

**Summary Minutes**  
**U.S. Environmental Protection Agency**  
**Science Advisory Board**  
**Chemical Assessment Advisory Committee Augmented for the Trimethylbenzene Review**

**Date and Time:** Thursday, January 29, 2015 2:00 PM – 5:00 PM EST

**Location:** Meeting conducted by teleconference

**Purpose:** Review and discuss the Science Advisory Board Panel’s December 22, 2014 draft review of the IRIS Toxicological Review of Trimethylbenzenes and Recommendations to improve IRIS assessments.

**Attendees:**

Chemical Assessment Advisory Committee Augmented for the Trimethylbenzene Review (TMB Panel)<sup>1</sup>

Members:

|                           |                         |
|---------------------------|-------------------------|
| Dr. Cynthia Harris, Chair | Dr. Lawrence Lash       |
| Dr. Mitchell Cohen        | Dr. Frederick J. Miller |
| Dr. Deborah Cory-Slechta  | Dr. Lorenz Rhomberg     |
| Dr. Gary Ginsberg         | Dr. Stephen M. Roberts  |
| Dr. Helen Goeden          | Dr. Emanuela Taioli     |
| Dr. Sean Hays             | Dr. Raymond York        |
| Dr. Robert A. Howd        |                         |

SAB Staff Office: Mr. Thomas Carpenter, Designated Federal Officer

Others Present: Please see Members of the Public Attending Meeting: Attachment A

**Meeting Materials:** All meeting materials are available on the SAB website at the Chemical Assessment Advisory Committee (CAAC) Augmented for the Review of the EPA’s Draft IRIS Trimethylbenzenes Assessment webpage

<http://yosemite.epa.gov/sab/sabproduct.nsf/a84bfee16cc358ad85256ccd006b0b4b/c30cfbee2522689c85257db0007b3b5d!OpenDocument&Date=2015-01-29>

**Convene Meeting**

The meeting was announced in the Federal Register<sup>2</sup> and proceeded according to the meeting agenda, as revised. Mr. Thomas Carpenter, Designated Federal Officer (DFO) for the Chemical Assessment Advisory Committee (CAAC) Augmented for the Review of the EPA’s Draft IRIS Trimethylbenzenes Assessment (TMB Panel), convened the meeting at 2:00 p.m. on January 29, 2015. He stated that the EPA Science Advisory Board (SAB) was a chartered federal advisory committee and reviewed Federal Advisory Committee Act (FACA) requirements. He stated the Panel members are in compliance with federal ethics requirements that apply to them and noted that the SAB Staff Office has determined that there are no issues with conflict of interest or appearance of a loss of impartiality for any of the Panel members.

As the DFO, Mr. Carpenter stated he would be present during the Panel's business and deliberations. He stated that summary minutes of the meeting would be prepared by the DFO and certified as accurate by the Chair.

### **Introduction of Members, Purpose of Meeting, and Review of the Agenda**

Dr. Cynthia Harris, Chair of the TMB Review Panel, hereafter referred to as the panel, provided introductory remarks.

Dr. Harris welcomed the panel and members of the public in attendance. She stated that the meeting was convened to review and discuss the Science Advisory Board Panel's December 22, 2014 draft review of the IRIS Toxicological Review of Trimethylbenzenes (August 2013) and EPA's progress in addressing the NRC recommendations to improve the development of IRIS assessments.

Dr. Harris reviewed the meeting agenda<sup>3</sup> and provided an overview of how the Panel would conduct their deliberations for the teleconference. She also acknowledged that there was one request from the public to provide oral comments for the panel's consideration. After the oral public comments, the panel members would discuss the sections of the report, noting substantive edits and identifying key recommendations for the letter to the Administrator and executive summary. She also urged members to identify recommendations that need to be made for the TMB assessment to be completed as distinct from other suggestions that would improve the TMB assessment. Dr. Harris asked panel members if they had any clarifying question. Hearing none, she proceeded to the agenda and introduced the agency staff for their presentations.

