



November 15, 2010

Angela Nugent, Ph.D.  
Designated Federal Officer (DFO)  
EPA Science Advisory Board (1400F)  
1200 Pennsylvania Avenue NW  
Washington, DC 20460

**Re: Comments for the November 22 SAB Review of EPA’s “Toxicological Review of Inorganic Arsenic: In Support of the Summary Information on the Integrated Risk Information System (IRIS)”**

Dear Dr. Nugent:

The following comments are provided on behalf of the Wood Preservative Science Council<sup>1</sup> to help EPA and the regulated community manage implementation of the proposed oral cancer slope factor (CSF) for inorganic arsenic in the Agency’s draft cancer hazard assessment for IRIS should the SAB approve EPA’s report. The WSPSC is deeply concerned with the scientific uncertainty, insufficient outside peer-review, and lack of transparency regarding EPA’s draft assessment, and how the proposed CSF will be used by EPA programs and Regional offices.

The scientific uncertainties and limitations in EPA’s assessment are substantial. Examples of these limitations are provided in the list below and are based on information in EPA’s 2010 revised draft assessment, and comments provided by the 2007 Science Advisory Board Arsenic Review Panel and the 2010 SAB Workgroup for the Arsenic Cancer Review:

1. EPA’s 2010 draft assessment indicates that insufficient or no data regarding essential exposure factors in the Taiwanese study population, on which EPA’s proposed CSF is based, are available, including concentration and speciation of arsenic in drinking water, daily volume of arsenic-contaminated water consumed, amount of arsenic consumed in the diet, nutritional status of the study population, and data on prevalence of smoking in the population.
2. Inadequate EPA response to 2007 SAB recommendations to the Agency to explore non-linear models, including analysis without the use of an outside comparison population and quantitative assessment of how different key exposure factors (e.g., arsenic drinking water concentration, arsenic dietary intake, etc.) affect the cancer hazard estimate when used in combination and not in isolation as EPA did in its revised 2010 draft assessment.

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<sup>1</sup> The WSPSC is a trade association of manufacturers of wood preservatives that supports and participates in objective, sound scientific analysis of wood preservatives with a focus on chromated copper arsenate (CCA). The WSPSC is supported by its members Arch Wood Protection Inc., and Osmose Inc.

3. No comprehensive outside peer-review of EPA's draft assessment. The 2010 SAB Workgroup, in the cover letter to its draft October 25 report to EPA Administrator Lisa Jackson, stated that "The SAB was not asked to conduct a full peer review of the assessment, including EPA's calculation of the cancer risk estimate."

Despite these limitations with EPA's 2010 draft assessment, the Agency is proposing a highly conservative CSF of  $25.7 \text{ (mg/kg-day)}^{-1}$  be used to assess potential cancer risk from oral exposure to inorganic arsenic for males and females in the U.S. EPA's draft assessment characterizes this CSF as the "95% upper bound...for the combined [bladder and lung] cancer potency" of inorganic arsenic for both sexes.<sup>2</sup> The WPSC believes that EPA needs to be transparent regarding the conservative nature of the CSF and that risk managers need to be informed that the proposed CSF reflects a highly conservative upper-bound cancer potency for inorganic arsenic.

Federal and state agencies will have significant challenges in implementing the new CSF because of its 17-fold increase over the current IRIS value, there are substantial uncertainties in the underlying data and analyses EPA is relying on for the proposed value, and none of the reported carcinogenic modes-of-action (MOAs) for inorganic arsenic in the peer-reviewed literature are consistent with the conservative linear dose-response modeling EPA used to calculate the CSF. Given these factors, the WPSC strongly recommends that EPA include guidance in the updated IRIS file for inorganic arsenic that risk managers can use that allows them flexibility regarding a specific CSF for regulatory purposes. Such guidance would enable managers to base their choice of CSF on policy rather than science.

For example, as mentioned above the peer-reviewed literature indicates that the carcinogenic MOAs for inorganic arsenic are consistent with calculating a CSF using non-linear dose-response modeling, which depending on how it is conducted, could result in substantially lower CSFs. Furthermore, the 2007 SAB recommended EPA conduct non-linear modeling to assess its effect on the CSF. Risk managers could use such an approach to calculate a CSF for the low arsenic exposure levels representative of the U.S. population. Alternatively, a manager could use a CSF based on linear extrapolation that uses different assumptions and/or model than what EPA used in its draft assessment, resulting in a more appropriate, less conservative CSF for a given regulatory need.

The WPSC believes the scientific uncertainty and published studies regarding the MOAs for inorganic arsenic support providing a range of CSFs. Such a range is also consistent with EPA being transparent regarding the uncertainty in the underlying science supporting its proposed CSF. EPA should provide flexibility for risk managers to choose a CSF that is appropriate for their regulatory needs instead of forcing them to use a single, highly conservative value.

Respectfully submitted,

Wood Preservative Science Council  
C/o Jim Hale, Executive Director

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<sup>2</sup> Page 131 in EPA's draft "Toxicological Review of Inorganic Arsenic, In Support of Summary Information on the Integrated Risk Information System (IRIS), February 2010".