

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

Date and Time: Thursday May 22, 2014 1:00 PM – 4:30 PM

Location: Meeting conducted teleconference

Purpose: The purpose of this meeting was to receive briefings on the development of the EPA's IRIS *Draft Toxicological Review of Trimethylbenzenes* (August 2013) and the HERO database from the EPA staff, take presentations from the public, and to discuss the EPA charge questions.

Attendees:

TMB Panel Chair: Dr. Cynthia Harris

Panel Members:	Dr. James V. Bruckner	Dr. Kannan Krishnan
	Dr. Mitchell Cohen	Dr. Lawrence Lash
	Dr. Deborah Cory-Slechta	Dr. Frederick J. Miller
	Dr. Gary Ginsberg	Dr. Lorenz Rhomberg
	Dr. Helen Goeden	Dr. Stephen M. Roberts
	Dr. Sean Hays	Dr. Emanuela Taioli
	Dr. Robert A. Howd	Dr. Raymond York
	Dr. James Klaunig	

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

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

Meeting Materials: All meeting materials are available on the SAB Web site at the Chemical Assessment Advisory Committee (CAAC) Augmented for the Review of the EPA's Draft IRIS Trimethylbenzenes Assessment web page

<http://yosemite.epa.gov/sab/sabproduct.nsf/MeetingCal/C99D0AF3224EA17F852579E2004F282D?OpenDocument>

Convene Meeting

The meeting was announced in the Federal Register¹ 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 1:00 p.m. on May 22, 2014. 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 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. Those determinations are summarized on the SAB web page².

He noted for this review, the SAB Staff Office had convened a Panel that included invited members of the Chemical Assessment Advisory Committee and additional experts to participate in the review of the *Integrated Risk Information System (IRIS) Toxicological Review of Trimethylbenzenes (August 2013)*. This Panel will develop responses to the charge for this peer review. The charge was two-fold and requested: (1) a review of the scientific and technical analyses used to develop reference concentrations and reference doses for the three trimethylbenzene isomers; and (2) advice and comment on the enhancements to the IRIS Program implemented to address the NRC recommendations for the program.

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 and DFO.

Welcoming Remarks

Mr. Christopher Zarba, Director of the EPA SAB Office, welcomed the Panel members and thanked them for providing advice to EPA on this IRIS assessment³.

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 receive briefings from the EPA and public comments to prepare for the June meeting. Dr. Harris reviewed the meeting agenda⁴ and provided an overview of how the Panel would conduct their deliberations for the teleconference. She noted that after the Panel discussions at the upcoming June meeting, the Panel would develop an advisory report for distribution among Panel members for further discussion with the goal of reaching consensus on the recommendations and advice.

Dr. Harris noted that EPA would provide introductory remarks to the Panel in addition to the overview for the assessment and access to the Health Effects Research Online (HERO) database and would be available throughout the meeting for clarifying questions as they arose. She also acknowledged that there were three requests from the public to provide oral comments for the Panel's consideration. After the oral public comments, the Panel members would consider the charge questions and seek clarification from the EPA and identify additional issues, (if any) that may not be addressed in the draft charge questions. 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.

Remarks from EPA's National Center for Environmental Assessment

Dr. Vincent Cogliano, Interim Director, EPA/NCEA/IRIS provided a more detailed presentation of the enhancements the agency has made to the IRIS process. He noted that the agency is implementing the enhancements in a phased approach. The TMB assessment was well under development when the NRC recommendation were published, but the agency incorporated as many of the recommendations as possible to in the TMB assessment.

Ms. Debra Walsh, Acting Deputy Director of NCEA, provided an overview of the Health and Environmental Research Online Database. This database houses the literature used in IRIS assessments and provides access to abstracts and full citations. Her presentation provides instructions on how Panel members can access the database⁵.

Mr. J. Allen Davis, TMB Assessment Manager in NCEA, presented an overview of the TMB Assessment. Mr. Davis' presentation⁶ is posted on the SAB website. He discussed the key aspects of the Toxicological Review, especially how toxicological similarities between TMB isomers and toxicokinetic modeling were used to fill in data gaps in isomer-specific databases and provided some clarification on science issues raised by public commenters on the August 2012 draft TMB Assessment.

One member asked whether EPA had considered deriving a mixture assessment using the C-9 fraction studies. EPA noted the need to have reference concentrations and reference doses for individual isomers due to detection of TMBs at Superfund sites.

Another member asked whether the EPA had considered the derivation of provisional peer reviewed toxicity values (PPRTVs), noting that a PPRTV was available for 1,3,5-trimethylbenzene. EPA noted that the duration for these studies was too short for a chronic assessment. A member followed up on the selection of a 90-day exposure and commented that it may not achieve a steady state. EPA staff noted that a 90-day study is the minimum preferred time frame for chronic exposure with an applied uncertainty factor and that the IRIS program prefers longer studies to ensure that steady state toxicity is achieved. Members also noted that the subchronic study (90-day exposure) applies an uncertainty factor of 3 to derive a chronic value based on subchronic data.

A member asked if there were analyses available to address the question of whether toxicity increased with increased time of exposure. EPA staff noted that acute and subchronic studies were available and the agency's analysis noted that doses were different for acute and subchronic studies. Another member followed up to ask if the current draft accounted for these differences as noted in the public comments on the 2012 draft assessment. EPA noted that the short-term studies did not report on the same endpoint as the subchronic studies. EPA also noted that the subchronic studies had similar observation with and without foot shock or hot plate stimulation.

