display U-shaped dose-response curve.
- **Combining default UFs of 10 can lead to double-counting. Therefore EPA, OEHHA and TCEQ have developed upper limits on total UFs for inhalation guidelines.**
  - **EPA (2002) and OEHHA (2008) limit total UFs for chronic inhalation exposures to 3,000. Similarly, TCEQ limits total UFs for acute inhalation guidelines to 300.**
- As our understanding of the issues has expanded over time, we're recommending the same guideline of 5 $\mu g/m^3$, but slightly different UFs between the petition and the publication.

Uncertainty Factors for Determining Proposed Acute Guideline for Mn[a]

	Mild LOAEL (mg/m^3)	Interspecies (UF_A)	Intraspecies (UF_H)	LOAEL to NOAEL (UF_L)	Subchronic (UF_S)	Database (UF_D)	Total UF	Resulting Guideline ($\mu g/m^3$)
ODEQ (2024) Proposed Range of Potential Options	1.5	3-10	10	2-10	1	1-6	300-1800	0.8-5
TCEQ (2017) 24-hour guideline	1.5	3	10	2	1	6	300[b]	5
ToxStrategies support for Petition to ODEQ (Nov 1, 2022)	1.5	10	10	3	1	1	300	5
Proposed 24-hour Acute Guideline for Mn (Perry et al. 2023)	**1.5**	**3**	**10**	**10**	**1**	**1**	**300**	**5**

[a] Colored columns indicate the three individual UFs that differ between the various entities (i.e., UF_A, UF_L, and UF_D).
[b]TCEQ's total calculated UF is 360; however, TCEQ guidelines (2015) limit actual UF to 300 for acute values. TCEQ's 2017 Manganese Development Support Document was published prior to developmental toxicity studies involving Mn noted for UF_D factors.

Addressing Uncertainty (cont.)

Uncertainty Factor	Recommended Value	Rationale
Interspecies (UF_A) Range in Framework: 3 - 10	3	• A UF_A of 3 was used since monkeys largely replicate the neurobehavioral effects of Mn observed in humans (Schroeter et al. 2011; Gentry et al. 2017) (UF_{A-D} of 3), and toxicokinetics between monkeys and humans in the Dorman et al. (2005) and Erikson et al. (2008) studies are essentially equivalent (UF_{A-K} of 1). • PBPK modeling was used as an additional line of evidence supporting consistent toxicokinetics between monkeys and humans.

Addressing Uncertainty (cont.)

Uncertainty Factor	Recommended Value	Rationale
LOAEL to NOAEL (UF_L) Range in Framework: 2 - 10	10	• Although effects were mild, a UF_L of 10 was used for conservatism and protectiveness, and since PBPK modeling showed tissue Mn levels did not immediately return to background levels following cessation of the 3-week continuous exposure (returned to background in <6 months). • This is a conservative assumption, since the respiratory effects were mild and no clinical effects were observed in monkeys in the Dorman et al. (2005) and Erikson et al. (2008) studies and the lack of data for a continuous 24-h exposure period. • Due to the study designs of Dorman et al. (2005) and Erikson et al. (2008), post-exposure recovery data are not presented for the 90-hour exposure group.

Addressing Uncertainty (cont.)

Uncertainty Factor	Recommended Value	Rationale
Database (U_D) Range in Framework: 1 - 6	1	General Considerations: Database insufficiency factor – "Adjusts for the possibility of identifying a lower (or more sensitive effect) if additional studies were available" (Dankovic et al. 2015). In determining UF_D - Evaluate the specific kinds of available data and weigh the likelihood that additional studies would reveal more sensitive toxicity/endpoints.

Addressing Uncertainty (cont.)

