

United States Environmental Protection Agency (U.S. EPA)
Science Advisory Board (SAB)
Teleconference Meeting
January 26, 2016
Meeting Minutes

Date and Time: January 26, 2016, 2:00 p.m. to 4:00 p.m.

Location: By teleconference only

Purpose: To review the SAB Draft (12/21/2015) Review of EPA's Draft Assessment entitled Toxicological Review of Benzo[a]pyrene (September 2014)

Meeting Participants:

SAB Members (see Roster¹)

Dr. Peter S. Thorne, Chair	Dr. Kimberly L. Jones	Mr. Richard L. Poirot
Dr. Joseph Arvai	Dr. Catherine J. Karr	Dr. Kenneth M. Portier
Dr. Kiros T. Berhane	Dr. Madhu Khanna	Dr. Kenneth Ramos
Dr. Sylvie M. Brouder	Dr. Francine Laden	Dr. Tara L. Sabo-Atwood
Dr. Ingrid Burke	Dr. Lois Lehman-	Dr. William Schlesinger
Dr. Michael Dourson	McKeeman	Dr. Gina Solomon
Dr. Joel J. Ducoste	Dr. Robert E. Mace	Dr. Daniel O. Stram
Dr. David A. Dzombak	Dr. Mary Sue Marty	Dr. Jay Turner
Dr. Elaine M. Faustman	Dr. Denise Mauzerall	Dr. Jeanne M. VanBriesen
Dr. Susan P. Felter	Dr. Kristina D. Mena	Dr. John Vena
Dr. William Field	Dr. Surabi Menon	Dr. Elke Weber
Dr. H. Christopher Frey	Dr. James R. Mihelcic	Dr. Charles Werth
Dr. Steven Hamburg	Dr. H. Keith Moo-Young	Dr. Peter J. Wilcoxon
Dr. Cynthia M. Harris	Dr. James Opaluch	Dr. Robyn S. Wilson
Dr. Robert J. Johnston	Dr. Thomas F. Parkerton	

SAB Staff:

Mr. Thomas Carpenter, Designated Federal Officer (DFO), for the Chartered SAB
Mr. Thomas Brennan, SAB Staff Office Deputy Director
Dr. Diana Wong, DFO, Chemical Assessment Advisory Committee Augmented for the Review of Draft Integrated Risk Information System Benzo[a]pyrene Assessment

Other Attendees: Names of those who requested the teleconference call-in number are provided in Attachment A.

Meeting Materials:

All materials for the meeting are available on the SAB webpage at:

<http://yosemite.epa.gov/sab/sabproduct.nsf/a84bfee16cc358ad85256ccd006b0b4b/e999ba302bda638a85257f16007c6b3f!OpenDocument&Date=2016-01-26>

Meeting Summary:

Convene the meeting

Mr. Thomas Carpenter, Designated Federal Officer (DFO) for the chartered SAB, formally opened the meeting and noted that this federal advisory committee teleconference was announced in the Federal Register² (published December 21, 2015, 80 FR 79337). The SAB is an independent, expert federal advisory committee chartered under the authority of the Federal Advisory Committee Act (FACA). The SAB is empowered by law, the Environmental Research, Development, and Demonstration Authorization Act (ERDDAA), to provide advice to the EPA Administrator on scientific and technical issues that support the EPA's decisions. The DFO noted that the Federal Register notice announcing the meeting had provided the public with an opportunity to provide written and oral comment.

The DFO stated that the SAB consists entirely of special government employees (SGEs) appointed by EPA to their positions. As SGEs, chartered SAB members are subject to all applicable ethics laws and implementing regulations. EPA has determined that advisors participating in this meeting have no financial conflicts of interest or appearance of a loss of impartiality under ethic regulations specified in 5 CFR 2635 relating to the topic of this meeting.

Purpose of the teleconference and review of the agenda

The SAB Chair, Dr. Peter Thorne, stated that the purpose of the teleconference was to conduct a quality review of the SAB Draft (12/21/2015) Review of EPA's Draft Assessment entitled Toxicological Review of Benzo[a]pyrene (September 2014). Dr. Thorne noted that the EPA staff were the only registered speakers.

Dr. Thorne reminded members that the purpose of the quality review is to determine if the report is ready to transmit to the Administrator as an SAB report and under what conditions. In reaching that determination he asked them to focus on the SAB's four quality review questions:

- Were the charge questions adequately addressed?
- Are there any technical errors or omissions in the report or issues that are not adequately dealt with in the draft report?
- Is the draft report clear and logical?
- Are the conclusions drawn or recommendations provided supported by the body of the draft report?

