

**Summary Minutes of the United States Environmental Protection Agency (U.S. EPA)
Science Advisory Board (SAB) Quality Review Teleconference
November 22, 2010**

Meeting of the Chartered SAB and SAB Liaisons¹

Date and Time: November 22, 2010, 2:00 p.m. – 5:00 p.m. Eastern Time

Location: By Teleconference

Purpose: To conduct a quality review of a draft SAB report entitled “SAB Report on the EPA’s Responsiveness to SAB 2007 Recommendations for the Revision of Cancer Assessment of Inorganic Arsenic (October 25, 2010 draft).”²

SAB Members and Liaison Participants:

SAB Members

Dr. Deborah Swackhamer, Chair
Dr. David Allen
Dr. Claudia Benitez-Nelson
Dr. Timothy Buckley
Dr. Ingrid Burke
Dr. Terry Daniel
Dr. George Daston
Dr. Costel Denson
Dr. Otto Doering
Dr. David Dzombak
Dr. T. Taylor Eighmy
Dr. Elaine Faustman
Dr. John Giesy
Dr. Jeffrey Griffiths
Dr. James Hammitt
Dr. Bernd Kahn
Dr. Agnes Kane
Dr. Madhu Khanna
Dr. Nancy Kim

Dr. Kai Lee
Dr. Cecil Lue-Hing
Dr. Lee D. McMullen
Dr. James Mihelcic
Dr. Jana Milford
Dr. Horace Moo-Young
Dr. Eileen Murphy
Dr. Duncan Patten
Dr. Arden Pope
Dr. Stephen Roberts
Dr. Amanda Rodewald
Dr. James Sanders
Dr. Jerald Schnoor
Dr. Katherine Segerson
Dr. Paige Tolbert
Dr. John Vena
Dr. Thomas Wallsten
Dr. Thomas Zoeller

Liaison Members

Dr. Pamela Shubat (Liaison with the Children's Health Protection Advisory Committee)

EPA presenters and representatives

Dr. John Vandenburg

SAB Staff Office Participants

Dr. Angela Nugent, Designated Federal Officer (DFO)

Dr. Vanessa Vu, Director

Teleconference Summary:

The teleconference was announced in the Federal Register³ and discussion generally followed the issues and timing as presented in the agenda.⁴

Convene the meeting

Dr. Angela Nugent, SAB DFO, convened the advisory meeting and welcomed the group. She noted that twelve individuals had requested to provide oral public comments and that written comments had been provided to SAB members and posted on the Web site.⁵

Purpose of meeting and review of the agenda

Dr. Deborah Swackhamer, the SAB Chair, welcomed SAB members and reviewed the purpose of the meeting. The SAB conducts quality reviews before an advisory report is transmitted to the EPA Administrator. Quality reviews focus on four questions:

1. Were the original charge questions to SAB Standing or Ad Hoc Committees adequately addressed?
2. Are there any technical errors or omissions in the report or issues that are not adequately dealt with in the Committee's report?
3. Is the Committee's report clear and logical?
4. Are the conclusions drawn or recommendations provided supported by the body of the Committee's report?

Overview of draft report

Dr. Elaine Faustman, Chair of the Work Group of the Chartered SAB for the Arsenic Cancer Review, provided an overview of the draft report. She noted that the work group focused on three areas: evaluation of epidemiological literature, dose-response modeling approaches; and the sensitivity analysis of the exposure assumptions used in the risk assessment. Her work group was not asked to conduct a full peer review of EPA's draft assessment. The work group considered public and SAB comment from the previous June 2010 quality review in developing the draft report. The draft report makes recommendations to improve the clarity and transparency of EPA's assessment and to strengthen the scientific basis of EPA's findings and conclusions.

Chartered SAB members had no clarifying questions for Dr. Faustman.

EPA Remarks

Dr. John Vandenberg of EPA's Office of Research and Development expressed thanks to the SAB work group and underscored the importance of EPA's assessment. EPA plans to complete its assessment in a timely fashion after the Agency has considered SAB and public comment. He provided one comment on the work group's draft report. He suggested that language be changed on page 1 lines 20 to insert the word "revised" before the word "assessment," since the SAB had conducted a full peer review of EPA's draft 2005 report. He also noted public comment for the teleconference criticizing EPA scientists' publication of an article in a peer reviewed journal. He clarified that EPA encourages Agency scientists to publish in the open literature.

Public comments

Dr. Swackhamer introduced twelve individuals who had requested public comment. She noted that each speaker had five minutes for comment.

Mr. Kevin Bromberg from the U.S. Small Business Administration provided oral comments related to the process for developing the work group's report and summarized his written comments. He asked the chartered SAB not to approve to work group report but to instruct the work group to meet in open session to address public comments.

