

**U.S. Environmental Protection Agency
Science Advisory Board
Chemical Assessment Advisory Committee (CAAC)
Augmented for the Review of Ethyl Tertiary Butyl Ether (ETBE)
and tert-Butyl Alcohol (tBA)**

**Public Teleconference
March 22, 2018 and March 27, 2018**

Minutes

Purpose:

To review the draft report of the SAB CAAC Augmented for ETBE/tBA, “SAB Review of EPA’s Draft Toxicological Review of Ethyl Tertiary Butyl Ether and Draft Toxicological Review of *tert*-Butyl Alcohol (*tert*-Butanol or tBA), 02-21-18”.¹

Participants:

CAAC Augmented for ETBE/tBA Members (See Roster² for full committee):

Dr. Janice E. Chambers (CHAIR)	Dr. William Michael Foster
Dr. Hugh A. Barton	Dr. Alan Hoberman
Dr. Janet Benson	Dr. Tamarra James-Todd*
Dr. Trish Berger*	Dr. Lawrence Lash*
Dr. James Bruckner	Dr. Marvin Meistrich
Dr. John Budroe	Dr. Maria Morandi
Dr. Karen Chou	Dr. Isaac Pessah*
Dr. Harvey Clewell	Dr. Lorenz Rhomberg
Dr. Deborah Cory-Slechta**	Dr. Stephen M. Roberts
Dr. Jeffrey Fisher	Dr. Alan Stern

*In attendance on March 22, 2018 only.

** In attendance on March 27, 2018 only.

SAB Staff:

Dr. Shaunta Hill-Hammond, Designated Federal Officer for the CAAC Augmented for ETBE/tBA

Dr. Sue Shallal, SAB Staff Office

Mr. Thomas Carpenter, SAB Staff Office

Other Attendees: See Appendix A.

Teleconference Summary:

The draft SAB report was discussed during two teleconferences; one occurred on March 22, 2018 and then continued on March 27, 2018. The discussion followed the topics as presented in the meeting agenda.³

Thursday, March 22, 2018

Opening of the Public Teleconference:

Dr. Shaunta Hill-Hammond, the Designated Federal Officer (DFO), convened the teleconference with a statement informing the participants that the Chemical Assessment Advisory Committee (CAAC) augmented for the review of ETBE and tBA (hereafter referred to as the CAAC-ETBE/tBA Panel or Panel) operates under the Federal Advisory Committee Act (FACA). Under FACA, Dr. Hill-Hammond noted that the SAB's deliberations are held in public with advanced notice given in the Federal Register.⁴ The SAB consists entirely of special government employees appointed by the U.S. EPA (hereafter referred to as the EPA or Agency) to their positions. As special government employees, all the members are subject to all applicable ethics laws and implementing regulations.

Dr. Hill-Hammond stated that for this SAB advisory activity, no conflict of interest or loss of impartiality issues were identified for any Panel member. Dr. Hill-Hammond then acknowledged the participation of Dr. Samuel Cohen, a current SAB board member. Dr. Cohen participated by providing his personal professional comments as a member of the general public. Dr. Hill-Hammond noted that Dr. Cohen's comments did not represent views or opinions of the chartered SAB. Further, as a result of Dr. Cohen's public participation in the teleconference and in previous meetings addressing the SAB review of EPA's draft ETBE and tBA assessments, Dr. Cohen will recuse himself from the quality review to be conducted by the chartered SAB.

Dr. Hill-Hammond reminded all participants that the teleconference materials were available on the SAB website. Dr. Hill-Hammond then conducted a roll-call of the Panel and turned the teleconference over to Dr. Janice Chambers, Chair of the CAAC-ETBE/tBA Panel.

Dr. Chambers offered welcoming remarks to Panel and noted that the Panel would hear comments from the public and the EPA. She then asked Dr. Hill-Hammond to proceed with the public comment period.

Public Comments:

Three individuals registered to present oral comments.⁵ Dr. Hill-Hammond invited each commenter to present his/her statements in accordance with the order of requests received by the SAB staff office.

