

**Comments Submitted by Dr. Russell Keenan on behalf of the American Chemistry Council
to the SAB Dioxin Review Panel on
*EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments***

June 24, 2010

Introduction

Good afternoon and thank you for providing this opportunity to address the SAB Panel. I am Dr. Russell Keenan, Vice President and Principal Toxicologist at Integral Consulting Inc., a national science and engineering firm providing interdisciplinary services in health, environment, technology, and sustainability. My comments today are on behalf of the Chlorine Chemistry Division of the American Chemistry Council.

It has been nearly 10 years since I last addressed the SAB on the Dioxin Reassessment, but much of my work over the last 25 years has been devoted to investigating the human health risks associated with exposures to dioxin and PCBs. During this time, I also co-developed the first private sector Cooperative Research and Development Agreement (CRADA) with EPA in the field of regulatory toxicology and risk assessment. The CRADA resulted in the research and application of Monte Carlo-based models for developing probabilistic reference doses for use in noncancer risk assessment. It is with this experience that I offer a few observations for your consideration as you begin your peer review of *EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments*.

Dr. Aylward has touched upon the key scientific questions and shortcomings of EPA's draft *Reanalysis* and these points are discussed in greater detail in her written comments. My focus is to encourage you to ask the question as to whether EPA consistently and appropriately followed its own guidelines and principles and applied a weight of evidence approach, using best available scientific information, in its evaluation of dioxin toxicity and risk. The need for a weight of evidence evaluation using best available science is at the heart of the recommendations made by the NAS Report and is fundamental to all of the other specific comments made by the NAS reviewers.

EPA's guidance and principles that address the use of best available scientific information is embodied in a variety of Agency documents, but the following are most relevant to risk assessment principles and weight of evidence.

- EPA's *Risk Characterization Handbook* was created as a single, centralized body of risk characterization implementation guidance (EPA 100-B-00-002, December, 2000). The Handbook states in their principles that "A risk characterization should be prepared in a

manner that is clear, transparent, reasonable, and consistent with other risk characterizations of similar scope prepared across programs in the Agency". The policy goes on to state that the principles of transparency, clarity, consistency, and reasonableness (TCCR) need to be fully applied throughout every aspect of the risk assessment process. I would urge you to apply this standard in your review of the *Dioxin Reanalysis*. For example, on pp. 5-60 to 5-61, beginning at line 27, the *Reanalysis* introduces the theory of "interacting background" to argue against the development of a nonlinear cancer dose-response and then cites an NAS (2009) report to support their decision. Please evaluate whether the adoption of such a fundamental concept absent peer review and public comment comports with these principles.

- EPA's *An Examination of Risk Assessment Principles and Practices* was published in March, 2004 (EPA/100/B-04/001) and began as an internal investigation of EPA's own approach to risk assessment. In this document, EPA makes a commitment to assessing all available scientific information using a weight of the evidence process that is consistent, comprehensive, balanced, and reproducible. I would urge the Panel to evaluate whether the draft *Dioxin Reanalysis* honors that commitment.
- EPA's *Guidelines for Carcinogen Risk Assessment*" (EPA/630/P-03/001F), published in 2005, embrace a weight of evidence approach as a key feature. In conducting the dose-response assessment, the *Guidelines* recommend starting with a critical analysis of all available data, rather than assuming a linear MOA. This analysis should include a complete evaluation of all existing data on tumor incidence rates and potential MOAs for tumor formation. The *Guidelines* are written to provide latitude and opportunity to use the published literature, to re-analyze previous data in light of new scientific understandings, or to conduct original research. Default assumptions must be employed only in the absence of critical information, or if the available data do not support a convincing alternative approach.

In fact, the *Cancer Guidelines* do not discuss specific criteria for conducting the MOA evaluation. When the *Cancer Guidelines* were being peer-reviewed before adoption, EPA disagreed with comments calling for the development of specific criteria by stating that "with the multitude of types of data, analyses, and risk assessments, as well as the diversity of needs of decision makers, it is neither possible nor desirable to specify step-by-step criteria for decisions to invoke a default option."

In light of this, I believe that it is important for you determine whether an important inconsistency exists between a straightforward reading of the *Cancer Guidelines* and the way in which EPA has interpreted them in order to justify its use of a linear, no-

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threshold cancer model in the *Dioxin Reanalysis*. For example, please refer to the statement made on p. 5-61 lines 27-28 of the *Reanalysis*, “The linear approach is used if there is sufficient evidence supporting linearity or if the mode of action is not understood (U.S. EPA, 2005).” Please evaluate whether EPA, at the very least, should have presented two dose-response assessments because the *Cancer Guidelines* do not require a full understanding of the MOA to support a nonlinear approach. In light of the NAS Report and their unequivocal recommendation that a nonlinear approach is scientifically justified, why hasn’t EPA presented one?

More detailed written comments on these and other issues will be provided to the Panel. I will also link these comments to specific examples in EPA’s *Dioxin Reanalysis*. Thank you for this opportunity to address the Panel today.