Uncertainty Factor	Recommended Value	Rationale
Database (U_D) Range in Framework: 1 - 6	1	• A UF_D of 1 was used because it is considered unnecessary to impose a UF_D factor for reproductive or developmental effects. • In a rat developmental drinking water study with Mn up to 4 mg/L, Oshiro et al. (2022) reported no cognitive impairment among offspring when combined with maternal stress. • Epidemiologic studies in children have shown cognitive effects in children associated with elevated blood manganese, but the range of blood Mn levels associated with cognitive effects varies considerably (Bhang et al., 2013; Haynes et al., 2015). Blood Mn levels in the PBPK model were consistent.

Addressing Uncertainty (cont.)

Uncertainty Factor	Recommended Value	Rationale
Database (U_D) Range in Framework: 1 - 6	1	• Similarly, Chung et al. (2015) observed neurocognitive deficits among the offspring of mothers with low and high blood manganese relevant to the U-shaped dose-response curve. • Although this uncertainty is not specifically accounted for, an additional uncertainty factor is not likely necessary because the PBPK modeling demonstrates that tissue Mn levels (blood, liver and brain) are not affected significantly at 24-hour exposures of 5 µg/m^3.

Proposed Acute Guideline is Conservative Relative to Chronic Thresholds

- The proposed acute guideline of 5 µg/m^3 is conservative relative to chronic inhalation values:
  - Bailey et al. (2009) proposed 2 µg/m^3 to 7 µg/m^3 as chronic reference concentrations.
  - Schroeter et al. (2011) and Gentry et al. (2017) predicted that homeostasis maintains Mn levels in the brain target tissue at airborne concentrations below 10 µg/m^3.
  - **Yoon et al. (2011) indicates that maternal and fetal blood Mn levels are not affected at airborne concentrations less than 10 µg/m^3.**

Conclusions

- Using PBPK methods, this study supports a 24-hour acute guideline for environmental exposures of 5 µg/m^3, which is equal to the value set by the TCEQ.
- Essential nutrients have unique pharmacological and toxicological properties, and therefore require alternative considerations in setting guideline levels and consideration of background tissue concentrations that are beneficial.
- PBPK modeling demonstrates that the guideline is protective of both respiratory and neurological effects, as Mn is not expected to accumulate in key tissues.

Conclusions (cont.)

- We recommend a combined UF of 300 applied to the POD of 1.5 mg/m^3, based on the following individual UFs:
  - UF_A: 3 for similarities in neurobehavioral effects and toxicokinetics between monkeys in humans
  - UF_H: 10 for sensitive human subpopulations (conservative due to PBPK modeling for sensitive life stages.)
  - UF_L: 10 for mild LOAEL to NOAEL (conservative)
  - UF_S: 1 since key study was 90 hours (longer than target of 24 hours)
  - UF_D: 1 since Mn is an essential nutrient and necessary for development. PBPK modeling indicates that the proposed 24-hour guideline of 5 µg/m^3 is not expected to significantly increase critical brain compartment, blood and other tissue compartments over background or NOAELs; and the guideline is low compared to chronic thresholds.