Dr. Steven H. Lamm from Consultants in Epidemiology & Occupational Health spoke from a written statement provided to SAB members that focused on the relationship of arsenic ingestion (based on data from the Southwest Taiwan study) to bladder cancer and lung cancer, as compared with exposure ranges relevant to the U.S. population. He also referenced his written comments provided to the chartered SAB on other arsenic-related issues.

Dr. Barbara D. Beck from Gradient Corporation presented oral comments on behalf of the Organic Arsenical Products Task Force. She briefly summarized her written comments on two points: the adequacy of EPA's response to SAB recommendations in 2007 for revising the arsenic cancer assessment and EPA's lack of consideration of important new post 2010 literature on mode of action and low-dose studies.

Dr. Lorenz R. Rhomberg from Gradient Corporation presented comments on behalf of the North American Metals Council. He briefly summarized his written comments. He noted that the 2010 IRIS draft proposes a value for the oral unit risk for assessing arsenic carcinogenicity that were 4.5 times higher than the 2005 IRIS draft. He stated that the limited work group review did not evaluate the entire potency estimate and that such a full review was needed.

Ms. Lynn L. Bergeson from Bergeson & Campbell, P.C. presented comments on behalf of Drexel Chemical Company. She noted that EPA had: 1) not fully assessed research results since 2001; 2) had not fully responded to SAB 2007 advice; and 3) allowed EPA scientists to engage in public advocacy through publication of an article in the journal Environmental Health

Perspectives, asserting the superiority of the Taiwanese data. She asked the chartered SAB to “refuse to accept” the new IRIS cancer value until recently published literature was fully considered and until EPA fully responded to 2007 SAB recommendations. She asked the SAB to conduct a full peer review.

Dr. Samuel M. Cohen from the University of Nebraska Medical Center summarized his written comments and spoke about arsenic’s mode of action and implications for risk assessments for exposure to inorganic arsenic and drinking water. He stated that all the known modes of action are nonlinear and that linearity has been excluded as a mode of action for inorganic arsenic. He stated that EPA’s 2005 Cancer Guidelines do not require specific evidence to demonstrate nonlinearity for nonlinearity to be assumed at low doses. He described research supporting toxicokinetic and cytotoxic bases for different kinds of cancer. He also noted that epidemiological evidence suggested a non-linear mode of action.

Dr. Joyce S. Tsuji from Exponent summarized written comments provided on behalf of the Wood Preservative Science Council. She called for EPA to conduct a full meta-analysis of studies of arsenic at low-doses. Such a meta-analysis should compare key exposure factors and their implications for linear and non-linear mode of action. She recommended that EPA examine the entire arsenic literature and not rely solely on conservative assumptions.

Ms. Tawny A. Bridgeford from National Mining Association provided brief public comments. Her association represents producers of coal, metals, and agricultural minerals. She expressed concern that a “scientifically indefensible cancer slope factor” might drive Superfund and drinking water regulated limits below background levels. She noted that the potentially broad implications of the IRIS assessment merited a “fuller” review of EPA’s science.

Dr. William J. Adams from Rio Tinto provided brief oral comment. He stated that the “key question is whether proposed change in cancer slope factor is strong enough scientifically to proceed.” He stated that, should EPA adopt the proposed cancer slope factor, drinking water standards for would be reduced below current well water levels to achieve a 1 in 100,000 cancer risk. He stated that most of the soil in the United States would be considered contaminated. He noted that the work group’s draft report (page 10) called for a “reality check” on estimated risk levels. He acknowledged that an IRIS assessment was not a full risk assessment, but expressed concern that an overly conservative risk assessment would not support good decisions.

Dr. Michal Eldan from Luxembourg-Pamol, Inc. noted that the 2007 SAB review called attention to substantial evidence for nonlinear dose mode of action for arsenic. She also noted that EPA’s Cancer Guidelines state that EPA should consider non-linear assumptions when they are scientifically possible, even if not proven, when there is no evidence for linearity.

Dr. Deborah Swackhamer then introduced two public speakers who provided late requests to provide oral comments.

Dr. Michael Kosnett from the University of Colorado School of Medicine provided oral comments and emphasized two points related to the work of the National Research Council (NRC) Subcommittee that evaluated the assessment of cancer risk associated with exposure to

inorganic arsenic in a 2001 report. The NRC subcommittee supported the use of a linear model to extrapolate human cancer risks from the epidemiological data and noted that *in vitro* studies show multiple genotoxic and nongenotoxic effects consistent with a linear response at low levels. This conclusion is consistent with the conclusion reached by the SAB work group concerning linearity. He also noted that any “reality check” or assessment of plausibility of cancer estimates needed to be done carefully. He noted language in the 2001 NRC report specified that “although the subcommittee’s risk estimates are of public-health concern, they are not high enough to be easily detected in U.S. populations by comparing geographical differences in the rates of specific cancers with geographical differences in the concentrations of arsenic in drinking water.”