Ms. Jessica Ryman-Rasmussen presented comments on behalf of API.⁶ Her comments were specific to the lack of pathology expertise in the development of the ETBE and tBA assessments, the derivation of toxicity values inconsistent with NRC recommendations, EPA guidelines, and the statements of other EPA offices, and the numerical value for the oral slope factor for ETBE.

Dr. Samuel Cohen of the University of Nebraska Medical Center, presented comments focused on the relevance of effects seen in animal studies to human health, lack of expertise in pathology on the assessment development teams and the peer review Panel and the lack of consensus noted within the draft report.⁷

Dr. James Bus of Exponent presented comments on behalf of LyondellBasell.⁸ In his comments, he stated his agreement with the Panel's recommendation that EPA should "refrain from conducting a quantitative analysis" of the cancer risks for both ETBE and tBA and agreement with the Panel's finding that PBPK modeling is not necessary or appropriate to support an extrapolation from inhalation-to-oral route for ETBE. He also asked that the Panel provide clarification throughout the report on points where no consensus was reached.

No questions were raised by the Panel to any of the public commenters. Dr. Chambers thanked the public commenters and then invited EPA representatives to present their comments.

Dr. Kris Thayer of the EPA National Center for Environmental Assessment, thanked the Panel for their work in reviewing the draft assessments. She noted that the EPA had a couple of clarifying questions on the draft report. She then provided a brief highlight of those questions, noting that the clarifying questions⁹ had been submitted in writing.

No questions were raised by the Panel to the EPA.

A second roll call of Panel was conducted by Dr. Hill-Hammond at the request of the chair. Dr. Chambers then reviewed the teleconference agenda for the day. She indicated that typographical errors and minor corrections as noted by the Panel would be addressed in the next report draft. She then offered a general correction to the report regarding the presentation of the key recommendations. Where the Panel presented no recommendations, the proposed change was to reflect this finding by stating: "The SAB has no specific recommendations at this time for this tier"; instead of "none". No objections were raised by the Panel. Dr. Chambers also indicated if no comments were raised on a particular section of the report by the Panel, then consensus with the draft text as presented in that section (including any minor typographical corrections made by the chair) would be implied.

Discussion of the draft report:

Dr. Chambers led the review of the draft report. The discussion proceeded as following: Dr. Chambers identified the report section and read the charge question. She then presented comments¹⁰ received regarding the corresponding report section and proposed changes to address the comments. She also invited additional comments and questions from the Panel during the review of each section.

Literature Search Strategy/Study Selection and Evaluation: Report Section 3.1

3.1.1 ETBE:

Dr. Alan Stern commented that the consideration of the National Research Council (NRC) recommendations was beyond the scope of the charge question and that utilization of NRC recommendations is a policy matter for EPA to decide.

Dr. Steve Roberts agreed that the suggestion to consider the NRC recommendations could be removed. Dr. Lorenz Rhomberg noted that implementation of the NRC recommendations was important for EPA and suggested that the Panel's recommendation that EPA comply with the NRC recommendations be noted as a tier 3 recommendation. Dr. Stern reminded the Panel that compliance with the NRC recommendations was not part of the charge question. Dr. James Bruckner asked if EPA could provide context for whether the inclusion of NRC recommendations within the report would be distracting. Dr. Thayer was available to respond and noted that the inclusion of NRC recommendations would not be distracting; however, she did not feel that the comment was needed. Dr. Rhomberg noted per EPA's comment, that the Panel could remove all references to NRC recommendations.

The Panel was in agreement with the proposal to remove all references to NRC recommendations within the draft report. Dr. Rhomberg and Dr. William Foster volunteered to revise the section. No further comments or changes were raised by the Panel.

3.1.2 tBA:

In order to remain consistent, the Panel agreed that changes made to section 3.1.1 for ETBE regarding NRC recommendations would also apply to section 3.1.2 for tBA. Drs. Rhomberg and Foster agreed to update this section. No additional comments or changes were raised by the Panel.

Hazard Identification - Chemical Properties and Toxicokinetics - Report Section 3.2

3.2.1.1 ETBE:

No comments or changes were raised by the Panel. Dr. Chambers noted the Panel's concurrence with the current report text.

