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January 21, 2013

Michael Baes
Pesticide and Environmental Toxicology Branch
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency
1515 Clay St., 16th floor
Oakland, CA 94612

Dear Mr. Baes:

The Chlorine Institute appreciates the opportunity to provide comments on the revised draft technical support document for a 1-µg/L PHG for perchlorate which was prepared by the Office of Environmental Health Hazard Assessment (OEHHA) within the California Environmental Protection Agency (CalEPA). The Chlorine Institute (CI) founded in 1924, is a 200 member, not-for-profit trade association of chlor-alkali producers worldwide, as well as packagers, distributors, users, and suppliers. The Institute's mission is the promotion of safety and the protection of human health and the environment in the manufacture, distribution and use of chlorine, sodium hydroxide, potassium hydroxide and sodium hypochlorite, plus the distribution and use of hydrogen chloride. The Institute's North American Producer members account for more than 93 percent of the total chlorine production capacity of the U.S., Canada, and Mexico.

Trace levels of perchlorates can be formed as a product of decomposition of sodium hypochlorite solution. Data indicate that perchlorate levels in sodium hypochlorite can increase over time as the sodium hypochlorite solution is stored. The amount of perchlorates formed is dependent on a number of factors including, but not limited to, the concentration of the sodium hypochlorite, the temperature of the sodium hypochlorite and the impurities in the sodium hypochlorite. As previously indicated, sodium hypochlorite is a mission chemical of the Chlorine Institute. For a variety of reasons, sodium hypochlorite is being increasingly used as a disinfectant for drinking water. Accordingly, the Institute has a strong interest in this matter.

The National Academies of Science (NAS) report on perchlorate health effects (NAS 2005) used iodide uptake inhibition as the critical effect for daily allowable perchlorate intake. Existing drinking water advisories and standards for perchlorate are all based on the assumption that a perchlorate higher than the NOEL observed over a 2-week exposure (Greer et al. (2002)) could result in chronic reduction in thyroid hormone production. As risk assessments are typically developed using a NOAEL the perchlorate RfD is overly conservative.

The effect of perchlorate on the thyroid is to inhibit the uptake if iodide from the blood into the thyroid follicle cells, where iodine is used to produce the hormone thyroxine (T4), which is then converted enzymatically to triiodothyronine (T3). OEHHA's perchlorate drinking water value is based on the data from Greer et al. (2002), in which 37 adults were given 0.007, 0.02, 0.1, or 0.5 mg/kg/day perchlorate (groups of 7-10 subjects) in drinking water for 14 days. After 2 and 14 days of exposure, the uptake of radioactive iodide (RAIU, a representative fraction of iodide in the whole body) into the thyroid was measured. In addition, blood levels of perchlorate and thyroid hormones T3, T4, and thyroid stimulating hormone (TSH) were measured before, during, and after cessation of exposure.
While significant inhibition of RAIU was observed at ≥0.02 mg/kg/day, there were not associated with changes in thyroid hormone levels. A lack of change in thyroid hormones is not surprising, as healthy adult thyroids contain sufficient stores of T3 and T4 to maintain normal hormone levels in the body for up to six months.

Studies published since the NRC (2005) assessment indicate that the human thyroid system compensates for inhibited iodide uptake from chronic environmental and occupational perchlorate exposure, maintaining adequate thyroid function in clinical volunteers (Braverman et al., 2006), perchlorate workers (Lamm et al., 1999; Braverman et al., 2005), and in iodine deficient women and pregnant women and their infants (Crump et al., 2000; Tellez et al., 2005; Buffler et al., 2006; Van Landingham and Gibbs, 2008; Pearce et al., 2008, 2010, 2011). Compensation for inhibition of iodide uptake is accomplished by stimulation of the thyroid to increase the capacity of iodide transport into the thyroid follicle cells. This is one of the functions of adaptive, resilient biological feedback mechanisms that are inherent in all humans to maintain homeostasis and normal thyroid health. Thus, a 2-week exposure (Greer et al., 2002) is not characteristic or predictive of long term functioning at such low levels of perchlorate exposure.

Derivation of a scientifically-valid, acceptable perchlorate drinking water level should be based on a dose estimate that is close to, but below, the actual threshold for onset of the most sensitive adverse effect (subclinical hypothyroidism). For perchlorate, this calls for chronic exposure data in humans that identifies an exposure level in which the thyroid has achieved non-adverse compensation for iodide uptake inhibition, while maintaining adequate thyroid hormone production. Short-term inhibition of iodide uptake is an inappropriate endpoint for deriving a safe drinking water level for perchlorate because (1) it is not an adverse effect, (2) it does not result in changes in thyroid hormone levels or function, and (3) the thyroid system compensates for the inhibition to maintain adequate thyroid hormone levels. A perchlorate drinking water level, based on a short-term NOEL, is no more health protective than higher levels that are based on a long-term No Observed Adverse Effect Level (NOAEL). The available human data for perchlorate indicate higher exposure levels than the Greer et al. (2002) NOEL that result in initial inhibition of iodide uptake, but produced no adverse effect on thyroid hormone levels or thyroid tissue health (i.e., a NOAEL).

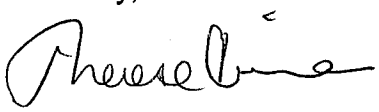
Since publication of the NAS (2005) report and the EPA RfD for perchlorate, clinical, occupational, and epidemiological studies have been published which indicate evidence of non-adverse thyroidal compensation for perchlorate-induced inhibition of iodide uptake. In

these studies, chronic exposure to perchlorate at doses higher than the (Greer (et al 2002)) NOEL resulted in no reduction in iodide uptake (measured by RAIU) or change in thyroid hormone homeostasis. While very short-term exposure to perchlorate may produce a transient change in thyroid hormone levels in response to inhibited iodide uptake, the resilient, adaptive mechanisms that maintain homeostasis (a dynamic and controlled balance) in humans restore the balance of iodide uptake and thyroid hormone levels in the thyroid and circulating blood. In people, even with long term exposure to perchlorate, the thyroid system is able to control these fluctuations and conserve thyroid hormone levels in the blood to maintain normal function. Thus, inhibition of thyroid iodide uptake is not an adverse effect unless extreme conditions occur, such as chronic inhibition from extremely high (i.e., therapeutic levels) exposures.

The low PHG being proposed by OEHHA takes none of the information provided above into consideration but instead uses uncertainty factors and overly conservative assumptions to in its technical support document.

If you have any question on the above information, or if the Chlorine Institute can be of any assistance, please contact me at (703) 894-4120.

Sincerely,



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