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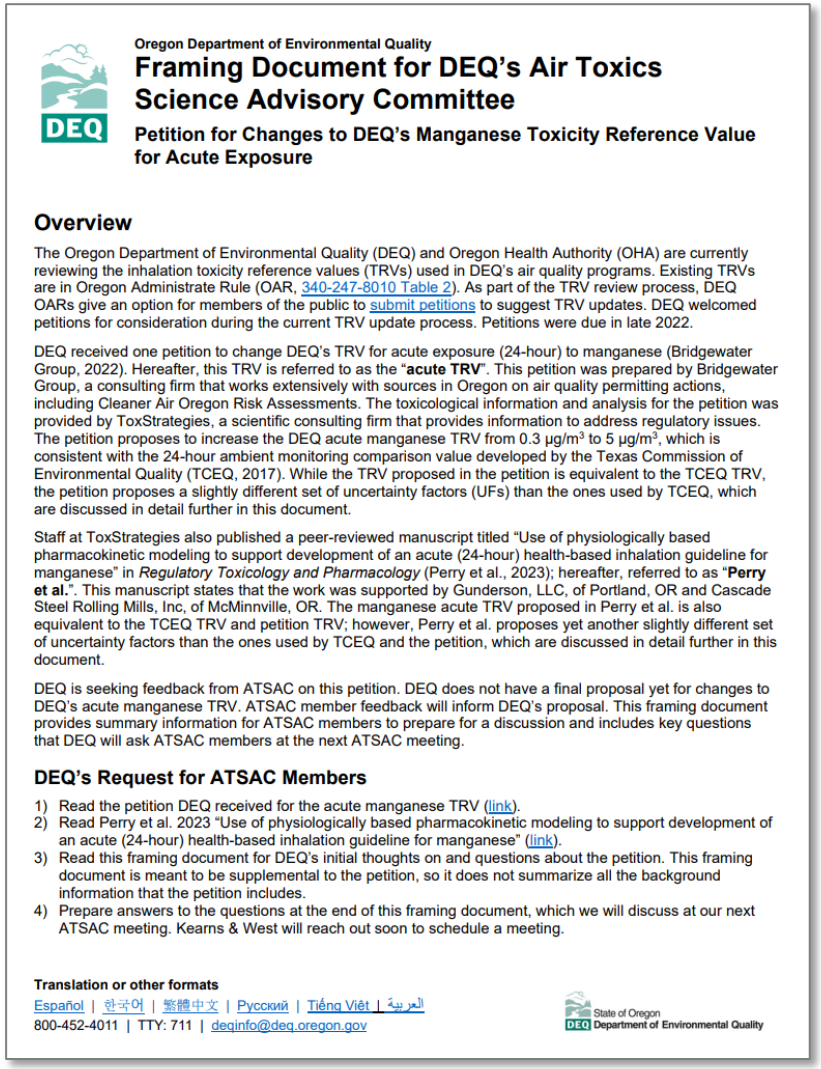
Review Tables in Manganese Framing Document

Holly Dixon, PhD
Oregon Health Authority



Oregon Department of Environmental Quality

Framing Document for DEQ's Air Toxics Science Advisory Committee

Petition for Changes to DEQ's Manganese Toxicity Reference Value for Acute Exposure

Overview

The Oregon Department of Environmental Quality (DEQ) and Oregon Health Authority (OHA) are currently reviewing the inhalation toxicity reference values (TRVs) used in DEQ's air quality programs. Existing TRVs are in Oregon Administrate Rule (OAR, 340-247-8010 Table 2). As part of the TRV review process, DEQ OARs give an option for members of the public to submit petitions to suggest TRV updates. DEQ welcomed petitions for consideration during the current TRV update process. Petitions were due in late 2022.

DEQ received one petition to change DEQ's TRV for acute exposure (24-hour) to manganese (Bridgewater Group, 2022). Hereafter, this TRV is referred to as the "**acute TRV**". This petition was prepared by Bridgewater Group, a consulting firm that works extensively with sources in Oregon on air quality permitting actions, including Cleaner Air Oregon Risk Assessments. The toxicological information and analysis for the petition was provided by ToxStrategies, a scientific consulting firm that provides information to address regulatory issues. The petition proposes to increase the DEQ acute manganese TRV from 0.3 $\mu g/m^3$ to 5 $\mu g/m^3$, which is consistent with the 24-hour ambient monitoring comparison value developed by the Texas Commission of Environmental Quality (TCEQ, 2017). While the TRV proposed in the petition is equivalent to the TCEQ TRV, the petition proposes a slightly different set of uncertainty factors (UFs) than the ones used by TCEQ, which are discussed in detail further in this document.

