

**Summary Minutes of the
U.S. Environmental Protection Agency
Science Advisory Board
Chemical Assessment Advisory Committee (CAAC)
April 2-3, 2013**

CAAC members:

Dr. Martin Philbert (Chair)
Dr. Daniel Acosta
Dr. Henry Anderson
Dr. Scott Bartell
Dr. James Bruckner
Dr. Deborah Cory-Slechta
Dr. William Michael Foster
Dr. Helen Goeden
Dr. Russ Hauser
Dr. Cynthia Harris – on the phone
Dr. Sean Hays
Dr. James E. Klaunig
Dr. Lawrence Lash
Dr. Maureen Lichtveld – did not participate
Dr. Abby Li
Dr. Maria Morandi
Dr. Victoria Persky
Dr. Kenneth Ramos – on the phone
Dr. Lorenz Rhomberg
Dr. Stephen M. Roberts
Dr. Robert Skoglund
Dr. Katherine S. Squibb
Dr. Leslie T. Stayner
Dr. Alan Stern
Dr. Rochelle Tyl

Purpose: The purpose of the CAAC meeting is to: 1) acquaint committee members with the work of the IRIS Program; 2) orient them to the process it uses to develop chemical assessments, also known as Toxicological Reviews; and 3) to discuss the role of the CAAC in this process.

Designated Federal Officer: Dr. Suhair Shallal

Other EPA Staff: see appended list of participants (Appendix A)

Public: see appended list of participants (Appendix A)

Meeting Materials and Meeting Webpage:

The materials listed below may be found on the meeting webpage at:

<http://yosemite.epa.gov/sab/sabproduct.nsf/a84bfee16cc358ad85256ccd006b0b4b/1363eb27571284ed85257b0f0062f32b!OpenDocument&Date=2013-04-02>

- Agenda
- Federal Register Notice
- Roster
- Public Comments
- Agency Briefing Material
 - IRIS: Toxicological Reviews and Process
 - Dose-Response Analysis
 - IRIS Hazard Identification
 - Science and Science Policy
 - Foundation for IRIS Assessments
- Invited Expert-provided Material
 - NRC Committees to Review the IRIS Draft Formaldehyde Assessment and the IRIS Process, presentation by Jonathan Samet
- Public comment submitted to the SAB Staff Office
 - Oral Comments presented by Charles Elkins
 - Oral Comments presented by Dr. Richard Denison
 - Presentation slides from Robert Fensterheim
 - Presentations slides from Nancy Beck, American Chemistry Council
 - Public Comments presented by Dr. Jennifer Sass
 - Public comments submitted by Charles Elkins
 - Public comments submitted by Dr. Kimberly Wise, ACC Center for Advancing Risk Assessment Science and Policy Public
 - comments submitted by Dr. Robert Fensterheim
- SAB Staff Office Material
 - SAB Committee/Panel Formation and the CAAC

Meeting Summary:

The discussion followed the general plan as presented in the meeting agenda.

Tuesday April 2, 2013

Opening Remarks

Dr. Shallal convened the meeting and announced that Drs. Ramos and Harris are participating via teleconference. Dr. Lichtveld did not participate due to illness and Dr. Williams withdrew due to other commitments. Dr. Shallal explained that all committee members are required to provide updated information on their confidential financial disclosure forms annually and to respond to questions regarding their impartiality on the issues being presented at the meeting. For today's meeting, she stated that the nature and scope of this SAB activity was examined and it was determined that it is a fact-finding activity where committee members will be briefed on the work of the EPA National Center for Environmental Assessment's IRIS program and the improvements that have been and are being implemented in response to recommendations by the National Research Council (NRC). Furthermore, she noted that no documents or other work products had been brought to this committee for their review at this time. However, when a review of a document is requested and advice is to be given, the SAB Staff Office Director will make the final determination as to who may serve as a member on that augmented committee based on the materials being reviewed.

She also reminded the audience and those participating via teleconference that all meeting materials were available on the SAB website. She then called on Mr. Chris Zarba, SAB Staff Office Acting Director, to present his welcoming remarks before turning the meeting over to Dr. Martin Philbert, Chair of the CAAC.

