



November 14, 2006

EPA Science Advisory Board (1400F)  
Dr. Angela Nugent, Designated Federal Officer (DFO)  
U.S. Environmental Protection Agency  
1200 Pennsylvania Ave., NW  
Washington, DC 20460

Subject: Draft SAB Report, "Advisory on EPA's Assessment of Carcinogenic Effects of Organic and Inorganic Arsenic"

On October 24, 2006, EPA announced a public teleconference of the Science Advisory Board (SAB) to consider the draft final report of the SAB Arsenic Review Panel (ARP) and solicited public input on relevant information that should be taken into consideration by the SAB<sup>1</sup>. The Wood Preservative Science Council (WSPSC)<sup>2</sup> believes that critical information has not been adequately taken into account by the ARP, thus jeopardizing the scientific integrity of the report as well as its utility in providing sound scientific advice to the Agency regarding the carcinogenic effects of inorganic arsenic.

### Critical Data and Information Has Not Been Considered

The WSPSC and other interested parties provided extensive and detailed information to the ARP on multiple occasions, including during development of the charge, for the September 2005 meeting, and for the January 24, February 23 and 28, 2006 teleconferences. The ARP has chosen to ignore the critical new information on the southwest Taiwan database which substantially changes the interpretation of results. Just because that database has "...been subjected to many years of peer review as part of published studies" (draft final report, page 41 at line 27-28) does not mean that significant new research documenting a major confounding factor should be ignored. In fact, new research demands that a detailed reconsideration of that

---

<sup>1</sup> 71 Fed. Reg. 62257, October 24, 2006

<sup>2</sup> The WSPSC is a trade association of manufacturers of water borne wood preservatives. It supports and participates in objective, sound scientific analysis of water borne wood preservatives with a focus on CCA. We are supported by our members, Arch Wood Protection, Inc., Chemical Specialties Inc., and Osiose Inc. The WSPSC consults with the nation's leading experts in the fields of environmental science, epidemiology, risk assessment, and toxicology.

dataset be made. Yet the draft final report fails to even acknowledge the critical new research, let alone direct that a detailed reconsideration be undertaken.

The draft final report also fails to consider many studies directly relevant to exposures in US populations, several of which are of similar size to the SW Taiwan dataset and actually provide a better estimate of exposure in the range of concern in the US. While a very few are mentioned (and in some cases incorrectly described), the majority are not discussed. Further, these studies are dismissed as lacking statistical power. However, the draft final report does not adequately identify that new and improved epidemiological tools, such as integrative analyses or meta-analyses, are essential to developing a clear understanding of responses and can greatly improve the statistical power and improve precision.<sup>3</sup> Such approaches should not be relegated to simply a sensitivity analysis or to secondary analyses. The use of such tools is clearly recommended and supported by EPA's own guidance for carcinogenic risk assessment<sup>4</sup>. In fact, reliance upon a single study that has acknowledged limitations and failing to fully consider all relevant information from all studies is not a scientifically defensible approach.

There is little doubt that chronic exposure to inorganic arsenic at high levels (>200 ppb concentrations in water) is associated with increased cancer incidence. However, the evidence is overwhelming that there is no association with increased cancer with exposure at low levels (below 150 ppb in drinking water). Evidence for a threshold comes from multiple studies conducted in the U.S. as well as studies outside the U.S. For the purposes of U.S. risk assessment, the greatest emphasis must be placed on analysis of exposures that are pertinent to the U.S. None of the U.S. studies has shown an increased incidence of cancer due to low exposure to inorganic arsenic when confounding factors are taken into consideration. What is known about the ongoing EPA study in Fallon NV also supports this conclusion.

#### Recommendations Should Address Good Science

There is no requirement in EPA's Guidelines which would mandate the use of a default linear model across the full range of observed data and extrapolation below that range, regardless of whether a clear mode of action has been identified. In fact, the use of such a model clearly is discouraged by the Guidelines when extensive data for inorganic arsenic clearly identify a nonlinear dose response. EPA's Guidelines provide a flexible approach to the assessment of the dose-response curve for a carcinogenic agent but clearly support the use of multiple approaches, weight of scientific evidence and full consideration of all available data.

The Panel's suggestion that there is some unknown "point of departure" below which human data are not available to characterize a dose response curve is unhelpful. In fact, extensive human data across multiple studies clearly documents a threshold to inorganic arsenic at concentrations at or below 150 ppb, below which there is no carcinogenic risk. This is within the range of observed data, and extrapolation below the observed range is not needed.

---

<sup>3</sup> US Environmental Protection Agency, Risk Assessment Forum. Guidelines for Carcinogen Risk Assessment" EPA/630/P-03/001F, March 2005, at page 3-13.

<sup>4</sup> Ibid.

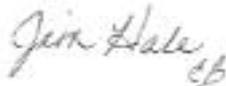
Letter to Science Advisory Board  
November 14, 2006

Given the overwhelming evidence for a threshold across multiple human studies, it is an abdication of scientific responsibility for the draft report to default to acceptance of a linear model that clearly is wrong and clearly inconsistent with the data. Regardless of whether the ARP believes it can identify an appropriate nonlinear dose response, or even whether it was asked to do so, the recommendations to the Agency should be based on the highest scientific credibility. Given the extensive and consistent data on inorganic arsenic, the clear recommendation should be that a linear model is not appropriate. The ARP should not conclude that linear extrapolation “is the method to be used” because of what EPA’s 2005 Guidelines appear to require.<sup>5</sup> The ARP should go well beyond simply “[encouraging] the Agency to test the sensitivity of the assumption of linearity.”<sup>6</sup>

### Conclusion

The Agency requested independent advice of a high scientific caliber. The SAB should ensure that the advice and recommendations provided to the Agency are transparent, scientifically credible, and complete. Where the SAB lacks critical information on which to base a decision, the datagaps should be identified. Where datagaps exist, the SAB should not rely upon clearly out-of-date and incomplete information to reach conclusions or make recommendations. Unfortunately, the conclusions and recommendations provided in the draft final report are based on out-dated information and assumptions, are incomplete, and excluded consideration of critical information provided to the Panel. Thus, the conclusions and recommendations fail to adequately respond to the Agency’s request. We suggest that the Board request a more complete response to the Agency’s request be prepared.

Sincerely,

A handwritten signature in cursive script that reads "Jim Hale" with a small "CB" or similar mark below it.

Jim Hale  
Executive Director

---

<sup>5</sup> Arsenic Review Panel draft final report, page 49 at line 28-29

<sup>6</sup> Ibid, page 49 at line 32-33