He noted there were no requests from the public to provide oral comment and one written public comment was available on the SAB website. The review would begin with a brief statement from EPA staff, then Dr. Elaine Faustman, Chair of the SAB Chemical Assessment Advisory Committee Augmented for the Review of Draft IRIS Benzo[a]pyrene Assessment (hereafter

referred to as the BaP Panel), would provide an overview of the report, followed by the lead reviewer comments and then comments from other board members.

EPA Remarks

Dr. Vincent Cogliano, Director, IRIS, National Center for Environmental Assessment thanked the BaP Panel for their thorough review. He noted there were many recommendations at differing levels of specificity and asked the SAB to consider prioritizing the recommendations. For example, one recommendation regarding studies that the BaP Panel thought were missing from EPA's assessment and should be included. The literature for this study was begun a prior to 2013 and there were limitations for the number of studies the agency could carry forward. He also noted that the agency is moving toward systematic reviews and this assessment was begun prior to that effort. He explained that the exclusion of studies was part process to select the most appropriate studies and part software technology capacity.

He asked if the SAB could identify recommendations that are necessary to finalize the report and those that may not be worth the level of effort or provide minimal improvement to the assessment. For example, the recommendation requiring additional analysis to update the carcinogenic research information. He noted that the International Agency for Research on Cancer (IARC) performed that analysis about five years ago will most likely not be worth the level of effort to replicate what IARC has already done with no resulting difference.

He noted that EPA is planning to continue more work on the development of the dermal slope factor with public engagement through workshops and other venues.

Presentation from the Panel Chair

Dr. Thorne introduced Dr. Elaine Faustman, Chair of the BaP Panel and asked her to provide an overview of the draft report as an introduction to the quality review discussion.

Dr. Faustman noted that the 26 member BaP Panel was one of the largest groups convened for an IRIS review by the SAB and attributed this to the importance of BaP as an environmental pollutant with a high degree of exposure. She thanked the BaP Panel and noted they included the most often recognized and prominent researchers working on BaP.

She highlighted several key points in the review of the assessment for the Board:

- Developmental effects presented in the assessment are the most appropriate non-cancer endpoints for deriving an RfD.
- Neurodevelopmental endpoints used are the most appropriate results however the Panel finds the discussion and rationale needs to be strengthened.
- The BaP Panel identified some areas where there should be additional critical studies listed in the literature review (i.e., mechanistic studies, immunological responses).

- The report commends the agency's efforts in deriving the IRIS Program's first dermal slope factor (DSF). However, the proposed DSF is not sufficiently supported scientifically and they recommend additional studies be included.

She acknowledged that that the report provides recommendations and suggestions to improve the assessment and the BaP Panel recognizes that some of these will require time. However, she noted the BaP Panel found the agency should not delay releasing an assessment while the agency implements additional research and analyses to address all the comments. She thanked the SAB members for their detailed comments on the report and thinks many of the comments can be addressed.

Chartered SAB Discussion and Disposition of the Report

After Dr. Faustman completed her remarks Dr. Thorne asked the lead reviewers to briefly summarize their comments³.

Dr. Francine Laden was the first lead reviewer and noted that the charge questions were very thoroughly addressed. She noted that the report provided suggestions and possible solutions in cases where the reviewers disagreed with the agency's approach. She suggested it would be helpful to summarize the discussed recommendations at the end of each section.

Dr. Gina Solomon, the second lead reviewer, agreed with Dr. Laden and stated that this was the most thorough report she has reviewed at the SAB and that it is a model for SAB reports. It was well organized, very clear and addresses all the quality review questions. She found no omissions. She noted that the pulmonary toxicology of BaP is discussed in the executive summary and should be brought forward into the letter to the Administrator.

She concluded by noting that her only concern is in regards to the greater scope of the IRIS assessment. If the goal is to help the program move forward more quickly, the reviewers are demanding a lot of detailed work from EPA. As reviewers, SAB members need to think about what is really important, critical to the document and make sure that EPA is identifying the appropriate hazards and developing well-supported toxicological assessments. But the SAB has to be careful not to get too carried away by trying to make each of these documents perfect.

Dr. Stram, the third lead reviewer, agreed with the previous reviewers and noted that this is an incredibly detailed report. This is particularly true where there is disagreement with EPA. In general, he agreed the recommendations and conclusions of the draft report are well supported. He found that the report may be too detailed.

He identified a potential technical error on page 42 of the draft SAB report. This has to do with whether the Sivak data were correctly modified by dividing by $(Le / 104)^3$. He referred members to his written comments that discuss the divisor, EPA's use of the Doll 1971 reference, and two possible approaches on EPA assumptions in this analysis.

