CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

Gavin Newsom, Governor
Jared Blumenfeld, Secretary for Environmental Protection
Lauren Zeise, Ph.D., Director

# MEMORANDUM

**TO:** Darrin Polhemus
Deputy Director, Division of Drinking Water
State Water Resources Control Board

**FROM:** Lauren Zeise, Ph.D.
Director

**DATE:** May 3, 2022

**SUBJECT:** REVIEW OF RECOMMENDATION FOR REVISED NOTIFICATION LEVEL FOR MANGANESE IN DRINKING WATER

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In response to your request dated April 7, 2022, the Office of Environmental Health Hazard Assessment (OEHHA) has reviewed the recommendation for a revised notification level (NL) for manganese developed by the Division of Drinking Water (DDW) scientific staff. Based on the potential risk for manganese induced neurotoxicological effects in bottle fed infants, DDW staff recommended a health protective concentration (HPC) of 20 μg/L, equivalent to 20 parts per billion (ppb), to serve as the basis for future recommended revisions to the current manganese notification and response levels of 500 μg/L and 5,000 μg/L, respectively. Based on a review of the information presented, OEHHA agrees with an HPC of 20 μg/L as the basis for the NL. OEHHA also suggests some additional steps, as outlined below, for future work on developing an HPC for manganese.

Manganese is an important pollutant to consider, given its ubiquitous occurrence in drinking water and food, high exposure potential in sensitive populations, and numerous human and animal studies suggesting neurotoxicity. The proposed NL is based on a study by Kern et al. (2010),[1] in which neonatal rats exposed to manganese over 21 postnatal days exhibited neurobehavioral deficits. There is merit in selecting this study and its point of departure (POD) of 25 mg/kg-day (a lowest-observed-adverse-effect level) for derivation of the NL because these were also the choice of several regulatory entities, including the Minnesota Department of Health,[2] Health Canada, Institut National de Santé Publique du Québec, and the French Agency for Food,

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3070959/pdf/nihms253360.pdf
[2] https://www.health.state.mn.us/communities/environment/risk/docs/guidance/gw/manganese.pdf

Environmental and Occupational Health and Safety (ANSES) in their health assessments of manganese.[3]

In an effort to continue to improve future iterations of the manganese NL, OEHHA has the following suggestions:

- *Literature evaluation of post-2010 studies:* There is a large number of human and animal studies published after the Kern et al. (2010) study. Thus, there is an extensive recent literature to inform the derivation of the HPC that appears to include well-conducted human studies. A systematic literature search and in-depth data evaluation is warranted for establishing a state-of-the-science HPC for the chemical.
- *Consider studies with lower PODs:* The DDW NL recommendation memo describes two studies cited by OEHHA for the development of a child-specific reference dose (chRD).[4] These studies, Dorman et al. (2000)[5] and Tran et al. (2002)[6] reported neurological effects of manganese in neonatal rats at 11 mg/kg-day and 8.3 mg/kg-day, respectively. Future analyses should indicate why they were not chosen as candidate critical studies. Ultimately the OEHHA 2006 chRD was based on a human dietary study and very similar to the acceptable daily dose ("ADD") developed by DDW.
- *Review Human Studies Database:* The "Human Data" section only describes the derivation of OEHHA's 2006 chRD. As noted above, there is a large number of human studies on manganese that should be reviewed in detail for potential use in deriving an HPC or future revised NL, and rationale should be given as to choices to include or exclude the studies from consideration.

Overall, OEHHA understands the need for an expedited assessment for establishing a more health protective NL. Until a more rigorous analysis can be done, which would take a considerable amount of time, OEHHA supports this intermediate approach, and agrees with the parameters used in the calculation of the HPC: use of the Kern et al. (2010) study, the composite uncertainty factor of 1,000, the relative source contribution of 0.2, and the drinking water intake based on infants 0−6 months.

[3] https://pdfs.semanticscholar.org/d118/8a6665043d1f09d1891f384069a364567232.pdf
[4] https://oehha.ca.gov/media/downloads/crnr/mn-pcpfinal-070306.pdf
[5] https://pubmed.ncbi.nlm.nih.gov/10797470/
[6] https://pubmed.ncbi.nlm.nih.gov/12428736/

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