3.2.1.2 tBA:

No comments or changes were raised by the Panel. Dr. Chambers noted the Panel's concurrence with the current report text.

3.2.2.1 ETBE:

No comments or changes were raised by the Panel. Dr. Chambers noted the Panel's concurrence with the current report text.

3.2.2.2 tBA:

No comments or changes were raised by the Panel. Dr. Chambers noted the Panel's concurrence with the current report text.

3.2.3.1 ETBE:

As a general discussion point, Dr. Chambers noted that the recommendations as presented were too long and proposed that they be revised to move the supportive background text into the introduction paragraph(s) where appropriate. Dr. Hugh Barton suggested that the text presented in the tier 2 recommendations could be moved to the introduction paragraph, leaving only the first and last sentences as the recommendation.

Dr. Roberts noted that mode of action information is addressed within the response to charge question 4a and suggested that the information not be repeated in this section. Dr. Barton commented that mention of the mode of action information in this section was appropriate as it serves as a reference point for recommendations presented later in the report. Dr. Jeffrey Fisher offered a comment that the charge question is about dose metrics which is dependent on mode of action.

Dr. Chambers summarized from the discussion that the text should be revised to provide a general statement on the mode of action and should refer to the response for charge question 4a.

Dr. Fisher agreed to provide revisions for this section of the report based on the Panel's discussion.

No additional comments or changes were raised by the Panel.

3.2.3.2 tBA:

No comments or changes were raised by the Panel. Dr. Chambers noted the Panel's concurrence with the current report text.

Break:

The Panel took a break at approximately 10:18 am. The teleconference resumed at 10:25 am and Dr. Hill-Hammond conducted a roll-call of the Panel before turning the teleconference back over to Dr. Chambers.

Hazard Identification and Dose-Response Assessment: Noncancer: Report Section 3.3

3.3.1.1 ETBE

Dr. Roberts proposed that the response to the charge question should focus on the Panel's discussions rather than providing a summary of the information presented by public commenters. He also stated that this section includes the first discussion of chronic progressive nephropathy (CPN) and that clarifications are needed to convey the Panel's points of consensus. Also as CPN hazards/effects could be associated with other chemicals, Dr. Roberts suggested, as a tier 2 recommendation, that EPA host a workshop to determine the criteria for when to consider CPN effects and also to develop a policy regarding CPN.

Dr. Maria Morandi noted that the EPA did not provide appropriate background information within the assessments regarding their position on CPN. Dr. Marvin Meistrich also commented that EPA needs to expand the information on the effects of CPN within their assessment. He then noted that the Panel's report should highlight issues regarding CPN where the Panel did not achieve consensus. Dr. Meistrich also noted that the Panel could include more information on the kidney effects by highlighting the points of agreement and disagreement among the Panel members.

Dr. Chambers asked Dr. Meistrich if he could identify areas where the Panel did reach consensus regarding the charge question. Dr. Meistrich suggested that consensus was reached regarding alpha 2u-globulin, effects that are specific to male rat and CPN specific to kidney effects.

Dr. Rhomberg stated that the Panel should be wary of additional discussions of consensus on CPN through report edits. Dr. Roberts agreed with him noting again the proposal for EPA to host a workshop for further discussion.

Dr. Karen Chou commented that the Panel did not reach consensus on CPN because the available scientific information is not clear enough to distinguish the CPN effects seen in rats from humans. She noted that the general toxicological assumption is that toxicity levels observed in lab animals can happen in humans. Without further research, the Panel cannot argue beyond the general toxicological assumption, thus no consensus among the Panel means that humans could suffer the same effects/potential outcomes as rats.

Dr. Rhomberg commented that exposures will vary among laboratory animals and humans. Dr. Chou responded in agreement but also noted that the high dose is a limitation in the assessment. Dr. John Budroe agreed with Dr. Chou, highlighting that bioassays are a risk management tool.