### **Clarifying Remarks from EPA's National Center for Environmental Assessment**

Dr. Vincent Cogliano, Interim Director of EPA/NCEA/IRIS, provided a summary of the EPA written comments that noted discrepancies across sections of the draft panel report. These comments are posted on the SAB webpage.<sup>4</sup>

### **Public comments**

Nancy B. Beck, Ph.D., DABT, with the American Chemistry Council, registered to address the Panel and provided written comments. Her oral statement is posted on the SAB web page.<sup>5</sup>

Members did not have any questions for the public commenter.

### **Discussion of the Responses to Charge Questions**

#### Enhancements to IRIS Assessments

Members discussed the recommendations and the need for clarity between recommendations that apply to future IRIS assessments and those that should be implemented in finalizing the TMB assessment. Members noted that they used the TMB assessment as a case study for the agency's progress in addressing the National Academy of Sciences (NAS) recommendations.

One member noted that some substantial issues identified by the panel need to be addressed in the TMB assessment. He also described how the stage of implementing the NAS recommendations may require the agency to be explicit in the preamble and other sections of assessment(s) to address the specific evaluation conducted rather than relying on boiler plate explanations in the preamble.

Another panel member pointed to the agency statements in the preamble to the assessment that funding source is a legitimate reason to downgrade a study, the inference that negative studies may carry less weight than positive studies, and that specificity is not a part of causal analysis. Members disagreed with this approach and noted that the study itself should be evaluated based on the quality of the science and rigor of the data rather than funding or concerns about using data from a single source or laboratory.

#### Hazard Identification

Members also noted some inconsistencies between the discussions in the Synthesis of Evidence section and other sections of the report. Another member noted that the recommendations could be improved by providing a clearer presentation of the Panel's thoughts on exactly how information on related compounds and mixtures (such as C9) should come into play in a toxicological review such as this. Members discussed the possibility that competing interactions for distributional phenomena, induction of detoxification systems or other unforeseen biological phenomena may mask the underlying toxicity of a particular isomer present as a minority of the C9 mixture.

Another member noted that EPA is setting reference values for Superfund National Priority List (NPL) sites where individual isomers are present, not all three isomers and not necessarily mixtures. Members also noted that the use of these types of studies should not be included in the initial literature searches and evaluations but should be used when the agency identifies data gaps and areas of uncertainty. In the face of well-done studies on individual isomers, the C9 mixture studies deserve lower weight but should be considered as potentially useful in filling data gaps.

One member noted that the response to the Synthesis of Evidence charge question consists primarily of criticisms: (1) that the EPA did not more fully utilize information on C9 mixtures; (2) that insufficient comparisons were made with other methyl-substituted aromatic compounds; and (3) that the neurological data used by the EPA to derive toxicity values were based upon unconventional endpoints and are of questionable relevance to humans. Other members noted that these were not consensus opinions, and in the case of neurological effect data, statements here contradict and undermine the panel response to later charge questions that specifically ask about this critical endpoint. Members discussed needed revisions to this section that included:

- suggestions for a structural change in this and future toxicological reviews in which a section is added at the end of synthesis section for discussion of relevant toxicity data from related compounds and mixtures;
- keep in mind that the objective of this section is to place information available for the topic chemical(s) in a somewhat broader context;
- discussion of toxicity information in this Hazard Identification is necessarily at a higher level (i.e., less detailed) than the synthesis sections focusing on the topic chemical(s); and
- information provided could include the extent to which data for the topic chemical(s) are consistent or inconsistent with related chemicals or mixtures, and whether information from related chemicals and mixtures suggests that important data gaps might exist for the topic chemical.

The panel suggests that, in EPA's TMB toxicological review, this section should include a discussion of the C-9 mixtures and other methyl-substituted aromatics. This section provides an

opportunity for the EPA to articulate, for transparency purposes, its view on how the C9 mixture data fit into the TMB assessment.

Some panel members suggested information on related aromatics such as xylene and toluene that could be included in this section. Members noted that there were differences of opinion among panel members on the extent to which information for the C-9 mixtures is relevant to an assessment of TMB isomers. Members agreed that these different viewpoints should be briefly summarized in a balanced way in the panel's response.

Dr. Harris asked Drs. Ginsburg and Rhomberg to revise these section of the draft report.