After Mr. Zarba welcomed the committee and audience members, he turned the meeting over to Dr. Philbert. Dr. Philbert reviewed the agenda and asked committee members to introduce themselves and to briefly explain their affiliation and areas of expertise. After all members introduced themselves, Dr. Philbert invited the Agency representatives to begin their presentations.

Dr. John Vandenberg was first to speak; he introduced Dr. Kenneth Olden, Director of the National Center for Environmental Assessment (NCEA), to make a few opening remarks. Dr. Olden outlined his vision for the IRIS program and his commitment to make improvements to the IRIS process. He stated that decisions regarding chemical safety must be made to protect the health of the public and chemical assessments must be anchored in the best science possible. He also talked about the work that has been done to reach out to the stakeholder community and the enhancements to the IRIS program that are being developed. Dr. Vandenberg then added his appreciation for the willingness of committee members to serve on the CAAC. He asserted that this committee would provide much needed continuity to the chemical assessment peer review process and would improve the final product.

Dr. Lynn Flowers was the next presenter (presentation posted on the SAB website). In brief, she focused on providing an overview of the IRIS program, the use of the assessments that are developed, the Health and Environmental Research Online (HERO) database, the chemical assessments that are currently under development and the role of the CAAC in the process. She stated that the program was embracing and implementing the NRC recommendations. This includes developing a standardized format for the assessments, unifying the cancer and non-cancer dose response framework, systematically identifying relevant studies, providing the rationale and criteria for evaluating and selecting studies that are used to calculate toxicity values.

Next, Dr. Jonathan Samet, the Chair of the National Research Council (NRC) Formaldehyde Review Committee, spoke via telephone about the recommendations that the NRC provided to the IRIS program (presentation posted on the SAB website). In summary, he explained that while reviewing the Formaldehyde assessment, the NRC committee noted a number of issues that were of general concern for other IRIS assessments as well. There were six major recommendations from the NRC committee. They include, the need 1) to reduce the volume of the text and eliminate redundancy and inconsistency, 2) to provide the criteria for including and excluding studies, 3) to standardize evidence tables, 4) to evaluate the strengths and weaknesses of critical studies, 5) to provide the rationale for selection of studies used in calculating RfC and unit risk, and finally, 6) the weight-of-evidence descriptions should indicate the determinants of "weight".

The next presenter was Dr. Vincent Cogliano (presentation posted on the SAB website). Briefly, he explained to the CAAC members the 5 steps in the process for developing a chemical assessment. These steps include: 1) identifying the evidence; 2) evaluating the evidence/studies; 3) integrating the evidence of each effect; 4) selecting studies for deriving the toxicity values;

and 5) deriving the toxicity values including the use of models, uncertainty values, reference dose/reference concentration (RfD/RfC). He further elaborated that chemical assessments are developed by interdisciplinary teams that incorporate all available information, using other risk assessments from other organizations (e.g., California Environmental Protection Agency (CalEPA), Toxicology Excellence for Risk Assessment (TERA), etc.), using models where appropriate, updating throughout the development process by adding new studies or other information, and including susceptible subpopulation (e.g., children). Members asked to have access to the Draft Handbook for Assessors; a URL was to be made available.

Dr. Samantha Jones was the next presenter (presentation posted on the SAB website); she provided a more in depth description of the hazard identification steps 1, 2 and 3. In brief, she explained that in step 1, a literature search is conducted and documented. She then described how studies are systematically reviewed and a project page is developed for each IRIS Toxicological Review. In step 2, she continued to explain that the studies are evaluated for relevance and quality. Members of the committee asked about the selection criteria that was used and how bias was avoided. She responded that 2 individuals reviewed the studies as a quality assurance step. She also indicated that the full text of the study is used to minimize the possibility of overlooking data. In step 3, Dr. Jones explained that data is synthesized and integrated by looking across human, animal and mechanistic evidence. A summary of the potential hazards and a rationale for those hazards that are carried forward in the dose-response analysis is provided at end of the Hazard Identification chapter of the IRIS assessment, she stated. A member of the committee commented that a meta-analysis approach may be useful to combine all the data. Others noted that the best data may not always be associated with the most relevant effects. Another member remarked that a balance needs to be established between a more streamlined process with concise information versus a more detailed narrative and then observed that a standardized weight-of-the-evidence approach may be a good approach.

