



January 28, 2014

Comments submitted to the SAB CAAC via email to Thomas Carpenter

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 Trimethylbenzene (TMB) Assessment.

Good Afternoon.

I am providing remarks today on behalf of the American Chemistry Council (ACC). We have read your draft report 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 that volunteering to be on this review panel is likely more of a time commitment than you expected. Not only is it important to get the TMB 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) **Public input is important.** We recognize that being a reviewer is no easy task. However, public input is a very important part of the Science Advisory Board process. While the amount of information may often be overwhelming, it is important that public input is considered. As you are likely aware, the ACC Hydrocarbon Solvents Panel submitted to you, before your last public meeting, the EPA Office of Pesticide Programs 2014 final rule exempting C-9 Rich Aromatic Hydrocarbons from tolerance requirements (Federal Register Vol 79, No. 187, September 26, 2014). This rule is an EPA final agency action and included a thorough review of the toxicity of C-9 hydrocarbons, including TMB. Not only has this rule not been discussed by this panel, it is not mentioned in your most recent draft report. At one point on the last call Dr. Harris noted wanting to get IRIS staff input on this rule, however that did not happen. We encourage this CAAC panel to review EPA's final regulation and

supporting toxicity documents which are available in the EPA docket and to also consult with the appropriate EPA scientific experts in the Office of Pesticide Programs regarding their toxicity conclusions and how they may be relevant to your review. This panel has already noted the importance of considering mixtures data as well as other relevant hydrocarbons. Final EPA regulatory actions, informed by similar science, should also be considered by this panel as part of the thorough review you are providing.

- 2) **Importance of C-9 data.** The draft report is clear that the “literature review and discussion should be expanded to include other closely related aromatic solvents and possibly mixtures” (at page 2). We support this recommendation as ACC agrees that most exposures to TMB occur in the presence of mixtures (particularly the C-9 fraction) and thus consideration of these studies is absolutely warranted. However, on page 13, there are still a variety of views among the panel regarding the role that testing of the C-9 fraction should have in the assessment. It is unclear why studies of xylenes would be important to the full CAAC, yet only some of the CAAC members support evaluation of C-9 mixtures (which contain xylenes and other closely related C-9 aromatics like isopropyl benzene). We recommend an approach that would include a robust evaluation of the C-9 data, before simply supporting EPA’s rejection of that data. Other parts of the draft report seem to support this approach and the language on page 13 appears inconsistent.

- 3) **The most useful recommendations are those that go beyond suggesting ‘further discussion’.** As we noted in our October 2014 comments, there are a few places in the report (e.g., the discussion of consideration of other solvents like xylene) where you recommend further or more robust discussion of a topic. In our experience, these types of recommendations are not as useful as ones that include a suggestion to also re-evaluate the determinations made in light of a more robust characterization of the topic of concern. The revised report is now very clear that the search criteria were too narrow and mixtures and other solvents can be very informative to a TMB assessment. The report appropriately recommends consideration and evaluation of this body of literature. However, the draft report also endorses the studies chosen for the points of departure and recommends specific uncertainty factors be used. This is logically inconsistent. The broader literature, including other solvents and mixtures, should be evaluated and incorporated into EPA’s evaluation of the appropriate critical effect, point of departure, and uncertainty factor. If your report endorses these decisions now, without consideration of the full body of literature, the recommendation to discuss the broader literature is essentially hollow, and will have no impact on the final quantitative values. EPA staff is likely to expand descriptions without a necessary re-evaluation of critical determinations in light of those descriptions. If the CAAC truly believes these data are important, the panel should not support EPA’s draft

determinations without seeing how the evaluation of this body of literature informs a complete weight of evidence evaluation.

- 4) **Clarifying the Cover Letter and Executive Summary.** It appears the cover letter and executive summary remain predominantly unchanged from the October 9, 2014 version. While the report covers many topics in depth, the cover letter and executive summary mention only a few of the report's findings and, appropriately, the depth of discussion is much more limited. Since not every topic area from the charge is addressed, it is unclear why certain topics are the focus of the cover letter and executive summary and others are not mentioned. It may be helpful to clarify which recommendations are most important to the CAAC. A thorough review of how the cover letter and executive summary relate to the full final report may be helpful.