Staff at ToxStrategies also published a peer-reviewed manuscript titled "Use of physiologically based pharmacokinetic modeling to support development of an acute (24-hour) health-based inhalation guideline for manganese" in *Regulatory Toxicology and Pharmacology* (Perry et al., 2023); hereafter, referred to as "**Perry et al.**". This manuscript states that the work was supported by Gunderson, LLC, of Portland, OR and Cascade Steel Rolling Mills, Inc, of McMinnville, OR. The manganese acute TRV proposed in Perry et al. is also equivalent to the TCEQ TRV and petition TRV; however, Perry et al. proposes yet another slightly different set of uncertainty factors than the ones used by TCEQ and the petition, which are discussed in detail further in this document.

DEQ is seeking feedback from ATSAC on this petition. DEQ does not have a final proposal yet for changes to DEQ's acute manganese TRV. ATSAC member feedback will inform DEQ's proposal. This framing document provides summary information for ATSAC members to prepare for a discussion and includes key questions that DEQ will ask ATSAC members at the next ATSAC meeting.

DEQ's Request for ATSAC Members

1) Read the petition DEQ received for the acute manganese TRV (link).
2) Read Perry et al. 2023 "Use of physiologically based pharmacokinetic modeling to support development of an acute (24-hour) health-based inhalation guideline for manganese" (link).
3) Read this framing document for DEQ's initial thoughts on and questions about the petition. This framing document is meant to be supplemental to the petition, so it does not summarize all the background information that the petition includes.
4) Prepare answers to the questions at the end of this framing document, which we will discuss at our next ATSAC meeting. Kearns & West will reach out soon to schedule a meeting.

Translation or other formats

Español | 한국어 | 繁體中文 | Русский | Tiếng Việt | العربية

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State of Oregon Department of Environmental Quality

Table 1. Information on the critical studies used in the TRVs for acute exposure to manganese.

	Critical Study Author and Year	Critical Study Species	Critical Effect Target Organ	Description of TRV Critical Effect	Duration of Exposure in Critical Study	Point of Departure (POD) Method	POD Value (mg/m^3)
Used in TCEQ, Petition, and Perry et al., 2023	Dorman et al. 2005	Male Rhesus Monkeys (20-24 months)	Respiratory System	Inflammatory airway changes (e.g., mild bronchiolitis, alveolar duct inflammation)	6 hrs/day, 5 days/week, 15 exposure days*	Lowest observed adverse effects level (LOAEL)◊	1.5
Used in Perry et al., 2023	Erikson et al. 2008 in addition to Dorman et al. 2005	Male Rhesus Monkeys (20-24 months)	Nervous System	Biochemical markers of oxidative stress in the brain (decreased glutathione levels and reversible increased glutamine synthetase protein with decreased gene expression)	6 hrs/day, 5 days/week, 15 exposure days†	LOAEL	1.5

Footnotes in framing document

Table 2. Information on the uncertainty factors (UFs) and other adjustments used in TCEQ's, the petitioner's, and Perry et al.'s TRV for acute exposure to manganese.

TRV Source	TRV ug/m³	Uncertainty Factor (UF) Information						Human Equivalent Concentration in TRV?	Time Adjustment in TRV?
		UF_A Inter-species	UF_H Intra-species	UF_L LOAEL	UF_S Sub-chronic	UF_D Database	Total UF		
TCEQ, 2017	5.0	3	10	2	NA	6	300*	No	No◊
Petition	5.0	10†	10	3	NA	--	300	No	No
Perry et al., 2023	5.0	3‡	10	10‡	NA	--	300	No	No

Footnotes in framing document

Table 3. TCEQ's statements on the UFs for manganese.