Dr. Lawrence Lash commented that the section currently includes some inconsistencies on the points of consensus among the Panel. He then suggested that the Panel's recommendations be presented per area of consensus with appropriate context information. He also noted that it would be useful for EPA to develop a general policy for CPN.

Dr. Trish Berger noted her agreement with the proposal for EPA to develop a CPN policy and also stated that additional research/data are needed.

Dr. Chambers asked Dr. Lash to provide context for the listed recommendations. Dr. Lash agreed to provide the revisions.

Dr. Hugh Barton asked for clarification on the third recommendation under tier 2. Dr. Lash responded that information to address the lack of mechanistic effects can be added for clarification.

Dr. Lash also commented regarding Dr. Berger's points on the need for additional research and data. He reminded the Panel that a publication is available by Melnick et al. (2012). Dr. Lash then asked the Panel to remember the focus of chemical assessments is public health and because of that the Agency should err on the side of caution.

Dr. Stern agreed with Dr. Lash regarding the public health focus of the Agency's assessments. He then shared that the process of risk assessment is not absolute science where there is proof of risk of harm when applied to environmental policy. He then noted that risk assessments are meant to be protective, not predictive. With that in mind, Dr. Stern stated that the EPA assessment was consistent with current EPA policy. EPA's approach is reasonable for the protection of human health.

Dr. Roberts noted that the points raised by Dr. Stern and others could be explained and included in the response for this section. Dr. Chambers asked for volunteers to lead the revisions for this section.

Drs. Roberts and Bruckner offered to provide the rationale for revising EPA's assessment. Drs. Lash and Stern offered to provide the rationale for maintaining EPA's assessment. No further comments or changes were raised by the Panel.

3.3.1.2 tBA:

Dr. Roberts indicated that the section could be revised by providing a reference back to the response for ETBE under charge question 3a. Dr. Roberts offered to draft a revision. No additional comments or changes were raised by the Panel.

3.3.2.1 ETBE:

The Panel discussed the formatting of this section. For consistency, members agreed that the section will be revised to remove the target subtitles.

Dr. Roberts noted a potential contradiction within this section as some Panel members did not agree that kidney effects are not relevant to human health. Dr. Meistrich offered to provide a revision to address Dr. Roberts concerns.

Dr. Chambers noted that EPA requested clarification on page 25 lines 28-30, regarding the phrasing "giving more emphasis". Dr. Meistrich commented that the text could be enhanced and offered to provide a revision to the Panel for their review. No additional comments or changes were raised by the Panel.

Recess:

The teleconference recessed at approximately 12:15 p.m.

Tuesday March 27, 2018

Dr. Hill-Hammond reconvened the teleconference at 2:00 pm. She reminded the audience that the CAAC-ETBE/tBA Panel operates under the Federal Advisory Committee Act (FACA). Dr. Hill-Hammond conducted a roll-call of the Panel and turned the teleconference over to Dr. Janice Chambers.

Dr. Chambers provided a review of the agenda, highlighting the charge questions pending for discussion for the day. She also provided a brief recap of the questions discussed on the previous day. The Panel then continued with their discussion of the report.

3.3.2.1 ETBE:

In response to Dr. Chambers' request, Dr. Meistrich affirmed that he would revise the section per the comments received and would address EPA's comments. Dr. Roberts commented that the Panel needs to include an explanation or some clarification of why EPA choose not to include the information on sensitive populations. Dr. Meistrich indicated that he would work with the assigned subgroup to address that point. No further comments or changes were raised by the Panel.

3.3.2.2 tBA:

Dr. Chambers, noted that the EPA requested clarification on the second tier 2 recommendation.

Specifically, what information regarding the metabolic and sedative actions of tBA on the exposed dams is being requested. EPA also wanted to know whether the recommendation was a request for more research in this area (and, if so, would it be considered a tier 3 recommendation).

