

April 3, 2013

David Allen, Ph.D.
Chair
US EPA Science Advisory Board
200 E Dean Keeton St. Stop C0400
Austin, TX 78712-1589

RE: Comments on Charter SAB Teleconference on March 29, 2013

Dear Dr. Allen:

Thank you for the opportunity to submit comments to the Science Advisory Board (SAB) report *SAB Advice (02/25/13 Draft) on Approaches to Derive a Maximum Contaminant Level Goal for Perchlorate* as well as the opportunity to make public comments on March 29, 2013. I have reflected upon the discussion on the teleconference and wanted to be clear about my comments as well as the edits to the SAB report that were requested by various members of the Charter SAB. We believe that these key additions will increase the scientific reliability of the SAB report and meet the scientific standard we know the Agency seeks.

My comments included the following:

- 1) Inclusion of the infant as the most sensitive population. We noted the excellent scientific work of the SAB committee in supporting the pregnant woman and her fetus as the most sensitive population. This is in stark contrast to the scant support for EPA's attempt to view the infant as the most sensitive population. We are concerned that despite repeated requests, there has been no attempt to rectify this major scientific deficiency. We request that the SAB provide a similarly rigorous assessment of whether the infant is as sensitive as the fetus in their report or that the SAB report require EPA to provide the same level of scientific support for the infant as THE most sensitive, assuming they believe that is true.
- 2) Absence of dose-response assessment in the report. We noted that many members of the Charter SAB requested that quantitative dose-response information be provided in the report so that the Agency can best understand what exposure levels are needed to cause thyroidal hormone effects. The absence of a dose-response assessment in the SAB report is a serious scientific deficiency. To have a sufficient level of scientific credibility the SAB report either should provide a dose-response assessment or explicitly require that EPA provide a dose-response assessment in their White Paper and future documents regarding perchlorate.
- 3) How to quantitate reduction in adverse health effects. As several reviewers noted, the SAB report does not actually address this charge question on how to quantitate

April 3, 2013

reduction in adverse effects. The SAB report stated that “the epidemiological studies provided to the panel are inadequate for quantitatively estimating reduction in adverse health effects that would result from regulating perchlorate in drinking water.” First, given the restricted time range of epidemiological studies (from 2005 to present) and the limited review of the large body of literature, the SAB report cannot address this question. It appears from the language in the SAB report that the authors are uncomfortable making this assessment, which is not surprising given the limitations they faced.

If the SAB panel had been required to review the 60 years of data on perchlorate, including clinical, occupational, animal, *in vitro*, and earlier epidemiological studies, they could have answered this question. Relatedly, had the SAB actually conducted a dose-response assessment, sufficient and scientifically reliable data would have allowed the SAB report to address this question. The perchlorate SAB Chair, Dr. Roberts, has suggested that the PBPK/PD model may be used to evaluate this. We think is a scientifically defensible approach, but the SAB report does not recommend this or address how EPA should do it. Since the Agency requested this information, the SAB report should explicitly provide that information to EPA.

Finally, it might be of interest to know that the article [“Evaluation of Perturbations in Serum Thyroid Hormones during Human Pregnancy due to Dietary Iodide and Perchlorate Exposure using a Biologically Based Dose Response Model”](#) was published electronically last week in *Toxicological Sciences* (Lumen et al., 2013). This is a timely paper that would help the SAB address the EPA charge questions (along with the points made above) in their report. This paper presents a PBPK/PD model that incorporates iodine intake and predicts changes in thyroid hormone levels. This is pertinent to the work of the SAB. Note that this paper states, At environmentally relevant ranges of perchlorate exposure including contributions from food and drinking water, the model predicted changes in the euthyroid maternal fT4 values are minimal and significantly less than the estimated 27% decrease in the maternal fT4 necessary to potentially cause hypothyroxinemic conditions (Table 9).

Thank you for the opportunity to provide these comments. We are happy to answer any questions or respond to any comments.

Sincerely,

INTERTOX, INC.

Richard C. Pleus, Ph.D.
Director / Toxicologist