#### Physiologically based pharmacokinetic modeling (PBPK)

Members noted that the PBPK section removed several recommendations. Panel members noted that the recommendations in the previous draft provided several paths the agency could use and the priority of these recommendations was not clear. For example, members noted that the recommendation to evaluate the work of Järnberg and Johansson and discuss why the model was not updated was more appropriate given the significant effort to update the model. Members noted that modifying the Hissink et al. (2007) model to predict the kinetics of inhaled TMB for repeated exposure scenarios was reasonable and appropriate.

#### Inhalation Reference Concentrations

One member expressed continued concern about the discussion of reversibility being added. He noted specifics, in the Supplemental Material (p.B-110) about the Korsak and Ryzdzynski (1996) study, it is clear that both tested isomers have very parallel patterns of decline in effect when examined 2-weeks after exposure termination. He believes the post-exposure declines are marked enough, the patterns similar enough across isomers, and the reversal effect notable enough in contrast to the smoothly increasing effect during the period of exposure that a real phenomenon seems to occur. Other member disagreed. They noted that the study's cohort grouping and reported statistical changes are not sufficient to support a reversible effect. Members agreed to include a discussion of the member's dissent in the report and the statistical difference between treated and control groups.

#### **Opportunity for brief clarifying remarks**

There were no requests to address the panel.

#### **Action Items and Next Steps**

Dr. Harris thanked the panel members for their efforts and asked for any revisions to be submitted to the DFO by February 13, 2015. The Chair and the DFO would then revise the Letter to the Administrator and Executive Summary based on the revisions and the discussions on this teleconference. A draft would be circulated to the panel for concurrence and then prepared for Quality Review by the Chartered SAB.

The Designated Federal Officer adjourned the meeting at 4:00 p.m.

Respectfully Submitted:

Certified as Accurate:

*/Signed/*

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Mr. Thomas Carpenter  
SAB Designated Federal Officer

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Dr. Cynthia Harris  
Chair  
Chemical Assessment Advisory Committee  
Augmented for the Trimethylbenzene Review

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by committee members during the course of deliberations within the meeting. Such ideas, suggestions, and deliberations do not necessarily reflect definitive consensus advice from the Panel members. The reader is cautioned not to rely on the minutes represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations

### **Materials Cited**

All meeting materials for the Chemical Assessment Advisory Committee Augmented for the Trimethylbenzene Review are available on the SAB website , <http://www.epa.gov/sab>. The materials cited below for this meeting are available at the following address:

<http://yosemite.epa.gov/sab/sabproduct.nsf/a84bfee16cc358ad85256ccd006b0b4b/c30cfbee2522689c85257db0007b3b5d!OpenDocument&Date=2015-01-29>

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- 1 Roster SAB Chemical Assessment Advisory Committee Augmented for the TMB Review
  - 2 Federal Register Notice Announcing the Meeting (79 FR 78428-78429)
  - 3 Meeting Agenda
  - 4 EPA Request for Clarifications in the SAB Revised Draft Report (12-22-14) on TMBs
  - 5 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.

**Attachment A**  
**Members of the Public Who Requested Call-in Information for the**  
**CAAC TMB Review Panel Teleconference**  
**January 29, 2014**

**Attendees**<sup>1</sup>

Dr. David Adenuga, ExxonMobil Chemical Company  
Dr. Nancy Beck, American Chemistry Council  
Mr. Jon Busch, ACC  
Ms. Patricia Casano, General Electric  
Ms. Angela Curry, Texas Commission on Environmental Quality  
Dr. Vincent Cogliano, US EPA  
Dr. Lynn Flowers, US EPA  
Ms. Maria Hegstad, Inside Washington  
Dr. Samantha Jones, US EPA  
Mr. J. Allen Davis, US EPA  
Mr. Andrew Kraft, US EPA  
Dr. Resha Putzrath, Navy and Marine Corps Public Health Center  
Ms. Bridget O'Brien USEPA  
Dr. Caroline English, NSF International  
Mr. James Kim, Office of Management and Budget  
Dr. Anita Myer, US Army Corps of Engineers

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<sup>1</sup> Based on members of the public requesting the teleconference dial in information