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c/o Dr. Angela Nugent, Designated Federal Official
EPA Science Advisory Board (1400 F)
1200 Pennsylvania Ave., N.W.
Washington, DC 10460

RE: SAB Arsenic Work Group Report

Dear Members of the Science Advisory Board:

For ten years I served on the EPA EPEC Science Advisory Board (SAB). I wish to take this opportunity to draw the attention of the SAB to key concerns with the 2010 SAB Inorganic Arsenic and Cancer Work Group report. I have reviewed many of these types of documents, and I am concerned that the Agency is not following its stated commitment to adhere to the best available science.

The draft report by the 2010 SAB Inorganic Arsenic and Cancer Review Work Group does not adequately address their limited charge questions, the issues raised by an earlier SAB in 2007, nor does it constitute a comprehensive independent review of the scientific basis of EPA's 2010 Draft Toxicological Review of Inorganic Arsenic. In the Agency's most recent document, many of the scientific deficiencies in EPA's approach for assessing the health risks of Inorganic Arsenic remain unaddressed.

EPA's general approach relies on selected conclusions of previous review committees (e.g., National Research Council (NRC) 1999, 2001, Arsenic in Drinking Water; Science Advisory Board, SAB, 2007 review) that support a very limited view of arsenic risk assessment (i.e., linear no-threshold from high doses in the SW Taiwan data set from the mid to late 1980's). EPA has resisted changes to this approach, despite increasing scientific knowledge on arsenic, potential for a threshold effect and additional human data. There are several continuing unaddressed methodological issues. For example, the comparison population that EPA uses to anchor the low end of their linear extrapolation has never been evaluated to ensure that it truly is representative of the people in the impoverished rural arsenic-exposed area in all ways but arsenic exposure (e.g., nutritional, health status, socioeconomics) to the comparison population (greater SW Taiwan including highly urbanized areas). In addition, although EPA states that neither the comparison population nor use of a linear or non-linear model affect the estimated risk substantially, they do not present a full sensitivity analysis (as recommended by SAB 2007) including non-linear model runs without the comparison population. I contend that indeed it does make a significant difference.

Moreover, EPA's Draft Toxicological Review of Inorganic Arsenic lacks a review of publications since 2007 on arsenic mode of action and low-level epidemiological studies. The recent literature reaffirms the earlier work on mode of action and addresses many of the uncertainties that were an issue for previous reviews such as NRC (2001) and SAB (2007). EPA insists that all low-level epidemiological studies (including this range of the SW Taiwan data) are unreliable because of exposure misclassification and lack of power, but has not adequately addressed scientific comments and publications to the contrary. The wealth of literature now available shows strong consistency among *in vitro* assays on mode of action, animal studies, and human epidemiological results. This weight of evidence (including studies by EPA scientists) has become even more robust in showing a non-linear mode of action for arsenic that is well within relevant human exposures corresponding to observed thresholds for cancer risk in human populations.

Even if EPA feels that the state of the evidence is still insufficient to warrant dispensing with default linear extrapolation models entirely, they should at least objectively present the full current scientific evidence and also perform calculations using non-linear approaches such as margin of exposure, in accordance with the weight of evidence, their 2005 Cancer Risk Guidance, and the recommendations of the SAB (2007).

Public comments to the Agency from leading scientists in the arsenic field describe the current state of the science, but unfortunately these comments were not provided to the 2010 SAB prior to their meeting (although they were submitted ahead of the deadline for receiving comments), which was very disappointing. Given the complexity of issues associated with arsenic and amount of material to review, one cannot expect a committee composed of individuals with little day to day involvement with arsenic to be able to provide a comprehensive review of even the very limited charge provided by EPA and to assess whether EPA followed the recommendations of SAB (2007) on certain issues, within the timeframe for the 2010 SAB's draft report. The 2010 SAB thus appears to have based their evaluation on EPA's statements that they followed the 2007 recommendations rather than comments to the contrary by members of the SAB (2007), the information provided in other public comments, or the 2010 SAB's independent review.

I would like to point out that there are two pivotal studies on the issues of threshold and mode of action for inorganic arsenic that are nearing completion, EPA Research Triangle Park and University of Nebraska, Dr. Sam Cohen. Both institutions have provided preliminary results showing that it appears that a threshold for inorganic arsenic will be identified. Dr Cohen testified at the SAB meeting earlier this year. I think it would be prudent to wait for the outcome of these studies. There is no rush to update the IRIS data set. The consequences of a wrong decision are enormous for both the public, the Agency and industry. An independent review of the science is called for by the 2007 SAB review, the comments to this SAB review from the five members of the prior 2007 SAB, and the EPA's own 2005 Cancer Risk Guidance.

In conclusion, I believe that the SAB Work Group report is premature, incomplete and does not constitute a thorough review of the state of the science for inorganic arsenic. This is not a report that will serve the Agency or the SAB well. I recommend that the SAB Work Group report should not be construed as a full and independent review of the science supporting EPA conclusions and I recommend that this report not be accepted as final.

I appreciate your review of my comments.

Yours sincerely

Bill Adams, Ph.D.
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Health, Safety and Environment