Dr. Weihsueh Chui followed with his presentation on the selection of studies and derivation of toxicity values (presentation posted on the SAB website). He began by explaining that toxicity values are intended to be public health protective. He described the process used in dose-response analysis and said it included evaluating and selecting studies for the derivation of toxicity values, consideration of mode of action (MOA), analysis of observed dose-response data in these studies, estimating a point of departure, and applying inferences at lower doses to derive a toxicity value. He then noted that in IRIS assessments, documentation of the conclusions and selections of the toxicity values is provided. He also talked about the new, improved structure of IRIS assessments and stated that Dose-Response Analysis and Hazard Identification are discussed separately in these documents. He also stated that a composite toxicity value based on multiple candidate values can be considered.

A committee member noted that there are physiologically-based pharmacokinetic (PBPK) models that do not have well characterized compartments. Another committee member asked about the use of uncertainty factors. Dr. Chui responded by noting that the new format provides this information in a transparent manner, listing all assumptions so that the reader is aware of the uncertainty associated with a model and/or a dose-response value.

After the end of the presentations, committee members had an opportunity to ask EPA representatives some clarifying questions. A discussion regarding the opportunity to provide input into the process of developing an IRIS toxicological review ensued. EPA representatives

indicated that they are interested in making modifications to their current process that would allow for more input. The most effective and feasible opportunities to engage the public is currently under review.

Dr. Shallal adjourned the meeting for the day at approximately 5:00 pm.

Wednesday April 3, 2013

Dr. Shallal re-convened the meeting at 8:30 a.m. and reminded the committee members and the audience that this meeting was a continuation of the first meeting of the EPA SAB Chemical Assessment Advisory Committee. The purpose of the meeting was to allow the committee to learn more about the IRIS program and the development of IRIS toxicological Reviews.

Dr. Philbert then summarized the previous day's proceedings and a short discussion period ensued where committee members provided their impressions. A committee member commented that earlier input into the planning of an IRIS assessment is needed. Another committee member observed that having an early opportunity to review the charge questions associated with a review of an IRIS assessment is also needed. Others agreed that early input is important but cautioned that this may cause delays in the development of the assessments. A committee member noted that the early stage where problem formulation occurs is critical and it would be useful to the Agency to have some input into the identification and selection of data/studies. Questions arose regarding the selection of committee members and how the CAAC would operate. To respond to this question, Dr. Philbert then asked Dr. Shallal and Mr. Fort to provide their presentation which was available on the SAB website.

Dr. Shallal began by presenting an overview of the process that the SAB uses when forming an advisory committee or *ad hoc* panel. She asked Mr. Daniel Fort, Ethics Officer with the EPA Office of General Counsel, to explain the ethics considerations that are included in the evaluation of prospective candidates. He presented information regarding the ethics requirements for Special Government Employees (SGEs). He noted that the members of the CAAC are all SGEs and would have to abide by the rule and regulations for SGEs concerning conflicts of interest and impartiality that are defined in the Code of Federal Regulations. Dr. Shallal then continued her presentation and explained the formation of the CAAC and the SAB Staff Office plan to augment the CAAC with chemical-specific experts for the review of individual IRIS documents. She elaborated that when a new review is requested, a Federal Register notice will be published soliciting nominations of experts. The process for adding chemical-specific experts will be the same as that followed in the formation of the CAAC, with an additional evaluation of prospective panel members in the context of each advisory activity to ensure there are no concerns regarding conflicts of interest or an appearance of a loss of impartiality.

After a short break, the 8 registered public commenters were invited to present their oral comments and given 5 minutes each. After each presentation, committee members were asked if they had questions for the commenters. These oral comments are briefly summarized below (see the SAB website for the full written version of these presentations or associated powerpoint slides).

