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March 26, 2014

VIA ELECTRONIC MAIL

Biomonitoring California
Office of Environmental Health Hazard Assessment
1515 Clay Street, 16th Floor
Oakland, CA 94612
biomonitoring@oehha.ca.gov

Re: Comments of the Manganese Interest Group: Proposed Listing of Manganese as a Priority Chemical

Dear Biomonitoring California:

On behalf of the Manganese Interest Group (MIG),[1] we are pleased to provide the following comments regarding the potential listing of manganese as a priority chemical under the California Environmental Contaminant Biomonitoring Program. Attached are comments submitted by MIG in November 2010 questioning the inclusion of manganese as a designated chemical under the program. Those comments remain equally, if not more, pertinent to consideration of the listing of manganese as a priority chemical for biomonitoring.

The following points are of particular significance:

- Manganese is a naturally occurring essential nutrient required to maintain human health. While an essential component of all bodily tissues, manganese accumulation is naturally regulated by the human body.

[1] MIG is an *ad hoc* coalition of industrial users of manganese. MIG members include steel producers, metalworkers, chemical manufacturers, and other similar stakeholders, some of which operate in California. Group members include: the American Iron and Steel Institute, the Steel Manufacturers Association, the Specialty Steel Industry of North America, the International Manganese Institute, the National Slag Association, Afton Chemical Corporation, Eramet Marietta, Inc., Felman Production, Inc., Nucor Steel, and U.S. Steel.

- Application of the human physiologically-based pharmacokinetic (PBPK) model for manganese[2] shows that chronic exposure does not materially alter tissue concentrations outside the normal fluctuations that occur due to changing dietary intakes.

- The PBPK model also suggests that blood and urine are not likely to be good biomarkers of manganese exposure at moderate to low levels of environmental exposure.

As noted in our previous comments, based on this information, MIG questions whether a biomonitoring program for manganese is likely to yield useful data. At minimum, the information poses significant issues concerning the design of, and utility of information generated from, a biomonitoring program for manganese.

The background document prepared in support of the Scientific Guidance Panel meeting on March 27, 2014, to consider the potential listing of priority chemicals for biomonitoring presents an incomplete and potentially misleading summary of the exposure and toxicity information available for manganese. In particular, the summary fails to mention the critical findings of the aforementioned human PBPK models. The information from these models is the most significant development in manganese exposure and toxicity assessment in at least the last two decades. The model provides insight into and broadens our understanding of how the human body regulates manganese uptake and accumulation, and should be considered as part of the SGP review process.

Further, the exposure data summary states that "CARB reported a statewide average ambient air concentration of 17.8 ng/m^3 in 2012." Such levels are well below even the most stringent estimates of safe levels of inhalation exposure for a lifetime. For example, the extremely conservative U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS) reference concentration (RfC) adopted in 1993 for manganese is 0.05 µg/m^3. More recently, in February 2013, the Agency for Toxic Substances and Disease Registry (ATSDR) issued a revised minimum risk level for manganese of 0.30 µg/m^3 for the respirable (PM_5) fraction. In evaluating the human PBPK models for setting an appropriate RfC for manganese based on the most up-to-date science, Toxicology Excellence for Risk Assessment (TERA)/International Toxicity Estimates for Risk (ITER) published a paper in 2011 proposing a manganese RfC in the range of 2-7 µg /m^3.

The SGP background document also states that "Elevated manganese blood levels have been measured in welders." While welders may be exposed to elevated manganese levels,

[2] A PowerPoint presentation describing the human PBPK model was presented to the U.S. Environmental Protection (EPA) Agency Integrated Risk Information System (IRIS) staff in June 2013. A copy of that presentation is attached. Further details on the human PBPK models are available in another EPA presentation from September 2010. A copy of that presentation also is attached (and is available at www.regulation.gov in docket EPA-HQ-OAR-2004-0074-0222).

this exposure scenario is not relevant to an assessment of manganese levels in the larger population. As the summary notes, "[m]ost manganese exposure occurs through diet."

Finally, the summary states that "CDPH reported there were detections above the health-based notification level of 0.5 mg/L for 384 drinking water sources across 46 counties (out of ~12,000 sources statewide) from 2006 to 2011." In adopting the notification level, the California Department of Public Health cites to "[s]imilar advisory levels for manganese … established by the US EPA , which has a manganese health advisory level of 0.3 mg/L (USEPA, 2004), and the World Health Organization (WHO), which has a manganese health guideline level of 0.4 mg/L (WHO, 2004)." EPA describes the advisory level as a recommended level of exposure that can be consumed over a lifetime without concern about potential neurological effects. In 2011, WHO discontinued its 400 µg/L drinking water guideline for manganese. The WHO decision was based on the conclusion that "this health-based value is well above concentrations of manganese normally found in drinking water, it is not considered necessary to derive a formal guideline value." (WHO, *Guidelines for Drinking-Water Quality*, July 2011). In sum, exceedance of the California notification level is not associated with adverse health effects. Such adverse effects only have been observed at significantly higher levels of manganese likely associated with occupational exposure.

MIG appreciates the opportunity to submit these comments and would be happy to provide additional information or address any questions OEHHA or the SGP may have. In particular, we would be pleased to arrange a meeting with experts in manganese toxicology to discuss further the issues related to biomonitoring of manganese. If MIG can be of any further assistance, please do not hesitate to contact me at (202) 342-8849 or JGreen@KelleyDrye.com.

Respectfully submitted,

Joseph J. Green
Counsel to the Manganese Interest Group

Attachments