Dr. Vena, the fourth lead reviewer, concurred with the other lead reviewers and stated he was overwhelmed with the thoroughness and comprehensive detail in the report main body, but that

did not generate concerns. He noted that the letter to the Administrator and the executive summary do not capture the sentiments of the full review report. For example, there are no statements in the cover letter indicating where the SAB agrees with the assessment as a whole. The consensus advice in the letter is overall well done and specific recommendations to improve specific details of the assessment are highlighted. He would like to see Appendix C be brought forward into the report.

Dr. Thorne thanked the lead reviewers for their comments. He then began the Board's general discussion of the draft report with Dr. Faustman addressing the lead reviewers' comments.

Dr. Faustman thanked the lead reviewers and noted that the letter and executive summary can be revised to address the comments. She also agreed that they could go through the recommendations to summarize them at the end of sections and more clearly distinguish "recommendations" from "suggestions" and identify which recommendations are needed to finalize the assessment.

Dr. Thorne thanked the lead reviewers and Dr. Faustman. He then opened the discussion to the remaining members on the teleconference. Several members agreed with the lead reviewers on the overall quality of the report.

One member commented that he was impressed with the overall report and the balanced panel. He noted he had three minor comments: 1) regarding the word choice used for the critical effect, 2) that there is a 500-fold difference between the reference concentration (RfC) and reference dose (RfD) that may not be specific to systemic toxicity, and whether a child-specific factor for BaP should be used to develop the RfC and RfD (and data are available for it) rather than using the default value. He noted that these are detailed in his comments. He noted there are also two concerns 1) the use of dose-response concordance and bimodal mode of action (MOA) he would like to discuss. Dose response concordance was stated for the tumor and mutations. He commented that adducts may form, yet they are not indicative of tumors being formed or causality to the chemical. He encouraged a recommendation for EPA to develop guidance for how to utilize dose concordance tables. He continued to note the MOA for BaP is bimodal. He noted that EPA explains the bimodality well and suggests that EPA guidelines are available and should be evaluated for BaP. He concluded noting the great job of the BaP Panel and chair describing it as quite remarkable.

Another member also recognized the tremendous amount of work done. Though one area remains confusing, the calculation of the dermal slope factor and choice of the dose metric. The report sets a precedent for dermal exposure, a very complicated issue, and notes that the appendix in the EPA assessment uses a choice of dose metric between absorbed and applied doses. She asked if there was discussion around developing methodology rather than developing a specific value as a guidance.

Dr. Faustman deferred to Dr. Cogliano to expand on his earlier statements on the agency's plan for the dermal slope factor. Dr. Cogliano noted the agency plans to conduct more work on the dermal slope factor. IRIS staff are developing a general dermal slope factor approach that may be difficult because many chemicals have different properties. He stated that there is an agency

need for a BaP dermal slope factor. He concluded by noting that the agency is planning a workshop to have public discussion. He highlighted the difficulty of developing a guidance document that is general. The agency's specific need for BaP dermal slope factor is important to many programs. Dr. Faustman added that BaP also provides a great deal of data, and addresses many factors that could be used to develop the more generic approach.

Dr. Faustman called upon Dr. John Kessel, a member of the BaP Panel, to describe some of the methods and assumptions used in the World Health Organizations guidance to address dermal exposure. He noted that the loading and exposure both need to be considered because it is possible to load too much material and depress the amount absorbed thus effecting the subsequent analyses. The WHO Committee on Dermal exposure, of which Dr. Kessel is a member, found it is possible to overload the dermal absorption to limit the rate absorbed across skin. He also commented on Dr. Stram's statement that the age adjustment factor in the report is a mistake and age adjustment was used for multi-stage analyses and the two analyses conducted on the Sevak data.

Dr. Faustman called upon Dr. John DiGiovanni, a member of the BaP Panel to address the dose concordance issues raised by SAB members. Dr. DiGiovanni noted that the BaP Panel discussed this subject at length. BaP is a mutagen and DNA damages occur prior to tumor formation. *In vitro* data clearly show that adduct formation and epoxide mutations occur with low frequencies and are difficult to detect. He noted that BaP is a complete carcinogen and the initial event is the mutagenic event followed by expansion of mutated cells. DNA adducts are induced in single applications of DMBA (7,12-dimethylbenz(a)anthracene). He noted that his research has shown that BaP can either induce tumors after a single topical application to mouse skin followed by repeated tumor promoter treatment or when given repeatedly in a complete carcinogenesis protocol. He noted much research tends to focus on a mutagenic MOA for BaP, as mentioned above, there is additional evidence for the role of promotion/proliferation in BaP carcinogenesis. Furthermore, both mutagenic and proliferative mechanisms occur simultaneously. A good example of this is the induction of mouse forestomach tumors by oral exposure to BaP. This discussion is included in the report and the BaP Panel found that the MOA must include both the initiating (mutagenic) effects and the promoting effects. Dr. Miriam Porirer, another BaP Panel member, agreed that adducts/mutations are difficult to detect and results depends on how a study detects and measures them.