UFs	Page Number	Direct Quote from TCEQ (2017)
UF_A Interspecies	21	"A UF_A of 3 was used to account for potential toxicodynamic differences between rhesus monkeys and humans."
UF_H Intraspecies	21	"A full UF_H of 10 was used for intrahuman variability to account for potentially sensitive subpopulations (e.g., children, the elderly, those with pre-existing medical conditions)."
UF_L LOAEL	8	"…Use of a minimal LOAEL-to-NOAEL uncertainty factor is justified as opposed to use of the 5-fold lower no-observed-adverse-effect-level (NOAEL of 0.3 mg Mn/m3) from the subchronic portion of the study due to the very conservative nature of the assessment for derivation of the acute ReVs (i.e., actual exposure duration far exceeding those of interest for the 1- and 24-h ReVs, use of a single day of a 3-week exposure for the 1-h ReV duration adjustment, minimal/mild airway inflammatory changes utilized as endpoints in the absence of observed clinical signs)."
	21	"A reduced UF_L of 2 was used for extrapolation from a LOAEL to a NOAEL since the observed pulmonary pathology was characterized as mild/minor airway inflammatory changes in the absence of observable clinical signs"
UF_S Subchronic		NA
UF_D Database	21-22	"A UF_D of 6 was used for limitations/uncertainties in the acute/subacute database including the lack of toxicological data on: (1) humans exposed acutely (or subacutely) to either less soluble forms of Mn or the more soluble forms of greater potential concern for the general population; and (2) whether acute/subacute exposure to inhaled Mn has a significant potential for adverse effects on numerous endpoints including developmental neurological effects, and if so (as suggested by the oral developmental database, as well as neurological/neurobehavioral changes being the critical effects based on the intermediate- and chronic duration databases), what exposure concentrations/durations induce them (ATSDR 2012). That is, additional studies involving neurobehavioral effects following gestational and postnatal exposure to airborne Mn are necessary. The addition of developmental neurotoxicology studies using a functional observational battery design and a wide range of well-established measures would result in a more complete inhalation (and oral) database, particularly if non-human primates are used considering that rodents may be a less-than desirable model for neurological effects in humans (i.e., rodent models do not appear to be as susceptible to Mn-induced neurotoxicity as humans and monkeys, somewhat diminishing the relevance of chronic Mn inhalation exposure rodent neurological results in regard to their ability to help identify the most sensitive Mn effects that may occur in humans) (see Section 3.12.2 of ATSDR 2012). Additionally, while some acute/subacute studies demonstrate either free-standing NOAELs or LOAELs/LOELs, they do not demonstrate these values in the context of studies adequate to fully characterize dose-response for the endpoints studied. These database limitations result in a low confidence in the acute/subacute database overall (TCEQ 2015), consistent with ATSDR (2012) not deriving an acute duration minimal risk level (MRL) (inhalation or oral)."

Table 4. Potential options for DEQ's acute manganese TRV for ATSAC to discuss.

TRV Proposal Name	TRV (ug/m^3)	Uncertainty Factor (UF) Information						Human Equivalent Concentration in TRV?	Time Adjustment in TRV?	Notes
		UF_A Inter-species	UF_H Intra-species	UF_L LOAEL	UF_S Sub-chronic	UF_D Database	Total UF*			
Option 1 TCEQ	5.0	3	10	2	NA	6	300	No	No	No changes to TCEQ's 2017 final acute Mn TRV. This includes TCEQ's policy that 300 is the maximum total UF allowed for acute TRVs.
Option 2 TCEQ with no total UF maximum	4.2	3	10	2	NA	6	360	No	No	Removes TCEQ's policy of capping the total UFs to 300 for acute TRVs.
Option 3 Petition	5.0	$10^{\lozenge}$	10	3	NA	--	300	No	No	The proposed TRV is the same as the TCEQ acute value, but some of the UFs are different.
Option 4 Petition with UF_D	0.8	10	10	3	NA	6	1800	No	No	Compared to the petition, includes an additional UF_D, which matches the TCEQ UF_D.
Option 5 Petition with UF_D and lower UF_A	2.8	3	10	3	NA	6	540	No	No	Compared to petition, includes the additional database UF_D, but a lower UF_A.
Option 6 Perry et al. 2023	5.0	3	10	10	NA	--	300	No	No	The proposed TRV is the same as the TCEQ acute value, but some of the UFs are different.
Other Suggestions from ATSAC members										Please let DEQ know if you think there is another good option that is not already on this table.