Public comments

Four individuals registered to address the Panel and provided written comments. The presentations are posted on the SAB website. The presenters were:

- M. David Adenuga, Ph.D, ExxonMobil Biomedical Sciences, Inc
- Richard H. McKee, Ph.D ExxonMobil Biomedical Sciences, Inc.
- Nancy B. Beck, Ph.D., DABT American Chemistry Council
- Patrick Beatty PhD, DABT American Petroleum Institute

Drs. Adenuga and McKee's presentation reviewed comments provided on the August 2012 Draft TMB assessment.⁷ Dr. Beck provided an oral statement that is also posted on the web page.⁸ Dr. Beatty was unable to attend the teleconference due to a change in his schedule. Additional written comments were provided by American Chemistry Council and are posted on the SAB website for this meeting.⁹ Members did not have any questions for the public commenters.

Discussion of EPA's Charge questions and Available Materials

Panel members discussed the Charge questions and asked the EPA staff clarifying questions on the charge questions. Members noted that there are overlapping issues between the charge questions for the TMB isomers.

Several members commented that question 2 on the dose metric selected seems to be a shift in the point of departure. EPA clarified that if the Panel were to recommend a different endpoint, the agency requests additional information to assist the agency in evaluating that advice.

One member asked if other Panel members had any concerns about the PBPK model and requested the physiologically based pharmacokinetic model's supporting files be provided to the Panel so they could perform a quality assurance quality control analysis. EPA agreed to provide that information and data to the Panel.

One member noted that the charge questions were organized in a chronologic series of steps that EPA follows to conduct the analyses. The member asked if this created a problem if the Panel did not agree with the agency's approach for a step and provided a different direction for the agency to pursue. That is, how should the Panel continue with the specific chronological progression predicated on the previous question when the recommendation differs from the option selected by the EPA? Members discussed the need to be facile and aware that the questions were indeed presented in the order in which one would conduct the toxicological analyses needed to derive an RfD or RfC. Members agreed that rather than rewrite the questions to be more generic they should consider any recommendations or changes to the EPA's analysis presented in a specific stage in the analysis and carry that recommendation forward. Recognizing that the charge questions may present a specific value the agency selected or derive comment on the value does not limit that Panel from comments on the next step when a different value is identified by the Panel.

EPA provided a clarification to question 4 in the general charge questions section. The clarification specifies that the Panel is asked to review the summary of public comments, not the original public comments received on the draft TMB Assessment (August 2012). The modified question was accepted by the Panel and incorporated into the charge posted on the SAB website.

Discussion of Next Steps

Dr. Harris reviewed the points the Panel members identified as key issues and asked the Panel for any additional thoughts. Panel members agreed that the key issues were identified and did not identify any additional issues or comments. Dr. Harris asked the DFO to summarize the next step for Panel members to develop the Advisory Report

Mr. Carpenter stated that the Panel would meet in Washington in June. Members were reminded that providing preliminary comments would help facilitate the discussion and report development. Those preliminary comments would be posted on the SAB website. He reminded Panel members of the tentative schedule for a teleconference to discuss the draft report followed by a quality review by the chartered SAB. Dr. Harris asked the Panel for any questions or clarifications. She then called upon the DFO to adjourn the meeting.

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

Respectfully Submitted:

Certified as Accurate:

/Signed/

/Signed/

Mr. Thomas Carpenter
SAB Designated Federal Officer

Dr. Cynthia Harris
Chair

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 SAB review of the IRIS Assessment for Trimethylbenzenes are available on the SAB Web site Panel. [Http://www.epa.gov/sab](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/MeetingCal/30192F9042ACA0CC85257C97004D7661?OpenDocument>

¹ Federal Register Notice Announcing the Meeting (79 FR 16324-16325)

² Determination Memorandum and Biosketches of Candidates

³ Draft *Toxicological Review of Trimethylbenzenes* In Support of Summary Information on the Integrated Risk Information System (IRIS) (CASRN 25551-13-7, 95-63-6, 526-73-8, and 108-67-8)

⁴ Meeting Agenda

⁵ HERO Health and Environmental Research Online Presentation

⁶ Overview of the Draft IRIS Assessment of Trimethylbenzenes. Mr. J. Allen Davis, IRIS USEPA

⁷ ACC Hydrocarbon Solvents Panel Comments on The Toxicological Review of Trimethylbenzenes presented at the EPA Trimethylbenzenes Listening Session August 1, 2012.

⁸ Comments submitted to the SAB CAAC. 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 Teleconference¹
May 22, 2014

Attendees

Dr. David Adenuga, ExxonMobil Chemical Company
Dr. Nancy Beck, American Chemistry Council
Mr. Jon Busch, American Chemistry Council
Mr. Kevin Bromberg, Small Business Administration
Dr. Lyle Burgoon, US EPA
Ms. Halie Choi, RegNet Environmental Services
Ms. Angela Curry, Texas Commission on Environmental Quality
Dr. Chuck Elkins
Mr. Robert Fensterhiem, RegNet Environmental Services
Dr. Lynn Flowers, US EPA
Ms. Maria Hegstad, Inside Washington
Ms. Maureen Johnson, US EPA
Dr. Samantha Jones, US EPA
Dr. Laura Keller, ExxonMobil Chemical Company
Dr. Richard McKee, ExxonMobil Chemical Company
Ms. Gina Perovich, US EPA
Dr. Resha Putzrath, Navy and Marine Corps Public Health Center
Mr. Lawrence Reichle, US EPA
Ms. Christine Ross, US EPA
Ms. Linda M. Wilson, Attorney General Office State of New York

¹ Based on members of the public requesting the teleconference dial in information