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Submitted Via Email

Mr. Michael Baes
Pesticide and Environmental Toxicology Branch
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency
1515 Clay Street, 16th Floor
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Attention: PHG Project
michael.baes@oehha.ca.gov

Re: Comments by the California Manufacturers and Technology Association on the Draft Public Health Goal Risk Assessment for Perchlorate as Proposed on December 7, 2012

Dear Mr. Baes:

The California Manufacturers and Technology Association (CMTA) has reviewed the revised draft public health goal risk assessment for perchlorate as proposed on December 7, 2012, and has several comments for your consideration. Our comments address three basic topics. First, we contend that the draft risk assessment runs counter to the weight of scientific evidence in concluding that exposure to perchlorate at levels typically found in the environment can have adverse health effects. Second, although it uses the no observed effect level (NOEL) determined by Greer et al. (2002), the point of departure derived from the NOEL is not justified. Finally, the proposed PHG would contribute significantly to water supply shortages and water rate increases that will undermine the future prosperity of the state. The available science does not justify these impacts.

1. The Draft Risk Assessment Runs Counter to the Weight of Scientific Evidence

The strong weight of scientific evidence demonstrates that exposure to environmental levels of perchlorate will have no adverse effects on exposed individuals, including all sensitive subpopulations. The draft risk assessment reaches a contrary conclusion by excluding certain scientific studies from its analysis, ignoring other studies, and re-analyzing several studies that found no effects from exposure to environmental levels of perchlorate to reach conclusions that differ from those reached by the authors of those studies. The draft risk assessment ultimately relies on a small number of studies, and principally upon those authored or re-analyzed by Dr.

Craig Steinmaus. Because the author of the draft risk assessment is the same as the author of those studies (i.e., Steinmaus), serious conflict of interest issues are presented.

A. The Weight of Scientific Evidence

In the single longest subsection of the draft risk assessment, OEHHA reviews the developmental and reproductive toxicity of perchlorate. Draft, pp. 38-64. This 27-page section reviews a total of 14 scientific studies on this topic: DHS (1997); Kelsh et al. (2003); Crump et al. (2000); Lamm & Doemland (1999); Li et al. (2000a); Li et al. (2000b); Brechner et al. (2000); Buffler et al. (2006); Steinmaus et al. (2010); Li et al. (2001); Chang et al. (2003); Tellez (2005); Amitai et al. (2007); and Cao et al. (2010). The strong weight of scientific evidence (11 of the 14 studies reviewed) indicates that exposure to environmental concentrations of perchlorate has no meaningful correlation with thyroid hormone levels. Only three of the 14 studies reported a positive association: Brechner et al. (2000); Steinmaus et al. (2010); and Cao et al. (2010). And these three studies all have methodological issues that may invalidate their results.

Notwithstanding this, the draft risk assessment reaches a conclusion opposite the strong weight of evidence—i.e., that exposure to environmental concentrations of perchlorate has a positive association with changes in thyroid hormone levels. This outcome is reached in several ways. First, data contained in several studies is re-analyzed or reinterpreted and the study is then re-categorized as a positive study rather than a negative study (e.g., Kelsh et al. (2003); Crump et al. (2000); Buffler et al. (2006); Li et al. (2000a)). Second, several negative studies are excluded for various disparate reasons (e.g., Tellez (2005); Li et al. (2000b); Amitai et al. (2007)). Cao et al. (2010) is also excluded. Finally, several studies are neither re-analyzed nor excluded, but are simply ignored in the analysis (e.g., DHS (1997); Lamm & Doemland (1999)). The remaining two studies (Steinmaus et al. (2010); and Brechner et al. (2000)), along with the re-analyzed studies, then form the basis for the conclusion of the draft risk assessment that exposure to environmental levels of perchlorate has a meaningful association with changes in thyroid hormone levels.

However, both Brechner et al. (2000) and Steinmaus et al. (2010) have been criticized by expert panels. The National Academy of Sciences (NAS) criticized Brechner et al. (2000) in its 2005 assessment of perchlorate, explaining that the apparently positive associations reported were explainable by other factors not evaluated or controlled. EPA's Science Advisory Board perchlorate panel criticized the four ecological studies conducted after the NAS perchlorate assessment, including Steinmaus et al. (2010), stating that such studies were "of little value" for establishing health level goals for perchlorate in drinking water. CMTA requests that OEHHA completely revise the health affect analysis in the draft risk assessment to be consistent with the weight of scientific evidence.

