



ATSAC Compiled Worksheets- Manganese

ATSAC Worksheet for 4-3-2024: Manganese Acute Exposure TRV Proposal Options

Instructions for ATSAC Members: If useful to you, you can fill out the green shaded portions of this worksheet before, during, and/or after the ATSAC meeting on 4-3-2024. You can send in this worksheet to DEQ after the meeting (email Apollonia Goeckner at apollonia.goeckner@deq.oregon.gov).

Excerpt from page 6 of the [Manganese TRV Framing Document](#): To aid ATSAC discussion, Table 4 outlines a range of potential proposals for DEQ’s acute manganese TRV. Not all potential options are in this table. DEQ wants to hear from ATSAC members on the benefits and drawbacks of the proposals in Table 4. DEQ also wants to know if ATSAC members think a better proposal option is available other than those listed in Table 4. ATSAC member feedback will inform DEQ’s final proposal.

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?	DEQ 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 ^o	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.

Translation or other formats

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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). DEQ has observed that this is regularly done by U.S. EPA and ATSDR.

Compilation of ATSAC Feedback Received

Here is a compilation of worksheets received from ATSAC members as of 5-10-2024. A complete summary of the ATSAC Manganese TRV Meeting, including ATSAC member feedback, is captured in the [ATSAC 4-3-2024 Meeting Minutes Document](#).

TRV Proposal Name	TRV (ug/m ³)	Uncertainty Factor (UF) Information						Human Equivalent Concentration in TRV?	Time Adjustment in TRV?	ATSAC Notes
		UF _A Inter-species	UF _H Intra-species	UF _L LOAEL	UF _S Sub-chronic	UF _D Database	Total UF*			
John Vandenberg 4-26-2024	1.25 µg/m ³	3 Monkey study	10 Concern about prenatal and youngest children	3 PBPK model	NA	3 Missing neurobehavioral data	300	-	Yes	LOAEL = 1.5 mg/m ³ from Dorman and Erikson studies with time adjustment from 6 hours to 24 hours yields POD = 1.5/4 = 0.375 mg/m ³ Rationale similar to Option 4 with time adjustment and use factor of 3 for UF _D due to lack of neuro data. I've revised this from my prior submission to not double-count lack of neuro data by changing UF _A to 3.
Daisy Dong 4-3-2024	1.25 µg/m ³	3	10	10	NA	1	300	UF _A =3 is equivalent as calculation of HEC	Yes, from 6h to 24h, POD = 0.375 mg/m ³	Agree with the LOAEL selection of 1.5 mg/m ³ from the two Rhesus monkey studies in combination; Agree with the UF selection based on arguments from the petition presentation. Disagree with no duration adjustment.
Susan Tilton 4-3-2024		3	10	2	NA	3	180	No	Yes	See below. Adaptation of Option 6 to include the time adjustment in TRV as part of the POD and not as an uncertainty factor. In addition, include UF _D to account for potential in utero/fetal neurotoxicity not included in PBPK model.
John Budroe 4-26-2024	0.21 µg/m ³	3	30	6	NA	3	1800	-	Yes	LOAEL = 1.5 mg/m ³ , time adjustment from 6 hrs to 24 hrs, POD = 1.5/4 = 0.375 mg/m ³ . UF _H reflects a subfactor of 3 (UF _{H,k}) to adjust for residual pharmacokinetic differences not accounted for by the PBPK model, and a subfactor of 10 (UF _{H,p}) to account for potential prenatal/child

											susceptibility due to pharmacodynamic differences with adults. UF _D reflects lack of developmental neurobehavioral data.
Jefferson Fowles <i>See meeting minutes</i>											
John Stanek 4-29-2024	1.25 ug/m ³	3*	10	10	-	-	300	PBPK used*	Yes 6/24 hr (to account for 24 hr value)		Value takes into account the 2 most relevant monkey studies as well as the findings from the PBPK model. In disagreement with not having a duration adjustment for determining a 24 hr value from a 6 hr exposure without having supportive data. A full UF for LOAEL is likely warranted as there is not a defined NOAEL under similar exposure conditions (without making a few assumptions). *If A TRV were based solely on lung effects (Dorman study), comparative species metrics from a particle-based dosimetry model (ie MPPD) would need to be presented to determine an HEC and support U _f a = 3.

Additional Notes from Susan Tilton 4-3-2024

UF_A – Recommend 3-fold to account for differences in toxicodynamics based on the fact that POD is from non-human primate study in rhesus monkeys and no adjustment is needed for dosimetry.

UF_H – Intraspecies uncertainty of 10-fold accounts for extrapolation to sensitive populations

UF_L – I recommend an extrapolation of 2-fold since the observed pulmonary pathology was characterized as mild/minor and reversible. Since I’m recommending to incorporate a time adjustment on the POD calculation, it’s not necessary to extend the UF here to account for the fact that the LOAEL is not based on 24 hr continuous exposure scenario.

UF_D – Recommend a value of 3-fold to account for uncertainty related to the possibility of identifying a lower POD if additional studies were available on the potential for neurotoxicity in offspring from in utero exposure. Should be considered that currently available reproductive and developmental effects were not observed in subchronic studies at higher doses for longer periods and that the incorporated PBPK model accounts for differences due to age during infancy and childhood. It is also important to note that:

- We are already using an UF_H of 10 to account for extrapolation to sensitive populations in humans
- Current studies suggest that under the exposure scenarios considered (24 hr exposure once per month or continuous exposure over 3 wks) that brain tissue levels were not predicted to be above background and that maternal and fetal blood levels were not changed at airborne concentrations less than 10 ug/m³ (Yoon et al. 2011)
- Therefore, inclusion of an UF_D would be considered conservative

Time adjustment in TRV-

I will leave it up to others to suggest how this is done, but if the time adjustment is not accounted for as an uncertainty (which several panel members noted that it should not be), then it should be applied to calculate the POD. The toxicokinetic data available suggest that a steady state is achieved with intermittent/shorter exposures of 6 hr/d, 5d/wk and so the time-adjustment would be a conservative approach. In this case, the UF_L does not need to account for additional uncertainty associated with the exposure period.

Overall comments,

The TRV for OR DEQ should be updated from 0.3 ug/m³ using the available data for acute respiratory effects. The LOAEL of 1500 ug/m³ is a reasonable value based on mild respiratory effects in rhesus monkeys for 90 hrs total.

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