Dr. Richard Wilson provided oral comments drawing on written comments provided to the committee. He noted that the Taiwanese data were not appropriate for deriving a dose-response relationship. He stated that EPA should look at other sources of epidemiological data.

After the public comments, the SAB Chair asked chartered SAB members if they had questions for any of the public commenters. Chartered SAB members had no questions.

Chartered SAB Discussion

Dr. Swackhamer introduced the lead reviewers to begin the SAB discussion by summarizing their significant comments. She noted that two of the lead reviewers, Drs. Jonathan Samet and Steven Heeringa, had provided written comments but were unable to participate in the call. Dr. Swackhamer introduced the other lead reviewers who summarized their major comments.

Dr. Paige Tolbert, the first lead reviewer participating in the teleconference, stated that the work group adequately addressed their original charge questions. She did not find technical errors or omissions, but voiced concern about the work group recommendation that EPA summarize major studies since 2007 since such a step might impose a substantial delay in finalizing EPA’s assessment. She stated that the report was clear and logical and that the report’s conclusions were supported by the body of the report.

Dr. John Vena, the second lead review participating in the teleconference, stated his conclusion that the work group did an excellent job in addressing each original charge question. He also expressed concern about the recommendation that EPA include an addendum in its final IRIS assessment summarizing major studies since 2007. He asked for information about the process for future updates to the IRIS assessment for arsenic and suggested that studies published since 2007 might be evaluated in a future assessment. He concluded his remarks by mentioning that his written comments include some suggestions for strengthening the SAB work group’s draft report.

Dr. Thomas Zoeller, the third lead reviewer participating in the teleconference, agreed with the previous reviewers. He commended the work group for a well drafted document and agreed that all the original charge questions had been addressed. He noted that his written comment identified some minor issues and points of clarification for the work group’s consideration.

Dr. Pamela Shubat (SAB Liaison: Chair, Children's Health Protection Advisory Committee), the fourth lead reviewer participating in the teleconference, noted that her quality review was also consistent with those of the other lead reviewers. She noted that the work group "had a tough job," but that it had adhered to its original charge questions and had fully addressed those charge questions. She agreed that the only "strong comment" across all the lead reviewers related to the recommendation that EPA conduct a review of literature published after 2007. Dr. Swackhamer also noted that Drs. Samet and Heeringa expressed concern about EPA's developing an addendum to its 2010 assessment summarizing recent literature. Dr. Shubat acknowledged EPA's need to "stay on top of the literature," but expressed the view that it might be appropriate to provide such a summary or bibliography in another format or venue. Her one other comment pertained to occasional differences in key language and emphasis in the body of the report, as compared to the executive summary and letter to the Administrator. She noted that additional editing for consistency would be helpful.

Dr. Swackhamer asked Dr. Faustman, the work group chair, to respond to lead reviewer comments. Dr. Faustman noted that the work group could easily make the editorial changes requested by the lead reviewers. The work group could clarify the report regarding the recommendation concerning the addendum identifying recent studies and improve consistency of language in the letter, executive summary, and body of the report.

Dr. Swackhamer then asked other chartered SAB members to provide comments. SAB members made the following points.

- The letter and report should acknowledge the genuine major public and scientific interest in the arsenic assessment and should encourage EPA's revised assessment to acknowledge this public interest more fully. The work group report should encourage EPA to describe more transparently how EPA will revise the arsenic assessment as additional studies become available.
- Given the public comment, the work group report might be revised to emphasize the importance of accelerating review of the literature published since 2007
 - o Dr. Swackhamer asked Dr. John Vandenburg to clarify when the next IRIS cancer assessment for arsenic would be scheduled. Dr. Vandenburg stated that EPA has a list of priority chemicals for future based on EPA program needs. EPA recognizes arsenic as a high priority chemical and is constantly surveying literature. He stated that he was not aware of the next scheduled time for a re-assessment of cancer effects for arsenic.
- The work group properly commends EPA for addressing data available as of 2007, but the report should add a concern about the lack of sufficient, reliable data for assessing the effects of inorganic arsenic and call for EPA to prepare for a future assessment by addressing these data gaps.
- Public comments regarding justification for the nonlinear mode of action differ significantly from the conclusions reached by the work group. Most public comments stated that EPA improperly used the "out-dated" Taiwan data set, but one commenter stated that use of other data sets did not make a significant difference. SAB members asked if the work group report could address this difference in veews.

- The SAB work group focused on narrow charge questions, rather than a full assessment of EPA's draft cancer assessment and the public and some SAB members are not comfortable with this narrow focus.

