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

$$\frac{\text{Reference Dose (mg/kg-day) X Relative Source Contribution X Conversion Factor}}{\text{Short-term Intake Rate (L/kg-day)}}$$

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

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_A = 10, UF_H = 10, UF_L = 10) UF_A is uncertainty due to interspecies variability to account for extrapolating from laboratory animals to humans, UF_H 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_L 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 moths 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 kcal/day

542.75 kcal/day x 5 µg/100 kcal = 27.1375 µg/day

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

(25 µg/kg-day x 6.47 kg – 27.1375)/ (25 µg/kg-day x 6.47 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 90th percentile, consumers only, combined direct and indirect water ingestion)

(1 mo x 219.7 mL/kg-day + 2 mo x 192.2 mL/kg-day + 3 mo x 143.3 mL/kg-day)/ 6 mo = 172.3 mL/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

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