- 5) **Comments on the preamble are very important.** We appreciate the time given to address the preamble of this and other IRIS assessments. We are already seeing other program offices refer to IRIS assessments as fully consistent with NAS recommendations and also consistent with systematic review approaches. As this is not the case, it is important that IRIS assessments, like the TMB assessment, are clear on this as well. Thus having a preamble that accurately describes approaches taken in the TMB assessment is important.
 - a. Your draft report notes (at page 6, line 12) that “to a substantial degree, the preamble provides a concise and clear description of the process that is followed.” We believe this sentence must be corrected. Since your report further notes that it is necessary to clarify what has been fully implemented and what is planned for subsequent assessments (at page 6, line 26), we cannot understand how the preamble can be seen as a “concise and clear description of the process that is followed.” As the panel members recognize the confusion in the preamble, it would be helpful to send a clear message to EPA regarding what should and should not be presented in the preamble.

 - b. The relevance of the preamble to a particular assessment may not be clear to readers of a final assessment and should be explicitly stated in the final IRIS assessment. While those that follow IRIS closely recognize that it will be a few more years before any IRIS assessment will be fully consistent with the NAS recommendations, many other users, including those that are interested in just one chemical, may not be aware of this. Thus, it is important that the preamble include a clear statement noting that it is not specific to the TMB Assessment and does not represent the methods and approaches that were followed as EPA developed the assessment. Alternatively, we recommend that the suggestion on page 6, lines 26-28, to clarify what was implemented and what is planned for future assessments be included in your recommendations on page 8, lines 11-16.

- 6) **Reliance on a reversible endpoint for the RfC/RfD may not be appropriate for all situations.** Historically, the IRIS program has not relied on reversible effects when setting IRIS values. While a chronic RfC is derived to represent a lifetime of exposure, in many situations, when used by state risk assessors and others, the duration is adjusted from 70 years to represent actual exposures (e.g. a 10 year, 25 year or 35 year exposure would all be considered chronic). As these time frames are frequently adjusted based on site specific information, the issue of reversibility would then become very relevant as there is indeed a post exposure period. If the IRIS value were based on a reversible endpoint, this value would need to be caveated noting that it may not be relevant for exposures that are less-than-lifetime as no adverse effect may be seen once the exposure is stopped. Derivations of values based on shorter term exposures would need to fully consider reversibility when interpreting the data. The panel may want to consider this when making their recommendations for the appropriate study and point of departure. Multiple approaches may be appropriate. While the IRIS glossary does not speak to reversibility, relying on reversible effects has not been the norm for the IRIS program and should not be considered lightly. Thus we ask the panel to consider these issues and also try to clarify their interpretation of the pain sensitivity endpoint and how it should and should not be used.
- 7) **Derivation of sub-chronic values should not be considered lightly.** While we are not necessarily opposed to the derivation of sub-chronic values by the IRIS program, we note that the IRIS program has been struggling for many years to develop their expertise to make the program the gold-standard for chronic non-cancer values and cancer values and to develop these assessments in a timely manner. This has not proven to be an easy task, as has been noted in multiple NAS reports. Many assessments take more than seven years to complete. While it may seem easy and logical to include sub-chronic derivations, our concern is that adding these values to IRIS assessments will slow down the process tremendously. In addition for this assessment, there should be an opportunity for public comment on a draft approach before EPA finalizes a newly derived value. Similarly, the issue of reversibility would become important and thus a discussion of what the correct points of departure are, in addition to a discussion of uncertainty factors, would also likely slow down the completion of the chronic assessment. We also note that other federal agencies, like ATSDR, provide sub-chronic and acute hazard values for chemical assessments.

The draft cover letter notes that regulatory agencies are frequently required to address risks associated with short-term exposures. Perhaps one recommendation could be that the problem formulation conducted for IRIS assessments include consideration of the exposure durations of concern before beginning the assessment. This may help in planning the

assessment, including collecting studies to consider, rather than trying to retrofit data to other exposure durations when the agency is at the final stages of the chronic assessment.

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