

Public Statement of Michael J. Kosnett, MD, MPH to the
Chartered SAB Second Quality Review for the SAB draft report reviewing EPA's
Inorganic Arsenic - Toxicological Review for IRIS 11/22/2010

Thank you for the opportunity to address the SAB.

My name is Michael Kosnett. I am a physician specializing in occupational and environmental medicine and medical toxicology. I am an Associate Clinical Professor in the Division of Clinical Pharmacology & Toxicology at the University of Colorado School of Medicine, and in the Department of Environmental and Occupational Health at the Colorado School of Public Health. I have had a long-term clinical and research interest in the human toxicology of arsenic. I served on the NRC Subcommittees on Arsenic in Drinking Water that issued reports to EPA in 1999 and 2001.

Although I am not speaking today as a representative of the NRC, I wanted to take this opportunity to emphasize two particular points that were noted by our NRC Subcommittees, and which remain quite valid today.

The first pertains to EPA's decision, in the recent IRIS Toxicological Review, to utilize a linear model to extrapolate human cancer risks from the epidemiological data. The Work Group accepted that ultimate decision. This was also the recommendation of the NRC Subcommittee. The Subcommittee noted that the human epidemiological data demonstrating cancer risk, particularly those from SW Taiwan and Chile, are consistent with a linear dose response, and that the range of extrapolation, or margin of exposure, between the arsenic doses associated with observed excess cancers and the low levels of arsenic exposure from environmental sources in the US is one of the narrowest for any carcinogen regulated by EPA. The Subcommittee also noted that in vitro studies have observed multiple genotoxic and nongenotoxic effects of arsenic in human and other mammalian cells that are consistent with a carcinogenic mode of action, and that these effects have occurred at concentrations that might exist in vivo at low levels of environmental arsenic exposure. A key question faced by EPA is not whether these potential modes of action might follow a nonlinear dose response at any dose, but rather whether there is convincing evidence that they exhibit a nonlinear dose response in the range of extrapolation relevant to contemporary environmental exposures to humans in the United States. In the absence of the demonstration of such nonlinearity in that dose range of interest, it is appropriate for EPA to utilize the linear dose response, which is also the default choice protective of public health.

My second point addresses concerns raised in the October 25, 2010 SAB draft review of the EPA IRIS report regarding a "reality check" relating the cancer slope factors for arsenic and the observed cancer rates in the US. This very point was addressed by the NRC Subcommittee in its 2001 Report. On page 221, in a section entitled "Plausibility of Cancer Risk Estimates" the Subcommittee wrote

“although the subcommittee’s risk estimates are of public-health concern, they are not high enough to be easily detected in US populations by comparing geographical differences in the rates of specific cancers with geographical differences in the concentrations of arsenic in drinking water.” I recommend that EPA and SAB take particular note of that section of the 2001 NRC report.