**Additional options include rounding the total UF to one significant digit (e.g., the total UF for Option 2 would be 400 instead of 360).*

Break

Manganese Petition
ATSAC Discussion Questions

Critical Study Question

1. What critical study option in Table 1 do you like the best and why? Would you propose another option for DEQ to consider?

UF Questions

2. Do you think the UF_A (interspecies) should be 3 or 10 or something else? Why?
3. Do you think the UF_H (intraspecies) should be 10 or something else? All proposals in Table 4 have a UF_H of 10.
4. Do you think the UF_L (LOAEL) should be 2, 3, 10, or something else? Why?

Database UF Question

5. Do you agree with the petitioners that there is enough evidence to not have a UF_D? Why or why not?

   Do you agree with the TCEQ UF_D of 6? Why or why not?

Total UF Question

6. Do you think we should put a cap on the maximum total UF like TCEQ does?

Best Option for DEQ's Acute Exposure TRV

7. What proposal option in Table 4 do you like the best and why?

   If you do not like any of the options listed in this document, why? Would you propose another option for DEQ to consider?

   Is there other information that DEQ needs to consider in order to choose a proposal option?

Final Thoughts?

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Next Steps

- Will circulate meeting minutes for you all to review in the next few weeks
- Using feedback from today's meeting, DEQ will put together a proposal for the acute manganese TRV
- DEQ and ERG will wrap up the quality control process over the next few months
- DEQ will then plan a series of ATSAC meetings to discuss the TRV review and selection process

EXTRA SLIDES

For Discussion as Needed

Overview of TRV Review Technical Process

Priority Toxic Air Contaminants (TACs) with **Existing** TRVs
~300 contaminants

Priority TACs with **Potentially New** TRVs
~100 contaminants

- Agency staff will review TRV information from all authoritative sources and gather information on TRVs that could be adopted from other organizations or developed
- Agency staff select TRVs using process discussed with ATSAC

We are here

- Contractor (ERG) completes quality control (QC) review of all TRV-related information
- Agency staff reviews QC findings and makes changes to TRV information

- In a series of meetings with ATSAC, agency staff will
  - Share results of the TRV selection process
  - Ask technical questions that arose and discuss tangential work
  - Ask for feedback if we have a proposal to deviate from the TRV selection process

Toxicity Reference Values (TRVs)

TRV Name	Definition
Chronic Cancer	Air concentration corresponding to a one in one million excess cancer risk, calculated by dividing one in one million (0.000001) by the inhalation unit risk when that air is breathed over a lifetime.
Chronic Noncancer	Air concentration below which noncancer health effects are not expected over a year or more of constantly breathing that air.
Acute Noncancer	Air concentration below which noncancer health effects are not expected over 24 hours or less from breathing that air.

Acute TRVs

Order of Preference	Agency Name	Name of Acute TRV	Assumed Exposure Time
1	ATSDR	Acute Minimal Risk Level (MRL)	Less than 2 weeks (includes 24 hours)
2	CalEPA	Acute Reference Exposure Level (REL)	1 hour
3	ATSDR	Intermediate MRL	2 weeks to 1 year

Chronic TRVs

Agency Name	Name of Chronic TRV	Type of TRV Available
US Agency for Toxic Substances and Disease Registry (ATSDR)	• Chronic Minimal Risk Level (MRL)	• Noncancer
US Environmental Protection Agency (EPA)	• Inhalation Unit Risk (IUR) • Reference Concentration (RfC)	• Cancer • Noncancer
California Environmental Protection Agency (CalEPA)	• IUR • Chronic Reference Exposure Level (REL)	• Cancer • Noncancer
Oregon DEQ in consultation with ATSAC*	• Chronic TRV	• Noncancer • Cancer

*Oregon DEQ in consultation with ATSAC was added to the list of authoritative sources by the Environmental Quality Commission in 2021. Currently, there are no TRVs from this authoritative source.