B. Serious Conflict of Interest Issues Are Presented

In reaching its key conclusions, the draft risk assessment relies principally on three studies: Steinmaus et al. (2007), Blount et al. (2006) and Steinmaus et al. (2010). The last of these is the study upon which the draft risk assessment relies for its conclusion that environmental levels of perchlorate cause changes in thyroid hormone levels—a conclusion that deviates from the weight of scientific evidence. The draft risk assessment also states that:

“Blount et al. (2006) and Steinmaus et al. (2007) are key studies supporting two of the potential susceptibility groups identified by OEHHA.” Draft, p. 75. These two papers receive extended discussion in the draft risk assessment, as does Steinmaus et al. (2010), although some of the discussion of this latter paper appears under the heading “Buffler et al., 2006.” Draft, pp. 46-48. (Steinmaus et al. (2010) is a re-analysis using the same datasets as those analyzed by Buffler et al. (2006)).

Serious conflict of interest issues are presented by the draft risk assessment, due to the fact that the author of the draft risk assessment, Dr. Craig Steinmaus, is also the author of two of the key studies upon which the draft risk assessment relies. The regulated community has the right to expect an impartial review of the scientific literature in the development of risk assessment documents. This impartiality cannot be assured when the author of the risk assessment must review, analyze and consider his own studies along with the studies of other researchers and make determinations as to which of the studies are of sufficient scientific merit to be included in the risk assessment and which of the studies should be excluded from consideration due to weaknesses in the studies’ designs. CMTA requests that a new draft risk assessment be developed by individuals with no conflicts of interest.

2. The Point of Departure Derived by the Draft Risk Assessment Cannot Be Justified

Although it uses the NOEL developed by Greer et al. (2002), the point of departure derived by the draft risk assessment cannot be justified. The draft risk assessment identifies Greer et al. (2002) as the critical study. However, the draft risk assessment fails to recognize that Greer et al. (2002) was one of five key clinical studies that the NAS found to be remarkably consistent. Because it fails to recognize the other four studies, OEHHA applies a benchmark dose analysis in the draft risk assessment to address perceived shortcomings that do not exist due to the fact that there are multiple relevant studies. Finally, the draft risk assessment treats the NOEL derived by Greer et al. (2002) at the very onset of iodide uptake inhibition (IUI) as an adverse effect. This is contrary to the fundamental science, which is well explicated by the NAS, that IUI is a non-adverse effect

A. Greer et al. (2002) is One of Five Key Clinical Studies

The draft risk assessment states that OEHHA has chosen the Greer et al. (2002) study as the critical study for purposes of deriving a public health goal. Draft, p. 111. The draft risk assessment states that the Greer study was selected because it was a clinical study in humans where subjects were given known doses of perchlorate and evidence of the very onset of a dose-response was observed. *Id.* The draft risk assessment goes on to say that several other studies might have been considered as “critical studies,” but these were either based on ecologic measurements or on only a single or few urinary perchlorate measurements. *Id.*

The draft risk assessment seriously misrepresents the scientific literature. As the National Academy of Sciences (NAS) pointed out, the scientific literature contains reports of no fewer than *five* clinical studies where subjects were given known doses of perchlorate and evidence of a dose-response was adduced: Brabant et al. (1992); Lawrence et al. (2000); Lawrence et al. (2001); Greer et al. (2002); and Braverman et al. (2004). The NAS stated that the results of these five studies were “remarkably consistent.” In each study, the subjects were

healthy adults, eating a self-selected diet (necessarily including exposures to perchlorate and other goitrogens in food). The effects of similar doses of perchlorate on iodide uptake were very comparable across all five studies. Daily doses of 0.030 and 0.040 mg/kg-day produced no effect in two of the studies; a dose of 0.020 mg/kg-day produced a small effect in one study; and a dose of 0.007 produced no effect in two of the studies. The dose of 0.007 mg/kg-day from Greer et al. (2002), was the lowest NOEL reported in the five clinical studies, resulting in the most conservative and most health-protective point-of-departure. CMTA requests that the draft risk assessment be revised to incorporate the full suite of consistent clinical studies.

B. Use of a Benchmark Dose Analysis is Not Justified

The draft risk assessment used a benchmark dose (BMD) method to derive a point-of-departure from the Greer et al. (2002) study. The draft risk assessment states that it selected Greer et al. as the critical study and then applied a BMD method because using a no adverse effect level (NOAEL), or, in this case, a NOEL, from a single study to derive a reference dose has several limitations, including: (1) this selection is limited to the doses chosen in the single study relied upon; and (2) it does not account for variability in the dose-response estimate. In this case, the effect of OEHHA's application of the BMD method is that the point-of-departure is lowered by approximately a factor of two. Draft, p. 111.

