



September 30, 2014

Comments submitted to the SAB CAAC via email to Aaron Yeow

Public statement from Nancy Beck, PhD, DABT, on behalf of the American Chemistry Council and the Center for Advancing Risk Assessment Science and Policy, to the Scientific Advisory Board Chemical Assessment Advisory Committee (CAAC) for the review of the Draft IRIS Ethylene Oxide (Aug 2014) Assessment.

Good Afternoon.

I am providing remarks today on behalf of the American Chemistry Council (ACC)¹ and Center for Advancing Risk Assessment Science and Policy (ARASP)². We greatly appreciate the willingness of each of you to volunteer your time to serve on this committee. Not only is it important to get the ethylene oxide science correct, but as this is one of the first semi-revised IRIS assessments you are reviewing, your comments on the structure, approach and methodologies used in this assessment will have precedent setting implications for many other IRIS assessments.

Many improvements recommended by the National Academies (NAS) have not been fully or partially implemented in this draft. Because it is now 3 years since the NAS issued its recommendations to the IRIS program, when the EO IRIS assessment is finalized, the public will assume that the assessment incorporates all of NAS's recommendations. In fact, other program offices within EPA are already describing all IRIS assessments as meeting the standards of systematic review, despite how old the assessments may be. Your review is important because it will help to ensure that this particular assessment is of high quality.

¹ ACC represents the leading companies engaged in the business of chemistry. ACC Members are committed to improved environmental, health and safety performance through Responsible Care[®]. For more details please see www.americanchemistry.com.

² ARASP is a coalition of 21 organizations focused on development and application of scientifically sound methods for conducting chemical assessments. ARASP promotes the use of transparent and consistent approaches for data identification, integration and evaluation in chemical assessment. For more details please see: <http://arasp.americanchemistry.com/>.

My comments focus on the importance of the charge questions, particularly as they pertain to cross-cutting issues. You will be hearing from other experts that will speak specifically to the ethylene oxide science.

- 1) Many of the charge questions focus on the modeling that has been conducted. As you evaluate the models and their fit, I ask you to keep the epidemiology literature as well as the biology in mind. While some models may fit the data better than others, your evaluation should look beyond the model fit statistics. It is important to keep asking yourself whether or not the model makes biological sense and is realistic. Similarly, I ask you to evaluate whether the unit risk values produced by the best fitting models are consistent with the epidemiology literature. For instance, Section 3.5.1 of the draft assessment is referred to as the characterization of the cancer hazard, and in appendix K EPA refers to this section as a weight of evidence evaluation. In this section, EPA acknowledges that “there is little strength in the associations, as reflected by the modest magnitude of most of the RR estimates” (at page 3-47), and EPA also notes that, for breast cancer, “the overall epidemiological evidence was judged to be more limited” compared to the evidence for lymphohematopoietic cancers (at page 3-48). However, when one looks at the recommended unit risk values (at page 4-73), it is not clear that the potency they imply is consistent with the potency implied by the relative risk estimates found in the epidemiology studies. Your evaluation of whether or not these findings are logical and consistent with the evidence is important and valuable to all stakeholders.
- 2) My second comment is related to the modeling as well as EPA’s responses to the SAB and public comments. As you will see, despite earlier SAB recommendations and public comments, EPA fails to conduct non-linear modeling, only linear modeling is presented. If one looks closely at the 2005 EPA Cancer Guidelines³, it is clear that invocation of the linear default requires two things: 1) that all available data are insufficient to establish the mode of action for a tumor site **AND** 2) when scientifically plausible based on available data, linear extrapolation is used as a default.” (at page 3-21 in the EPA Cancer Guidelines). Your opinions on whether the linear modeling is supported by the data are important. You will hear more on this from Dr. Albertini.

Similarly, EPA discounts some of the available data noting, that the “other MOAs proposed by the ACC are speculative” (at page L-3). If one looks closely at the EPA Cancer Guidelines, it is clear that ascertaining a nonlinear mode of action is not necessary if there is significant biological support.⁴ EPA Cancer Guidelines state (page 3-21), “Where alternative

³ See: http://www.epa.gov/raf/publications/pdfs/CANCER_GUIDELINES_FINAL_3-25-05.PDF.

⁴ The EPA Cancer Guidelines state (at page 3-23) “Nonlinear extrapolation having a significant biological support may be presented in addition to a linear approach when the available data and a weight of evidence evaluation support a nonlinear approach, but the data are not strong enough to ascertain the mode of action applying the Agency’s mode of action framework.”

approaches with significant biological support are available for the same tumor response and no scientific consensus favors a single approach, an assessment may present results based on more than one approach.” Furthermore, the previous SAB recommendations were explicit, “With appropriate discussion of the statistical and biological uncertainties, several Panel members strongly advocated that both linear and nonlinear calculations be considered in the final EtO Risk Assessment.” Clearly, there is not scientific consensus in support for only using a linear extrapolation approach and we recommend that both approaches be presented. Your evaluation of the biological support is important and I ask you to look critically at all the evidence and to consider whether EPA has used consistent and standard criteria to judge the quality and strength of the studies accepted and the studies discounted. The use of standard criteria to evaluate all studies has been recommended by the NAS, however this is a recommendation that EPA has only partially implemented and the current draft does not appear to apply standardized criteria to the animal and mechanistic data that are discussed.

- 3) As you have seen, the ACC has recommended some edits to charge question 7, the question asking you to evaluate the response to comments. The edits suggested are consistent with the charge language that is being used in the CAAC ammonia review and we recommend that a similar charge be used here to ensure that your review evaluates all the significant public comments.

Lastly, consistent with previous recommendations from the SAB/BOSC⁵, we encourage this panel to recommend that EPA put in place strategies to ensure that recommendations from the public and peer reviewers on this draft are appropriately addressed. Adequate response to public comments is an important component of the assessment development process. Similarly, it will be important to ensure that the final draft is responsive to your recommendations. Currently, EPA staff responsible for writing and producing the assessments are the sole judge and jury of the adequacy of the final responses.

Thank you again for the time and energy you will put into this important review. I would be happy to answer any questions.

⁵ See SAB/BOSC 2012 report available at: [http://yosemite.epa.gov/sab/sabproduct.nsf/3822EB089FCCB18D85257A8700800679/\\$File/EPA-SAB-12-012-unsigned.pdf](http://yosemite.epa.gov/sab/sabproduct.nsf/3822EB089FCCB18D85257A8700800679/$File/EPA-SAB-12-012-unsigned.pdf).