

## Derivation of Montana's Health-Based Guidance for Manganese

Montana has updated health-based guidance for Manganese. The health-based guidance includes a 100 µg/L value protective of the most sensitive population, formula-fed infants less than one year of age. This guidance is meant to protect against neurodevelopmental effects observed in human epidemiology studies and rat toxicity studies (Khan, 2011, and 2012; Kern et al., 2010 and 2011; Beaudin et al., 2013). Because of the extensive nervous system changes and maturation that occurs until a child is approximately 6 years old, DEQ recommends children under 6 should not consume drinking water if the manganese concentration is greater than 100 µg/L.

Montana's health-based guidance is also consistent with the U.S. Environmental Protection Agency (EPA) Lifetime Health Advisory (HA) of 300 µg/L for children older than six years of age and adults See *Drinking Water Health Advisory for Manganese*  
<https://www.epa.gov/sites/production/files/2018-03/documents/dwtable2018.pdf>.

Also refer to *Manganese in Drinking Water: Montana Fact Sheet* found on the MT DEQ Manganese in Drinking Water webpage.

### Non-Cancer Health-Based Guidance Derivation

Reference Dose (mg/kg-day) X Relative Source Contribution X Conversion Factor  
Short-term Intake Rate (L/kg-day)

$$\frac{.025 \text{ mg/kg-day} \times .8 \times 1000 \text{ } \mu\text{g/mg}}{.1723 \text{ (L/kg-day)}} = 116 \text{ } \mu\text{g/L} \text{ rounded to one significant figure} = 100 \text{ } \mu\text{g/L}$$

**Reference Dose/Concentration (RfD)** = LOAEL/UF = 25 µg/kg-day

**Lowest Observable Adverse Effects Level (LOAEL):** Health Effect: Neurodevelopmental effects in neonatal rats (Kern et al., 2010, 2011; Beaudin et al., 2013); LOAEL = 25 mg/kg-day

**Uncertainty Factor (UF):** 1000 (UF<sub>A</sub> = 10, UF<sub>H</sub> = 10, UF<sub>L</sub> = 10) UF<sub>A</sub> is uncertainty due to interspecies variability to account for extrapolating from laboratory animals to humans, UF<sub>H</sub> is for intraspecies variability to account for variability in the responses w/in the human population because of intrinsic and extrinsic factors and the UF<sub>L</sub> is because a LOAEL and not a NOAEL was used in the derivation (EPA, 1993).

**Relative Source Contribution (RSC):** The RSC accounts for potential exposure from other environmental media and was calculated by subtracting manganese in infant formulas from the LOAEL to give a RSC of .833, rounded to .8 (EPA, 2000)

Details: Manganese in infant formula: FDA mandates commercial infant formula provides 5 micrograms of manganese per 100 kcal/day (21 CFR 107.100). The average estimated energy requirement for an infant from birth to 6 months is 542.75 kcal/day (Infant Nutrition and Feeding, USDA, Chapter 1, Table 1, time weighted average for males and females combined). The average ingestion from infant formula is 27.1375 micrograms/day.

$$(472 + 567 + 572 + 548 + 596 + 645 + 438 + 500 + 521 + 508 + 553 + 593)/12 = 542.75 \text{ kcal/day}$$

$$542.75 \text{ kcal/day} \times 5 \text{ } \mu\text{g}/100 \text{ kcal} = 27.1375 \text{ } \mu\text{g}/\text{day}$$

Using the subtraction approach (Box 12 of Exposure Decision Tree) the Relative Source Contribution (RSC) is calculated as 0.83.

$$(25 \text{ } \mu\text{g}/\text{kg-day} \times 6.47 \text{ kg} - 27.1375)/ (25 \text{ } \mu\text{g}/\text{kg-day} \times 6.47 \text{ kg}) = 0.83$$

The SDWA and CWA limits the RSC to a maximum of 0.80. That value is used instead of 0.83

**Drinking Water Ingestion Rate:** 172.3 mL/kg-day (EPA, EFH, Updated Chapter 3, Feb 2019, Table 3-21, time weighted upper 90<sup>th</sup> percentile, consumers only, combined direct and indirect water ingestion)

$$(1 \text{ mo} \times 219.7 \text{ mL}/\text{kg-day} + 2 \text{ mo} \times 192.2 \text{ mL}/\text{kg-day} + 3 \text{ mo} \times 143.3 \text{ mL}/\text{kg-day})/ 6 \text{ mo} = 172.3 \text{ mL}/\text{kg-day}$$

**Critical effect(s):** Neonate manganese exposure resulted in hyperactivity, disinhibition of exploratory behavior, learning deficits, and altered expression of dopamine transporters and receptors in the prefrontal cortex, nucleus accumbens and dorsal striatum of young weanling male rats (Kern, 2010). Fine sensorimotor dysfunction (Beaudin et al., 2013).

## References

Beaudin, SA., Nisam, S., and Smith, DR. 2013. Early life versus lifelong oral manganese exposure differently impairs skilled forelimb performance in adult rats. *Neurotoxicology and Teratology* 38:36-45.

EPA. 1993. Reference Dose (RfD): Description and Use in Health Risk Assessments. Background Document 1A. <https://www.epa.gov/iris/reference-dose-rfd-description-and-use-health-risk-assessments>

EPA, 2000 Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health <https://nepis.epa.gov/Exe/ZyPDF.cgi/20003D2R.PDF?Dockey=20003D2R.PDF>

EPA 2019, Update for Chapter 3 of the Exposure Factors Handbook Ingestion of Water and Other Select Liquids. EPA/600/R-18/259F [https://www.epa.gov/sites/production/files/2019-02/documents/efh -  
\\_chapter\\_3\\_update.pdf](https://www.epa.gov/sites/production/files/2019-02/documents/efh_-_chapter_3_update.pdf)

Khan K, Factor-Litvak P, Wasserman GA, Liu X, Ahmed E, Parvez F, et al. Manganese exposure from drinking water and children's classroom behavior in Bangladesh. *Environ Health Perspect.* 2011; 1003397:1501–1506.

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Kern, CH., and Smith, DR. 2011. Prewaning Mn exposure leads to prolonged astrocyte activation and lasting effects on the dopaminergic system in adult male rats. *Synapse* 65:532-544.

Kern CH., Stanwood, GD., and Smith, DR. 2010. Prewaning manganese exposure causes hyperactivity, disinhibition, and spatial learning and memory deficits associated with altered dopamine receptor and transporter levels. *Synapse* 64:363-378.

United States Department of Agriculture, (USDA), Infant Nutrition and Feeding, March 2009. 21 CFR, Food and Drugs. Part 107 Infant Formula. 107.10 Nutrient Information.