The draft risk assessment ignores the fact that there was not one critical experimental human study, but five such studies. The fact that five human studies have been conducted and that the studies produced remarkably consistent results, serves to account for variability in the dose-response estimate. The NAS analyzed the results of these five studies in multiple ways and concluded that the experimental results were clear—in healthy subjects, a dose of 0.007 mg/kg-day has no effect on iodide uptake, and doses in the 0.020 to 0.040 mg/kg-day range have minimal or no effect. Further, the draft risk assessment applies the BMD method to a NOEL, which is a departure from the accepted practice of applying this method only to lowest observed adverse effect levels (LOAELs) or no observed adverse effect levels (NOAELs). Selecting the most conservative of the five studies, ignoring the other four, and then applying a BMD method to the most conservative of the five studies to select a point-of-departure resulted in an unjustifiably conservative point-of-departure. CMTA requests that the draft risk assessment be revised to eliminate the benchmark dose overlay and to instead use the point of departure derived directly from Greer et al. (2002), as recommended by the NAS.

C. The Draft Risk Assessment Treats IUI, a Non-Adverse Event, as Adverse

The lowest dose level from Greer et al. (2002), 0.007 mg/kg-day, was used by the NAS as its point-of-departure for developing a reference dose for perchlorate. The NAS explicated a mode of action for perchlorate in which IUI is the first step in a potential progression of health effects. However, the NAS was very clear that IUI is itself not an adverse effect, but rather a non-adverse precursor event. IUI is a common event, and variability in IUI can range from 7% to 26% in a 24-hour period. NAS stated that it would take a dose of perchlorate sufficient to inhibit iodide uptake by 75% over an extended period of time (measured in months) to lead to an adverse effect. At levels below those that can cause any IUI, there can be no progression to adverse effects. The NAS acknowledged that it was departing from the traditional risk assessment approach by basing the calculation of an acceptable risk level on a non-adverse

event. According to the NAS, use of a non-adverse effect that is upstream of adverse effects is a conservative, health protective approach to perchlorate risk assessment.

The draft risk assessment treats IUI as an adverse effect. The draft risk assessment states that it treats decreased uptake of iodide as the critical event and that adverse health effects of perchlorate are associated with thyroid hormone imbalance. Draft, pp. 1, 37. The draft risk assessment does not explain how perchlorate at levels below that known to produce IUI can be associated with impaired thyroid function or can alter thyroid hormone levels. The draft risk assessment does not present an alternative mode of action assessment or link purported hormone thyroid effects with IUI. OEHHA's inference that low levels of perchlorate are associated with thyroid hormone level changes, and potentially to adverse developmental and other adverse effects, runs contrary to the conclusions reached by the NAS and other authoritative bodies (US EPA's Office of Inspector General-2010; Agency for Toxic Substances Disease Registry-2008), based on the findings of Greer et al. (2002). CMTA requests that the draft risk assessment be revised so that IUI is properly recognized as a non-adverse effect. CMTA further requests that revisions be made throughout the draft risk assessment consistent with the recognition of IUI as non-adverse.

3. Anticipated Economic Impacts Are Not Justified

OEHHA continues to dismiss the practical realities of establishing a lower perchlorate PHG for millions of water users in California who already face the prospect of rapidly increasing water rates. CMTA recognizes that the Department of Public Health (DPH) is responsible for evaluating the feasibility and affordability of treating affected water sources to a lower level. However, it is OEHHA's interpretation of the available science that largely frames the public debate about where the state should set the drinking water standard. OEHHA's proposal to lower the PHG from 6 ppb to 1 ppb is a vote of no confidence in the safety of the current drinking water standard. Many California communities depend on ground water with residual perchlorate concentrations below the current 6 ppb drinking water standard, but absent further treatment, would exceed a 1 ppb standard. Some systems do not actively treat to remove perchlorate, but instead blend impacted groundwater with perchlorate-free surface water. At 1 ppb, this practice would require much larger volumes of surface water and would likely be infeasible. The only other option available to affected utilities is to install anion exchange or biological treatment systems which are extremely expensive to build and operate. Treatment cost per capita will be especially high in suburban and rural areas where water systems serve smaller populations and perchlorate contamination originates from sources other than legacy industrial operations.

Recent legislative mandates such as SBX7 7 (Steinberg, 2009) also promise disproportionate increases in water rates and conservation requirements for commercial, institutional and industrial water users. In the current water policy environment, new standards that effectively strand otherwise viable water supplies, or require new treatment systems at the expense of water ratepayers, become another significant impediment to the sustainability of manufacturing operations located in affected communities. Taking this action without any scientific evidence that it will further public health protection is simply irresponsible.

CMTA appreciates OEHHA's consideration of our comments on its revised draft perchlorate public health goal, and we look forward to another iteration of the PHG document that addresses the scientific shortcomings detailed above.

Sincerely,



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