

Dr. Angela Nugent
Designated Federal Officer
Arsenic SAB
USEPA Headquarters
Ariel Rios Building
1200 Pennsylvania Avenue, N. W.
Mail Code: 1400F
Washington, DC 20460

Dear Dr. Nugent:

I am writing as a member 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.

As a group, several members of the 2007 SAB panel submitted comments regarding the February 2010 draft document "Toxicological Review of Inorganic Arsenic in Support of Summary Information on the Integrated Risk Information System (IRIS)". I was a member of the group submitting these comments.

In light of the June 16, 2010 SAB conference call, which I understand will focus on the extent to which EPA addressed the 2007 SAB panel comments, I am submitting the original letter detailing our comments on this very issue. In brief, the letter provides important details regarding where the signatories felt the EPA did not adequately address comments made by the 2007 SAB panel. Thus, they are directly relevant to the June 16 review and should be considered important background information for the full SAB.

The letter is submitted as a courtesy to the current SAB to ensure continuity and completeness in the information they will utilize to reach their own conclusions

Respectfully,

Justin Teegarden, PhD, DABT

Date: March 25, 2010

Dr. Sue Shallal, DFO
EPA Science Advisory Board Staff
U.S. Environmental Protection Agency
(Mailcode 1400 F)
1200 Pennsylvania Avenue, NW
Washington, DC 20460

RE: Comments Submitted to the Workgroup of the Chartered Science Advisory Board upcoming review (on April 6-7, 2010) of the USEPA draft "*Toxicological Review of Inorganic Arsenic in Support of Summary Information on the Integrated Risk Information System (IRIS). February 2010*"

Dear Dr. Shallal:

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 regarding the February 2010 draft document review April 6-7, 2010 by a Work Group of the Chartered SAB.

First, we note that in 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 ≤ 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 µg/day and 200 µg/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 µg/day of non-water arsenic intake for the assessment appears excessively low for this population.

Sincerely,

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Yvonne P. Dragon, Ph.D.
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Senior Scientist
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Janice W. Yager, Ph.D., MPH
Adjunct Professor, Department of Internal Medicine
University of New Mexico

Attachments (1)

References

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