The first registered commenter was Mr. Chuck Elkins. He addressed the panel regarding 4 issues. He explained that the CAAC will have a unique opportunity to identify overarching issues as they gain experience after reviewing several IRIS assessments. He also suggested that the charge questions should be discussed before panels are formed. Then he noted that more time should be allotted to public comments and they should be used as a resource for the panel. Finally, he commented that the CAAC should remain independent from the Agency and provide critical advice.

The next presenter was Mr. Bob Fensterheim. He presented his suggestions on revising the charge before a panel is formed. He also offered his thoughts on the IRIS process and stakeholder involvement. In addition, he suggested ways that the CAAC could be augmented by chemical-specific experts.

He was followed by Dr. Kim Wise. Her presentation included comments on ways to determine which assessments would be reviewed by the CAAC and the need to review other NCEA products, e.g., guidance documents. She also discussed the need to develop a clear charge. She then noted that opportunities for public comments should be afforded during meetings and teleconferences of the CAAC.

Dr. Pat Casano was the next presenter and she commented on having the CAAC be involved early in the development of the IRIS assessments. She told committee members that they should be involved in the planning and scoping stage before an assessment is written. She suggested that the CAAC should help determine if a chemical causes an adverse effect. She further discussed the use of causation charts and then determining if the data is adequate to estimate risk.

She was then followed by Ms. Anne LeHuray. She talked about the intersection of science and science policy. She outlined several questions that should be answered when developing an IRIS assessment. For example, when is data sufficient to make a decision; how should issues of background and endogenous levels of a chemical be addressed; etc.

The next presenter was Dr. Nancy Beck. She indicated that oversimplification can be problematic. In the new structure of IRIS documents, the preamble seems disconnected from the assessment, she noted. She then elaborated that scientific plausibility of an effect should be the first consideration when developing an assessment. She reiterated that guidelines are complex and should not be oversimplified.

Dr. Jennifer Sass followed with her comments. She noted that the National Academy of Sciences released several reports recommending modernization of chemical health evaluations. She continued and summarized four main recommendations from these reports. They recommended, she said, that the EPA should: 1) incorporate variability in human exposure and vulnerability into health assessments, 2) if data is not available, use scientifically-based default assumptions that will protect health, rather than waiting for more data, 3) incorporate information about the potential impacts of exposure to multiple chemicals and, other factors, such as exposure to biological and radiological agents and social conditions, 4) presume that even low exposures are not risk free. Finally, she commented on the need for vetting of the members of the CAAC to eliminate bias and conflicts of interest.

The next speaker was Dr. Richard Denison. His comments were focused on 2 issues, 1) the conflict of interest and bias of committee members, and 2) the timeliness of IRIS assessments. He stated that some members were principals or founders of consulting firms which may create a conflict. He also stated his concerns regarding spending too much time on revising assessments which could cause delays in finalizing IRIS assessments.

Committee members voiced their concern regarding Dr. Denison's assertions that CAAC members had conflicts of interest. Another member agreed that timeliness of assessments is important, but stated that it was also important for assessments to be transparent with regard to the uncertainty of the risk estimates.

Since there was time available for more public comments, Dr. Philbert, the Chair of CAAC, invited other non-registered members of the public to address the CAAC. He called on Mr. Jamie Conrad, who had asked for an opportunity to present oral comment to the CAAC after the stated deadline. Mr. Conrad was not present and did not provide any comments. Mr. Kevin Bromberg was then called to provide his oral presentation. He introduced himself and stated that his office represented the voice of small business. He encouraged the committee to provide early input in the development of IRIS assessments. He also reinforced the need to engage public commenters and to consider their comments seriously as the committee develops its advice.

A committee member questioned the feasibility of responding formally to public comments. Members then entered into a discussion of the importance of having an opportunity to provide early advice on IRIS assessments. Others believed that providing advice too early may be counterproductive and too prescriptive. Another member suggested that the committee should have an opportunity to at least be observers in the early stages of developing an IRIS assessment so they gain an understanding of the issues associated with that assessment. Others added that the assignment of CAAC members to the review of a specific chemical should be done early.

As the discussion concluded, CAAC members did agree that some early involvement before an IRIS assessment has been developed is needed. EPA representatives indicated that enhancements to the IRIS development process may allow this to occur in a more systematic way in the future. CAAC members also commented that charge questions should also be discussed prior to the selection of the final augmented committee so that experts with the appropriate expertise could be included. Furthermore, CAAC members suggested that there should be flexibility in responding to public comments.

