

March 25, 2010

## COMMENTS

**Docket ID No. EPA-HQ-ORD-2010-0123**

U.S. Environmental Protection Agency  
Office of Environmental Information (OEI) Docket  
Mail Code: 2822T  
1200 Pennsylvania Ave., NW,  
Washington, DC 20460

Subject: Draft Toxicological Review of Inorganic Arsenic: In Support of the Summary  
Information on the Integrated Risk Information System (IRIS)  
Docket ID No., EPA-HQ-ORD-2010-0123

*Submitted electronically*

As members of the SAB Arsenic Review Panel (2007) that reviewed the 2005 draft "Toxicological Review of Inorganic Arsenic in Support of Summary Information on the Integrated Risk Information System (IRIS)" document, we submit the following comments on the February 2010 draft document that will be reviewed on April 6-7, 2010 by a Work Group of the Chartered SAB.

First, we note that the Introduction section of the February 2010 draft in the section titled "External Peer Reviewers" (p. xii), our names are listed under the title "Science Advisory Board Review Panel" members as having reviewed this present February 2010 draft, when in fact, we reviewed the 2005 draft version of the document. We firmly request that you remove reference to our having reviewed the February 2010 draft since we have not been formally requested to do so or amend this section of the current report to make clear that we reviewed the 2005 draft in our deliberations culminating in the report of 2007, but that we have not reviewed this February 2010 draft. We ask that you please correct this misconception as a procedural matter.

Second, as cited in the February 2010 draft, while the SAB Arsenic Review Panel (2007) advised that the Taiwanese dataset (Wu 1989; Chen et al., 1988, 1992) "remains, *at this time*, (italics added) the most appropriate choice for estimating bladder cancer risk among humans, [due to exposure to inorganic arsenic] though the data have considerable limitations that should be described qualitatively or quantitatively to help inform risk managers about the strength of the conclusions." (SAB, 2007, p. 7). SAB (2007) also recommended that EPA evaluate other recent published epidemiology studies using a uniform set of criteria and document these findings in a weight-of-evidence assessment with the implication that recent studies with more robust study designs (i.e., prospective studies vs. currently utilized ecological studies) be sought for utilization in the assessment. Recent studies document lower exposures in populations more similar to the U.S. population in genetic background, diet and lifestyle. In the five years that have ensued since our review of the 2005 draft document, epidemiology studies (with a more robust prospective study design and individual exposure assessment) have examined cancer

outcomes at reasonably well documented arsenic drinking water levels  $\leq 100 \mu\text{g/L}$ . While the February 2010 USEPA draft document did review a large number, but not all, of these studies and presented tabled results (Appendix B) as suggested by SAB (2007), the draft did not present a review of each study conducted by systematic consistent application of the uniform performance criteria called out in the 2007 SAB Arsenic Review Panel report (SAB, 2007, p.39). For example, in Appendix B of the February 2010 draft, the availability of smoking status documentation is still inconsistently cited in the critical review of each study even though a large body of epidemiological literature has documented smoking behavior as a co-carcinogenic or synergistic factor in bladder and lung cancer causation. Smoking status information is also lacking in the Taiwan based studies utilized to derive the cancer slope factor. Other key factors such as degree of exposure misclassification, temporal variability in assigning past arsenic levels from recent measurements, study response/participation rates, reliance on imputed exposure levels, estimates of exposure variability, control selection methods in case-control studies, number of persons at various arsenic drinking water concentration categories and the influence of these factors on the magnitude and statistical stability of risk estimates are likewise not consistently evaluated.

Similarly, an extensive compilation of *in vitro* study references with brief descriptions is presented in the February 2010 draft text and Table C-3 thus complying with the SAB (2007) recommendation to review *in vitro* mode of action studies, however, in the body of the text and the conclusion of this table, no coherent critical integration and evaluation of these data is presented to address potential discrimination of key events in inorganic arsenic's carcinogenic mode of action. Meanwhile, other scientists have successfully evaluated, integrated and published critical reviews of this data base.

And finally, sensitivity analyses on arsenic water intake and non-water intake values for the Taiwan population were conducted as recommended by SAB (2007). When proportional changes in cancer risks are evaluated for non-water arsenic intake input assumptions in the exposed Taiwanese population of 100  $\mu\text{g/day}$  and 200  $\mu\text{g/day}$  as recommended, estimated cancer risk for male and female lung and bladder cancer risk *decrease* by 5 to 20% (USEPA draft "Toxicological Review of Inorganic Arsenic in Support of Summary Information on the Integrated Risk Information System (IRIS), February 2010, Tables 5-8 and 5-9). The proportionate decrease in estimated cancer risk across cancer types and sexes appears quite stable. Given available data on total and inorganic arsenic levels and intake values for non-water sources in Taiwan and especially for rice (Schoof et al. 1998; Lin et al. 2004; DOH, Taiwan, 2009), the determination that 50-60% of total arsenic in rice is inorganic arsenic (EFSA, 2009), and the known reliance on rice as a food staple in this region, the assumption of 10  $\mu\text{g/day}$  of non-water arsenic intake for the assessment appears excessively low for this population.

Sincerely,

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Attachments (1)

## References

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