



February 19, 2015

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, to the Scientific Advisory Board Chemical Assessment Advisory Committee (CAAC) for the review of the Draft IRIS Ethylene Oxide (EO) Assessment.

Good Afternoon.

I am providing remarks today on behalf of the American Chemistry Council (ACC). We have read your draft report on the IRIS Ethylene Oxide Assessment and want to thank you all again for the time and energy you are putting into this review. It is clear that each of you is taking your responsibilities seriously and we recognize the effort that has gone into conducting this review. 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.

There are many recommendations in the draft report that ACC supports and due to the time constraints I will not point them out. Thus my comments today will focus on areas where public input may help to improve the clarity of your recommendations.

- 1) **Further Clarification for Support of Linear Modeling is Necessary.** As you may recall, during the first teleconference in September 2014, I raised a few points where ACC felt your input was very important. One of these areas was EPA's decision to present only linear cancer modeling. I noted that, despite earlier SAB recommendations and public comments, EPA failed to conduct non-linear modeling and only linear modeling was presented. Your current draft report, in explaining your support for this approach states (at pages 4 and 22): "conditions for including a non-linear assessment per EPA *Guidelines for Carcinogen Risk Assessment* (EPA, 2005) are not met in the case of EtO, and therefore a non-linear modeling approach need not be included". However, it is unclear why you believe that the conditions are not met. This is not described in your comments and further elaboration would be helpful.

The 2005 EPA Cancer Guidelines<sup>1</sup> are clear that the linear default should be invoked only: 1) when all available data are insufficient to establish the mode of action for a tumor site **AND** 2) when “scientifically plausible based on available data.” (page 3-21). Additionally, the Cancer Guidelines state on 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.”

Evaluation of all the available information indicates that it would most certainly be appropriate for EPA to present non-linear modeling approaches, if for no other reason than as a useful and plausible comparison. You heard multiple times throughout your review from Dr. Albertini who explained that EO is a weak carcinogen and described further mechanistic information supporting the plausibility of a threshold. Dr. Albertini also cited, and provided you with citations, new literature that shows that indeed genotoxic compounds can have thresholds. If the CAAC finds this information unconvincing, it would be extremely helpful to understand why this is the case. Your opinions on whether the linear modeling is supported by the data are important; however, they are only useful if the basis for your conclusion is explained clearly and transparently. We ask that you evaluate the full body of literature, including information provided by Dr. Albertini, and provide a clear rationale for your support of the interpretation that only linear modelling need be presented.

**2) Further Clarification Regarding Rejecting the Union Carbide Dataset is Necessary.**

Similar to the concerns raised above, ACC has suggested and provided information, and experts, to support the consideration of the Union Carbide dataset. The current draft report notes (at pages 4 and 22) that the CAAC “concur with the decision not to use the Union Carbide Cohort data for unit risk derivation.” Unfortunately the draft report provides no justification for this concurrence. Page 25 of the draft report notes that the 2007 SAB review suggested that EPA consider this study and page 31, in discussing the EPA response to comments in their draft report, notes that, regarding use of this study, “the EPA response is concise and clear.”<sup>2</sup> Nevertheless, what is missing is the panel’s rationale for why the Union Carbide study should not be considered.

At the public meeting, experts presented information regarding the Union Carbide dataset. However there was no subsequent robust discussion of these data. Some CAAC members, however, suggested that that dataset not be considered as it was funded by industry. As Dr. Ramos, a CAAC member, and former Society of Toxicology (SOT) President, can explain, the SOT states that “Research should be judged on the basis of scientific merit, without

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<sup>1</sup> See: [http://www.epa.gov/raf/publications/pdfs/CANCER\\_GUIDELINES\\_FINAL\\_3-25-05.PDF](http://www.epa.gov/raf/publications/pdfs/CANCER_GUIDELINES_FINAL_3-25-05.PDF).

<sup>2</sup> The draft report misstates (at page 31) that the SAB, in 2007, supported discounting of the Union Carbide data.

regard for the funding source or where the studies are conducted (e.g., academia, government, or industry).”<sup>3</sup> The panel should fully discuss the strengths and weaknesses of the Union Carbide data, in light of the strengths and weaknesses identified in the NIOSH dataset. Thereafter, the panel should include its rationale in its report as to whether the Union Carbide dataset should be considered.

**3) Responses to Charge Question 7 (Responses to Public Comments) Should be Improved.**

In the first teleconference of this panel, ACC suggested that charge question 7, addressing EPA’s response to public comments, needed to be revised to ensure that this panel weighs in on the substance of the responses. Unfortunately, the current draft report does not provide your thoughts on whether or not you agree with EPA’s responses nor does it discuss the substance of the responses. The draft report notes that responses are often “clear,” “concise” and sometimes “appropriate,” but no consideration is given to the substance of the responses. Rarely is a judgment on the EPA response provided. For instance, regarding comment #6 (at page 31), the draft report notes that “the EPA response methodically presents the reasoning behind this conclusion”. What is not clear is whether or not the CAAC agrees with EPA’s reasoning and conclusions. For example, does the panel agree that the Parsons 2013 study is flawed? Without weighing in on the substance of the response, the CAAC review of this section of the EPA draft assessment becomes a box-check exercise that lacks the substantive input that stakeholders, including ACC, would have hoped to see and that EPA needs to hear to truly improve the scientific assessment. With a bit more explanation, we believe that your review could indeed make the responses to this charge question substantive and extremely useful, particularly for the charge questions where disagreement among stakeholders and EPA still exists.

Thank you again for the time and energy you have put into this important review. There are many areas in the draft report where your comments are extremely helpful and will be very useful as EPA works to finalize the EO IRIS assessment. Your efforts are greatly appreciated. I would be happy to answer any questions.

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<sup>3</sup> See SOT position statement available at: <http://toxicology.org/pr/PrinResearch.asp>