

September 18, 2012

Stephen M. Roberts, Ph.D.  
Chair, Science Advisory Board Perchlorate Advisory Panel  
c/o Mr. Tom Carpenter, US EPA Designated Federal Officer  
US Environmental Protection Agency  
Washington, D.C.  
*Submitted via email*

RE: US EPA Science Advisory Board (SAB) Draft Advisory Report

Dear Dr. Roberts:

The Perchlorate Study Group (PSG) appreciates the opportunity to respond to the recent draft document *Science Advisory Board (SAB) Draft Advisory Report* dated September 5, 2012 (SAB Draft Report). Our comments are organized below into areas of agreement and remaining concerns. In sum, we applaud the SAB's efforts and encourage further review and analysis of the important issues raised by the SAB panel.

### **Areas of Agreement**

- **PBPK Modeling**: PSG agrees with the SAB Draft Report that the use of the Physiologically-based Pharmacokinetic/ Pharmacodynamic (PBPK/PD) modeling is a superior, scientific approach to deriving the MCLG, and is preferable to using an algebraic approach. The SAB Draft Report reflects a sound understanding of the fundamental toxicological and pharmacological science of perchlorate. Although it is not clear how the SAB recommends that EPA use the PBPK/PD modeling, PBPK/PD generally provides a robust scientific tool that can address questions related to changes in physiological function in response to exposure, such as changes in iodine uptake inhibition (IUI) or thyroid hormones.

We also agree with the SAB that the PBPK/PD model should be extended to describe changes in thyroid hormone levels and downstream effects, since the current model generates data only on IUI, an effect that is mechanistically upstream from any adverse effects. Recognizing the short timeline EPA has committed to, it may be challenging to develop a fully-expanded model. Based on the fundamental science, we understand changes in thyroid hormones are expected only when IUI exceeds approximately 75% for several months or longer. We also understand that the PBPK/PD model predicts a very low level of IUI change (less than 3.4%<sup>1</sup>) from exposures to environmental levels of perchlorate.

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<sup>1</sup> Corresponding to a 7-day old, bottle fed infant drinking water containing perchlorate at 24.5 ppb and the contribution of 0.1 µg/kg-d from food (Table A-4, US EPA White Paper).

- The Need for Peer Review: We concur with the SAB's concerns that any modifications EPA incorporates into the peer-reviewed, published PBPK model should also be subject to independent peer review with opportunity for comment by scientific experts. The SAB recommended that the scientific basis for all data inputs and methodologies used to derive the MCLG be described clearly and transparently. Further the PSG agrees with the SAB that its novel approach in using the PBPK/PD model to derive the MCLG should be "carefully implemented with attention to data quality and methodological rigor to include "a critical evaluation of the available data and describing the strengths and limitations" and that a "robust explanation of the approach and modeling used for the derivation of the MCLG is necessary." As we have previously commented, the current PBPK/PD model incorporates policy decisions that are not scientifically defensible (*e.g.*, model inputs not chosen from consistent points in their distributions) and is neither transparent, nor easily translatable to the lay person. As such, the PSG agrees that a peer-reviewed technical document that provides transparency and documents any additions to the PBPK/PD model is necessary.
- Adverse Effect: The PSG agrees with the SAB panel that EPA has failed to adequately define the adverse effect. The SAB panel stated that to move toward the goal of quantitative dose-response and reduction in adverse health effects assessment for perchlorate, EPA must first define the adverse effect. The PSG notes that EPA determined that regulation of perchlorate would present a meaningful opportunity for risk reduction, and found that "the contaminant may have an adverse effect on the health of persons" before it defined the adverse effect.
- Impact of Other Goitrogens. The PSG agrees with the SAB panel that co-exposures to other goitrogens, such as thiocyanate and nitrate, should be considered in future studies and analyses. As the SAB panel indicated, the NHANES dataset (and perhaps other datasets) provide an opportunity to evaluate the extent to which the U.S. population is co-exposed to other goitrogens. We note that all goitrogens competitively inhibit the uptake of iodide and that, at environmental levels, perchlorate generally accounts for less than 2 percent of the total goitrogenic load on a daily basis.
- Breadth of Scientific Literature. The SAB stated that while its charge focused on literature published since the release of the NRC's 2005 report, EPA clearly should consider and incorporate the entire body of scientific literature related to the ingestion of perchlorate into its analyses of perchlorate. The PSG agrees with this statement. The PSG wishes to reemphasize the breadth and depth of the toxicological literature on perchlorate and the prior work of authoritative bodies in summarizing the toxicological data on perchlorate.
- Cost/Benefit Analysis: The PSG agrees with the SAB panel's recommendation regarding assessing costs and benefits of the draft MCL/MCLG. While the SDWA (as amended) already requires EPA to conduct a Health Risk Reduction Cost Analysis (HRRCA), the SAB panel's recommendation underscores the major import of this exercise in determining the utility of such a regulation.

### Remaining Concerns

We continue to have concerns regarding some other aspects of the SAB Draft Report.

- Dose Response Assessment Not Considered: We note the lack of a dose-response assessment in the SAB Draft Report. Dose-response assessment would provide a substantial foundation from which the SAB could address some of its questions and concerns.

- Lack of Scientific Citations to Support Conclusions: Finally, there are many instances within the report where statements are presented without a citation (*e.g.*, no scientific citation that hypothyroidism is more relevant than hypothyroxinemia). To this end, PSG is prepared to provide the SAB more information to address these issues if the SAB is given the time and scope.

Unfortunately, the SAB was directed to assume that EPA is correct in its determination to regulate perchlorate. The SAB was not asked, nor did it consider, requirements of the SDWA or the public health implications of regulation. Given the restraints on available public resources, it would seem reasonable for this question to be raised, rather than unnecessarily spend time and resources taking regulatory actions that will have no public health benefit on a chemical that the overwhelming balance of scientific research shows does not present a health concern at environmental levels.

We appreciate your consideration of these and our previous comments. We have attached our previous comments for reference and would welcome the opportunity to discuss these issues further.

Sincerely,

Jonathan Bode  
Chair  
Perchlorate Study Group

cc:

Hon. Lisa Jackson, Administrator, U.S. EPA  
Hon. Bob Perciasepe, Deputy Administrator, U.S. EPA  
Thomas Carpenter Designated Federal Officer Science Advisory Board (MC-1400R)  
Dr. Vanessa T. Vu, Director, U.S. EPA Science Advisory Board Staff Office  
Nancy Stoner, U.S. EPA Acting Administrator for Water