

November 16, 2020

Office of Environmental Health Hazard Assessment  
1001 I Street  
P. O. Box 4010, MS-12B  
Sacramento, California 95812-4010

**Re: Announcement of the Developmental and Reproductive Toxicant Identification Committee Meeting Scheduled for December 10, 2020**

On behalf of the Consumer Healthcare Products Association (CHPA)<sup>1</sup> and the Council for Responsible Nutrition (CRN),<sup>2</sup> enclosed herein are comments on the recent notice from the California Office of Environmental Health Hazard Assessment (OEHHA) regarding 22 chemicals to be discussed at a December 10, 2020 meeting of the Developmental and Reproductive Toxicant Identification Committee (DARTIC). The comments provided herein address manganese (Mn).

**Manganese**

A significant body of literature exists for Mn demonstrating its safety and effect on human health, including information on the essential nature of this naturally-occurring element in enzyme regulation, bone formation, and immune response.<sup>3</sup> Commonly found in a wide variety of foods, dietary supplements, as well as drinking water, Mn is considered an essential nutrient for human health for which Dietary Reference Intakes (DRI) have been established by an expert committee of the Food and Nutrition Board of the Institute of Medicine (now the National Academy of Medicine).<sup>4</sup> To prioritize Mn for review as a reproductive or developmental toxicant would mislead consumers to believe this essential nutrient is a health concern and discourage consumption of a substance essential to human health.<sup>5</sup>

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<sup>1</sup> The Consumer Healthcare Products Association (CHPA), founded in 1881, is the national trade association representing the leading manufacturers and marketers of over-the-counter (OTC) medicines, dietary supplements, and consumer medical devices. Every dollar spent by consumers on OTC medicines saves the U.S. healthcare system more than \$7, contributing a total of \$146 billion in savings each year. CHPA is committed to empowering consumer self-care by preserving and expanding choice and availability of consumer healthcare products.

<sup>2</sup> The Council for Responsible Nutrition (CRN), founded in 1973 and based in Washington, D.C., is the leading trade association representing dietary supplement and functional food manufacturers, marketers and ingredient suppliers. CRN companies produce a large portion of the functional food ingredients and dietary supplements marketed in the United States and globally. Our member companies manufacture popular national brands as well as the store brands marketed by major supermarkets, drug stores and discount chains. These products also include those marketed through natural food stores and mainstream direct selling companies. CRN represents more than 150 companies that manufacture dietary ingredients, dietary supplements and/or functional foods, or supply services to those suppliers and manufacturers. Our member companies are expected to comply with a host of federal and state regulations governing dietary supplements and food in the areas of manufacturing, marketing, quality control and safety. Our supplier and manufacturer member companies also agree to adhere to additional voluntary guidelines as well as to CRN's Code of Ethics. Learn more about us at [www.crnusa.org](http://www.crnusa.org).

<sup>3</sup> Aschner M and Erikson K, 2017 Manganese *Adv Nutr* 8(3):520-521.

<sup>4</sup> The DRI for Mn available at <https://www.nap.edu/read/11537/chapter/39>.

<sup>5</sup> This concern is not idle speculation, as federal agencies have already recognized adverse effects from manganese deficiency. For example, the U.S. Environmental Protection Agency (U.S. EPA) has noted that "the potential adverse

The available science for Mn as a reproductive or developmental toxicant is unsettled, as demonstrated by the inconsistent findings in the Mn studies identified in the OEHHA prioritization document, and does not support prioritization of the review of Mn as a reproductive or developmental toxin under Proposition 65.<sup>6</sup> In addition to the studies identified by OEHHA, a recent systematic literature review of epidemiologic studies of developmental Mn exposure and neurodevelopmental outcomes<sup>7</sup> found that a causal relationship was not established between Mn exposure and validated neurodevelopmental outcomes. This review included 22 human epidemiologic studies in which Mn exposure was measured during neurodevelopment (gestation up to approximately 15 years). Prioritizing Mn for a listing review would be premature given the currently available science, which does not support a casual association between developmental toxicity and manganese exposure. A listing is also very likely to interfere with federal nutrition policy.

When assessing the potential for toxicity, it is important to consider the route of exposure. The primary source of excess Mn exposure for the general U.S. population is through inhalation of air contaminated with particulate matter containing Mn.<sup>8</sup> OEHHA indicates that occupational exposure to high levels of Mn via inhalation, as seen in welders, may result in adverse outcomes, though this is far from settled.<sup>9</sup> High-level, work place, inhalation exposure, however, does not translate to a concern with Mn through other routes of exposure, particularly oral consumption levels typically found in food and dietary supplements. Yet, if OEHHA's prioritization does not recognize different routes of exposure, it leaves the very products that provide this essential nutrient (food and supplements) vulnerable to legal challenge under Proposition 65. Additionally, possible confounders, including co-exposure to other toxicants should also be taken into consideration when reviewing the science related to this nutrient.

CHPA and CRN urge OEHHA not to prioritize Mn for review due to its status as an essential nutrient and the current science regarding whether exposure causes reproductive or developmental toxicity does not demonstrate a relationship. If OEHHA moves forward with prioritizing Mn for review, based on the concerns identified in this letter, CHPA and CRN request review only for non-oral consumption routes, such as inhalation. Absent this, we ask OEHHA to consider adopting a maximum allowable dose level for oral consumption to ensure that consumers do not avoid food and dietary supplements containing this essential nutrient. For oral consumption routes, safety of the form and amount of a nutrient are already heavily regulated at the federal level by the Food and Drug Administration (FDA). As such, OEHHA review of oral consumption routes for Mn would be redundant and is unnecessary.

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effects from manganese deficiency may be of greater concern than potential toxicity from over-exposure". U.S. Environmental Protection Agency, *Health Effects Support Document for Manganese*, at 1-2 (2003).

<sup>6</sup> <https://oehha.ca.gov/media/downloads/crn/dartprioritization100120.pdf>

<sup>7</sup> Leonhard MJ, Chang ET, Loccisano AE and Garry MR, 2019 A systematic literature review of epidemiologic studies of developmental manganese exposure and neurodevelopmental outcomes. *Toxicology* doi: [10.1016/j.tox.2019.03.004](https://doi.org/10.1016/j.tox.2019.03.004)

<sup>8</sup> ATSDR toxicological profile for manganese <https://www.atsdr.cdc.gov/toxprofiles/tp151-c2.pdf>

<sup>9</sup> <https://www.cdc.gov/niosh/topics/manganese/>.

Thank you again for the opportunity to submit these comments.

Sincerely,

A handwritten signature in black ink that reads "Jay E. Sirois". The signature is written in a cursive style with a large initial "J" and "S".

Jay E. Sirois, Ph.D.

Senior Director, Regulatory & Scientific Affairs  
Consumer Healthcare Products Association

A handwritten signature in blue ink that reads "Megan Olsen". The signature is written in a cursive style with a large initial "M" and "O".

Megan Olsen

Vice President & Associate General Counsel  
Council for Responsible Nutrition