Dr. Rhomberg inquired as to whether the Panel's recommendations for additional research would prohibit the Agency from moving forward without it. Dr. Meistrich stated that the request for additional research could be included as a tier 3 recommendation. Drs. Stern and Alan Hoberman were in agreement. Dr. Budroe inquired as to whether the Panel could retain the tier 1 recommendations as presented, only removing the research request. Dr. Barton inquired as to whether the subgroup could confirm what data are available in the Agency's assessment. Dr. Meistrich responded indicating that he would work with the subgroup to address revisions to recommendations and the identification of available data. Dr. Barton also noted that if there is a modified NOAEL or LOAEL, additional revisions to this section would be needed. No further comments or changes were raised by the Panel.

3.3.3. 1 ETBE:

Dr. Deborah Cory-Slechta proposed that the last two recommendations in tier 1 be moved to tier 2. The first bullet under tier 1 would also be revised to remove the word "examine". The Panel then had some discussion about whether the section considers nephropathy in addition to urothelial hyperplasia. Dr. Roberts commented that depending on the revisions to 3b regarding the male rat data, there could be another endpoint. No further comments or changes were raised by the Panel.

3.3.3. 2 tBA:

The Panel agreed that the tier 3 recommendation bullets 3 and 4 should be moved to tier 2. The Panel also discussed changing the word "encourage" to "consider" in the tier 2 recommendations. Dr. Cory-Slechta agreed to make the revisions, also including those proposed for ETBE. No further comments or changes were raised by the Panel.

3.3.4 1 ETBE:

Dr. Stern suggested deleting the tier 2 recommendation which suggested alternate endpoints be used for deriving the reference concentration for inhalation (RfC). Dr. Morandi noted that kidney weight was not a specific endpoint; however, there were consistent changes in kidney weight for both male and female rats. Dr. Bruckner commented that other than CPN, kidney weight was the only effect seen and suggested that the Panel retain it as an option for deriving the RfC. Dr. Rhomberg asked whether kidney weight was secondary to other effects and if EPA could consider it as an independent effect. He then asked the Panel if additional language could be added to the recommendations and introduction paragraphs to clarify the Panel's suggestion. Dr. Morandi noted that she would work with the subgroup to revise the recommendations with consideration of linking the endpoints to reproductive effects.

Dr. Morandi also noted that she would include parts per million (ppm) conversions throughout the section. No further comments or changes were raised by the Panel.

3.3.4.2 tBA:

No comments or changes were raised by the Panel. Dr. Chambers noted the Panel's concurrence with the current report text.

3.4 Hazard Identification and Dose–Response Assessment: Cancer

3.4.1.1 ETBE:

The Panel engaged in a brief discussion about the tier 2 recommendations, specifically, whether the third bullet under tier 2 should be moved to tier 1. Ultimately, the Panel decided to make no changes to the recommendations as presented. No further comments or changes were raised by the Panel. Dr. Chambers noted the Panel's concurrence with the current report text.

3.4.1.2 tBA:

Dr. Roberts offered to provide cross references throughout the text to identify related/key report sections. The Panel agreed that would be helpful for context. Dr. Roberts confirmed that no recommendations were proposed by the subgroup regarding the cancer mode of action. The Panel then discussed and agreed to remove the final paragraph in this section. No further comments or changes were raised by the Panel.

3.4.2.1. ETBE:

The Panel discussed the phrasing “preponderance of data” as it appeared in this section. The Panel decided to revise the phrase changing it to “preponderance of evidence”. Dr. Bruckner agreed to make the revisions and to also include more information on the database. No further comments or changes were raised by the Panel.

3.4.2.2. tBA:

No comments or changes were raised by the Panel. Dr. Chambers noted the Panel's concurrence with the current report text.

Clarifying Public Comments:

Dr. Hill-Hammond acknowledged receipt of two requests for clarifying comments.¹¹

Dr. James Bus presented comments¹² specific to the consideration of alternative endpoints and the selection of multiple endpoints for deriving the RfC and reference dose (RfD) values.

Kevin Bromberg presented comments¹³ specific to providing clarity to the report especially in areas where the Panel did not reach a consensus view and highlighting the importance of public comments.

Teleconference Adjournment:

Dr. Chambers asked Dr. Hill-Hammond to review the next steps for the Panel. Dr. Hill-Hammond noted that another teleconference will be needed so the Panel could complete the discussion of the draft report. She noted that she would work with the Panel members to determine their availability and stated that a Federal Register Notice would be published announcing the upcoming teleconference date. She then asked Panel members currently tasked with providing revisions to the report to submit them by April 6, 2018.