Another Board member noted that the report is an exceptional document. She asked why the BaP Panel feels comfortable using the mixture data and to consider providing this explanation early in the report. Dr Ken Portier, a BaP Panel member, noted that there is a discussion on mixture uncertainties on pages 37-38 of the report.

Dr. Thorne thanked Dr. Faustman for her responses. He then asked SAB members if they had additional comments they would like to bring up. Hearing none he proceeded with the disposition of the report. He noted that the report should not be returned to the BaP Panel for additional review based on the Board's recognition of the report's quality and the member's discussions provided suggestions to address the dermal slope factor dosimetry and other issues raised in the quality review. He reminded members that the recommendations for pulmonary toxicological values and mixtures should also be discussed in the letter to the Administrator and

the Executive Summary of the final report. He then proposed two options for the Board's consideration.

Option 1: The SAB chair and Dr. Faustman address the comments to finalize the report and forward it to the Administrator.

Option 2: Dr. Faustman and the lead reviewers address the comments raised in the discussion for this review and forward the final report to the Administrator.

He then asked for a motion to dispose of the report.

Dr. Indy Burke moved that the Board use Option 1 to finalize the report and Dr. Steven Hamburg seconded the motion.

Dr. Dourson asked why not use option 2, the lead reviewers revise the report with the Chairs. Dr. Burke replied that the discussion leads her to believe that the changes can be made with minor editing and revision to the text as discussed. She finds that could be accomplished by the BaP Panel Chair.

Dr. Thorne invited SAB members to discuss the motion.

SAB members did not have any further comments on the motion and agreed to vote. The motion was approved unanimously with no abstentions.

The DFO adjourned the meeting at 3:30 p.m.

Respectfully Submitted

Certified as Accurate

/signed/
Mr. Thomas Carpenter
SAB DFO

/signed/
Dr. Peter S. Thorne
SAB 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 BaP 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.

Attachment A: Names of those who requested the teleconference call-in number

Michael L. Richards, Exxon Mobil Corp
Chris Saranko, PhD, DABT Geosyntec Consultants
Allison D. Foley, Esq., Venable LLP
Alan H Stern, EPA-SAB CAAC for BaP
John C. Kissel, PhD, PE, Professor Environmental and Occupational Health Sciences University
of Washington
Bhagavatula Moorthy, Baylor College of Medicine
H. Shen, Shell Oil Company
Fred Reitman, Shell Oil Company
Sue Shallal, US EPA, SABSO
W. Michael Foster, BaP Panel member
Miriam Poirier, National Cancer Institute
Stephen Roberts, University of Florida
Joanne Caroline English, NSF International
Kathleen Newhouse, US EPA
Annette Bunge, Colorado School of Mines
Maria Hegstad, Inside EPA
Vincent Cogliano, PhD, Director, Integrated Risk Information System (IRIS)
Anita Meyer, Army Corps Engineers
Annette Rohr, Electric Power Research Institute
Rayna Laiosa, PSEG
Anne LeHuray, PhD, Pavement Council
Felix Ayala-Fierro, ITG Brands
Resha Putzrath, Navy and Marine Corps Public Health Center
James Kim, Office of Management and Budget
Nancy B. Beck, PhD, DABT, American Chemistry Council
Pat Rizzuto, Chemicals Reporter, Bloomberg BNA, Inc.

Materials Cited

The following meeting materials are available on the SAB January 26, 2016, meeting webpage:

<https://yosemite.epa.gov/sab/sabproduct.nsf/a84bfee16cc358ad85256ccd006b0b4b/e999ba302bd638a85257f16007c6b3f!OpenDocument&Date=2016-01-26>

SAB Draft (12/21/2015) Review of EPA's Draft Assessment entitled Toxicological Review of Benzo[a]pyrene (September 2014)

¹ Roster

² Federal Register Notice Announcing the Public meeting

³ Quality Review Comments from Members of the Chartered SAB on the SAB Draft Report as of 1/25/2016.