Dr. Shallal adjourned the meeting at approximately 1:00 pm

On Behalf of the Committee,

Respectfully Submitted,

/s /
Suhair Shallal, Ph.D.
Designated Federal Officer

Certified as Accurate:

/s/

Martin Philbert, Ph.D.
Chair, SAB Chemical Assessment Advisory Committee

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 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

EPA/Public Sign on April 2, 2013		
First Name	Last Name	Affiliation
Pat	Ambrosio	RNA
Nancy	Beck	ACC
Patrick	Bently	American Petroleum Institute
Ted	Berner	US EPA
David	Bottimore	Versar
Tom	Brennan	US EPA/SABSO
Sarah	Bresolin	SBA/Advisory
Kevin	Bromberg	SBA/Advisory
Tom	Carpenter	SAB Staff
Pat	Casano	GE
Weihseh	Chiu	US EPA
Vincent	Cogliano	US EPA/IRIS
Richard	Denison	Environmental Defense Fund (EDF)
David	Dunlap	KCPS
Chuck	Elkins	CETA
Bob	Fensterheim	RegNet
Anthony	Flood	IFIC
Lynn	Flowers	US EPA/NCEA
Martin	Gehlhaus	US EPA
Mara	Hegstad	Inside EPA Newsletter
Samantha	Jones	US EPA/NCEA
James	Kim	OMB
Anne	LeHuray	NCI
Keely	Maxwell	US EPA/AAAS
Lindsay	McCormick	ASPH/EPA Fellow

Angela	Nugent	US EPA/ SAB
Ken	Olden	US EPA
Glenn	Paulson	US EPA
David	Reynolds	Inside EPA Newsletter
Susan	Rieth	US EPA
Pat	Rizzuto	BNA
Jim	Rollins	Policy Navigation Group
Stephanie	Sanzone	US EPA/OSAB
Jen	Sass	NRDC
Alissa	Sasso	Environmental Defense Fund (EDF)
Alli	Schultz	Regnet Environmental Service
Rachel	Shaffer	Environmental Defense Fund (EDF)
Sue	Shallal	US EPA/SAB
Jamie	Strong	US EPA
Patricia	Underwood	DOD/ ATTL
John	Vandenberg	US EPA
Elizabeth	Wask	Beverage & Diamond
Debra	Watson	US EPA/NCEA
Phillip	Wexler	National Cobray Medicine
Kimberly	Wise	American Chemical Council
Diana	Wong	SAB Staff
Linda	Wonnorrton	NASA HQ
Aarron	Yeow	US EPA/SAB
Chris	Zarba	US EPA/SAB
Cheryl	Hogue	Chemical & Eng News

EPA/Public Sign on April 3, 2013		
First Name	Last Name	Company
Pat	Ambrosio	BNA

Patrick	Beatty	API
Norman	Birchfield	CEQ
Tom	Brennan	US EPA/SAB Staff Office
Sarah	Bresolin	SBA/Advisory
Kevin	Bromberg	SBA/Advisory
Tom	Carpenter	SAB Staff
Pat	Casano	GE
Weihshueh	Chiu	US EPA
Vince	Cogliano	EPA/IRIS
Richard	Denison	Environmental Defense Fund
Chuck	Elkins	CETA
Lynn	Flowers	US EPA/NCEA
Dan	Fort	US EPA
Maria	Hegstad	Inside EPA Newsletter
Samantha	Jones	US EPA
James	Kim	OMB
Anne	LeHuray	NCI
Lindsay	McCormick	US EPA/ASPH
Jim	Rollins	Policy Navigation Group
Jen	Sass	NRDC
Rachel	Shaffer	Environmental Defense Fund
John	Vandenberg	US EPA
Shi	Vu	
Debra	Walk	US EPA/NCEA
Elizabeth	Wask	Beverage & Diamond
Kimberly	Wise	ACC
Diana	Wong	SAB Staff
Aaron	Yeow	US EPA/SAB