Finally, all teleconference participants were thanked for their attendance and the teleconference was adjourned at approximately 3:57 pm.

On Behalf of the Committee,
Respectfully Submitted,

Certified as True,

/s/

/s/

Shaunta Hill-Hammond, Ph.D.
Designated Federal Officer

Janice Chambers, Ph.D.
Chair, Chemical Assessment Advisory
Committee Augmented for the ETBE/tBA
Review

NOTE AND DISCLAIMER: The minutes of this public teleconference reflect diverse ideas and suggestions offered by committee members during the course of deliberations within the teleconference. Such ideas, suggestions, and deliberations do not necessarily reflect definitive consensus advice from the Panel members. The reader is cautioned to not rely on the minutes to represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations may be found in the final advisories, commentaries, letters, or reports prepared and transmitted to the EPA Administrator following the public meetings.

Appendix A

**List of Participants and Requests for Call-In Information for the Chemical Assessment
Advisory Committee (CAAC) Augmented for the Review of *ETBE and tBA*
Public Teleconference
March 22 and 27, 2018**

Name	Affiliation
James Avery	US EPA
Dahnish Shams	US EPA
Ravi Subramaniam	US EPA
Tina Bahadori	US EPA
Amanda Persad	US EPA
Janice Lee	US EPA
Kris Thayer	US EPA
Paul Schlosser	US EPA
Vicki Soto	US EPA
Channa Keshava	US EPA
Kathleen Newhouse	US EPA
Mary Ross	US EPA
James Weaver	US EPA
Edmond Bourke	Not available
Nagu Keshava	Not available
Tiffany Stecker	Not available
Maria Hegstad	Inside EPA
James Bus	Exponent, Inc., on behalf of LyondellBasell
Samuel Cohen	University of Nebraska Medical Center
Kevin Bromberg	SBA Advocacy
Jessica Ryman-Rasmussen	American Petroleum Institute
Michael Honeycutt	Texas Commission on Environmental Quality
Rebecca Hersher	National Public Radio
Barbara Hayes	Hyundai America Technical Center, Inc.
Karen Martin	U.S. EPA
Joanne Caroline English	Independent Consultant
Katy Goyak	ExxonMobil Biomedical Sciences, Inc.
Todd Menssen	Uponor, Inc.
Andrew Pawlisz	P66
Kashyap Thakore	California Department of Public Health
Garrett Keating	State of California - Cal/OSHA
Sylvia Carignan	Bloomberg Environment
Gulan Sun	Motiva Enterprises LLC

Materials Cited

The following teleconference materials are available on the SAB webpage at:

<https://yosemite.epa.gov/sab/sabproduct.nsf/a84bfee16cc358ad85256ccd006b0b4b/46495425f4649f7e85258227003ec276!OpenDocument&Date=2018-03-22>.

¹ SAB Review of EPA's Draft Toxicological Review of Ethyl Tertiary Butyl Ether and Draft Toxicological Review of tert-Butyl Alcohol 2.21.18.

² Roster.

³ Agenda.

⁴ Federal Register Notice Announcing the Meeting.

⁵ 03-22-18 List of Registered Public Speakers.

⁶ Written comments submitted by Jessica Ryman-Rasmussen on behalf of the American Petroleum Institute (API).

⁷ 03-19-18 Written comments submitted by Samuel Cohen.

⁸ 03-22-18 Oral comments presented by James Bus on behalf of LyondellBasell.

⁹ U.S. EPA comments on the 02/21/2018 SAB Draft Peer Review Report.

¹⁰ 03-08-18 Compilation of Panelist comments on the SAB Draft ETBE/tBA Report.

¹¹ 03-27-18 List of Registered Public Clarifying Commenters.

¹² 03-27-18 Clarifying comments submitted by James Bus on behalf of LyondellBasell.

¹³ 03-27-18 Clarifying comments submitted by Kevin L. Bromberg