



Oregon Department of Environmental Quality

Compilation of ATSAC Responses to Manganese Email on 4-12-2024

Copy of DEQ Email

From: GOECKNER Apollonia * DEQ <Apollonia.GOECKNER@deq.oregon.gov>
Sent: Friday, April 12, 2024 11:10 AM
To: John Budroe; Dong, Qiaoxiang@CDPR; Jeff Fowles; Tilton, Susan C; Stanek, John; John Vandenberg, Ph.D.
Cc: Holly Dixon; Farrer David G; MACMILLAN Susan * DEQ; GISKA JR * DEQ
Subject: ATSAC Meeting 3: Follow Up Manganese Questions
Attachments: Compiled Worksheets - ATSAC Mn TRV Proposal.docx; Dorman et al. 2005.pdf; Erikson et al. 2008.pdf

Hi ATSAC Members,

Thank you all again for your participation and thoughtful feedback during the ATSAC meeting last week.

New Update: This week we received a [document from ToxStrategies](#) that includes further clarifications and follow-up after the ATSAC meeting. We also received an [email](#) from the author of the Texas Commission on Environmental Quality (TCEQ) Manganese Development Support Document, Joseph Haney, about the exposure duration adjustment. We wanted to immediately share these documents with you.

Request: Based on these additional materials, we compiled three additional questions for you all to answer. Please read the ToxStrategies response document and TCEQ email to provide full context for the questions.

Please reply-all to this email with your answers to these questions before 4/26.

1. Does Dorman et al. 2005 (see Table 2 specifically) support ToxStrategies' statement on page 3 of their response document?

"As such, we would not expect lung tissue levels to be higher following a single 24 hour exposure than that for 6 hours per day, for 15 days (or a total of 90 exposure hours), which is the exposure at the POD." – ToxStrategies Response pg. 3

If you have questions about Dorman et al. 2005 methods, we attached the paper directly to this email. Figure 1 in Dorman et al. is an overview of the experimental design. Exposure and necropsy procedures are detailed on page 3; for example, Dorman et al. states that "necropsies were performed the day following the last inhalation exposure (i.e., 12-18 hr after termination of the final inhalation exposure)."

2. ToxStrategies highlights TCEQ's guidance related to time adjustments:

"TCEQ guidance recommends that 'if it is reasonable to assume that steady state has been achieved, or toxicodynamics indicate that no additional toxic effect would be expected to occur with the subacute exposure duration, the POD from the subacute study can be used as the 24-hour POD without adjustment.'" – ToxStrategies Response pg. 3

Do you agree that the conditions mentioned in this quote from TCEQ guidance are met in the Dorman et al. 2005 and Erikson et al. 2008 study? Do you agree with the TCEQ guidance?

3. Given the additional information from ToxStrategies and TCEQ, what is your current recommendation about an exposure time adjustment and/or uncertainty factors and why? Attached is a compilation of the three worksheets we received after the 4/3 meeting (see page 2). Please edit the worksheet attachment, if applicable, and email it back to us.

Kearns & West and DEQ are still working on meeting minutes for the 4/3 ATSAC meeting. We will send those to you all to review once they are ready.

Thank you,
ATSAC Governance Team



Apollonia (Apple) Goeckner | Program Coordinator
Oregon Department of Environmental Quality
700 NE Multnomah St., Suite 600
Portland, Oregon 97232 - 4100
P: 503.869.0026
Pronouns: She/Her/Hers

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ATSAC Responses

ATSAC Member	ATSAC Member Responses
<p>Dr. John Budroe 4-26-2024</p>	<p><u>Question 1:</u> The Dorman et al. (2005) and Erickson et al. (2008) Mn exposures of 6 hr/d, 5 d/wk for 15 days would result in a lesser day-1 exposure than that of a human breathing Mn at the same concentration for the acute TRV time period (24 hours). This indicates that a time adjustment from 6 to 24 hours is appropriate (noted in worksheet).</p> <p><u>Question 2:</u> I would be more likely to support the TCEQ guidance if it read "steady state has been achieved, AND toxicodynamics indicate that no additional toxic effect would be expected to occur with the subacute exposure duration...". In this case, there is no toxicodynamic data available that would justify not using an exposure duration adjustment.</p> <p><u>Question 3:</u> As noted in the response to question 1, an exposure time adjustment should be employed (POD x (6 hours/24 hours) - included in attachment). Uncertainty factors are listed in the attachment.</p>
<p>Dr. Daisy Dong 4-26-2024</p>	<p><u>Question 1:</u> No, an exposure scenario of 6 hours/day, 5 days/week is different from a continuous exposure of 24 hours, which may cause adverse effects that is irreversible.</p> <p><u>Question 2:</u> No, there is no data indicate that the TK and TD are similar between 6 hour and 24 hour exposure. I would agree with the TCEQ guidance if TK reaches steady state AND TD indicates no additional toxic effects. Duration adjustment should be applied for the 24-hour TRV calculation unless there are experimental data proved to be unnecessary.</p> <p><u>Question 3:</u> My recommendations remain same: need to adjust for duration from 6 hours in Monkeys to 24 hours in humans, UF-A of 3, UF-H of 10, UF for LOAEL-to-NOAEL of 10. It is worth to mention that a LOAEL to NOAEL of 10 is not overly conservative given that the critical effects include neurotoxicity and many brain neurotoxicity biomarkers did change at the LOAEL in monkeys. Also I have less concern of in utero exposure as Mn accumulation in the brain is mainly through inhalation route.</p>
<p>Dr. Jefferson Fowles</p>	<p><i>DEQ did not receive an additional follow-up response.</i></p>
<p>Dr. John Stanek 4-26-2024</p>	<p><i>Emailed DEQ TRV worksheet.</i></p>
<p>Dr. Susan Tilton 4-26-2024</p>	<p>I don't have any additional recommendations from my prior comments except to comment that an adjustment for time should either be accounted for as uncertainty as part of the UF-L or should be applied to calculate the POD, but it does not need to be accounted for in multiple places. Because of that, I believe the recommendation for a reduced TRV is appropriate and one approaching 0.3 ug/m³ is reasonable.</p>
<p>Dr. John Vandenberg 4-26-2024</p>	<p>Thanks for sending the materials - I reviewed the ToxStrategies response and attachment, the email from Joseph Haney, and the Dorman and Erickson papers.</p> <p>My response to the questions: The Dorman and Erickson exposure conditions of 6 hr/d for 5/wk for 15 days does not address the amount of exposure and accumulation of Mn in the body that would occur for a human breathing 24 hours a day i.e., the duration of the acute TRV. The total exposure after 24 hr would be greater than for 6 hr if the Dorman/Erickson study had used continuous (24 hr) exposures (I do</p>

appreciate a 24 hr inhalation exposure would be extremely difficult to implement in a laboratory study). I am not convinced that the data obtained at 15 days relates to this time adjustment. In the summary table I retained a time adjustment from 6 to 24 hours to align the study exposures with the duration of the acute TRV.

I've updated the summary table and revised my UFa from 10 to 3 in order to not double-count the lack of neurobehavioral data. I retained a UFd of 3 due to lack of neurobehavioral data and evidence from the Erickson paper showing brain effects at 15 days. As Dorman states in the first sentence of the abstract "Neurotoxicity and pulmonary dysfunction are well-recognized problems associated with prolonged human exposure to high concentrations of airborne Mn. "

With the time adjustment and application of a combined UF of 300 the TRV result that I derive is 1.25 ug/m³.

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