Following this discussion, Dr. Swackhamer asked whether the Board would like to suggest that the SAB review EPA's revised IRIS cancer assessment at the same time the SAB reviews ORD's draft noncancer IRIS assessment, since the SAB Staff Office announced plans for reviewing ORD's draft noncancer IRIS assessment in May 2010. Such a review could provide a full integrated review of cancer and non-cancer effects. SAB members asked if such a proposal would delay release of EPA's draft cancer assessment. Dr. Swackhamer asked Dr. Vandenburg to explain EPA's plans for revising the draft IRIS cancer assessment and for developing the draft IRIS noncancer assessment. Dr. Vandenburg responded that EPA currently planned to revise its cancer assessment based on SAB comments and then submit it for internal EPA and interagency review, with the goal of completing the cancer assessment in four to six months. In parallel, EPA's Office of Research and Development is preparing for a preliminary internal EPA and interagency review of its noncancer assessment with the goal of developing a draft report for SAB peer review.

Board members expressed concern that such a proposal for linking the review of the cancer and noncancer assessments might delay EPA's planned completion of the draft IRIS cancer assessment. Other SAB reviewers endorsed the idea of a re-examination of the cancer assessment in the context of the noncancer review since the noncancer assessment may examine "precursor events that come before cancer" and shed light on cancer mode of action. Still other SAB members suggested that SAB also note the complex relationship between IRIS assessments and EPA risk management decisions. It may be useful at some future time to address how EPA integrates IRIS assessments into decision making. The SAB Chair expressed concern that such an activity may involve the SAB in providing advice on policy, rather than scientific issues, and involve the Board in issues beyond its proper scope.

A Board member moved that the draft report be approved subject to changes suggested in members' written and oral comments and re-review by the lead reviewers. The move was seconded.

Board members discussed that key revisions would include:

- o Clarifying language, as indicated in Board comments;
- o Better aligning the letter with the executive summary and body of the report
- o Some better acknowledgement of the existence of public concerns regarding the plausibility of a linear mode of action and research pointing to a non-linear mode of action beyond language on page 8, line 30 of the draft.
- o Clarifying that the literature addendum recommended should involve characterization of major epidemiological studies conducted since 2007
- o Including mention of possible SAB review of arsenic cancer mode of action as part of the SAB upcoming draft IRIS non-cancer review. Possibly include language such as "The SAB welcomes the upcoming opportunity for the Board to review the IRIS Assessment of the non-cancer effects of arsenic, and based on this review of the IRIS Assessment of cancer effects, we would be willing to also

include the most current mode-of-action data for cancer in that review to inform the non-cancer effects. This would also provide for a more integrated approach to the consideration of this important drinking water pollutant."

Dr. Swackhamer asked for a voice vote to approve the motion. There was universal approval with members of the SAB work group abstaining.

The Designated Federal Officer adjourned the meeting at 5:00 p.m.

Respectfully Submitted:

Certified as True:

/s/

/s/

Dr. Angela Nugent
SAB DFO

Dr. Deborah L. Swackhamer
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 panel members. The reader is cautioned to not rely on the minutes 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.

Materials Cited

The following meeting materials are available on the SAB Web site,

<http://www.epa.gov/sab>, at the following address:

<http://yosemite.epa.gov/sab/sabproduct.nsf/a84bfee16cc358ad85256ccd006b0b4b/138473f4b37b3225852577b300516041!OpenDocument&Date=2010-11-22>

¹ Roster, Chartered SAB Members and Liaisons

² Draft SAB report entitled “SAB Report on the EPA’s Responsiveness to SAB 2007 Recommendations for the Revision of Cancer Assessment of Inorganic Arsenic (October 25, 2010 draft).”

³ Federal Register Notice Announcing the Meeting

⁴ Agenda

⁵ Written public comments:

- Comments from Barbara Beck regarding Need to Include and Evaluate Relevant Recent Literature in the 2010 IRIS Arsenic Assessment
- Comments from Barbara Beck regarding unresolved scientific issues
- Comments from Exponent and Pamela Mink, Emory University on behalf of the Wood Preservative Science Council.
- Comments from Kevin L. Bromberg
- Comments from Lorenz R. Rhomberg
- Comments from Lorenz R. Rhomberg regarding interpretation of Cancer Guidelines
- Comments from Michael J. Kosnett,
- Comments from Michal Eldan on behalf of the Organic Arsenical Products Task Force with 2001 Gibbs et al. article from Environmental Health Perspectives
- Comments from Richard Wilson
- Comments from Samuel Cohen with attachments: article submitted to Toxicological comments and March 2010 previous comments
- Comments from Steven H. Lamm
- Comments from the Wood Preservative Science Council
- Comments provided by the Arsenic Coalition
- Data workbook from Steve Lamm with standard mortality ratio elements for the villages using the SW Taiwan population as the reference population
- Graph provided by Steve Lamm showing Standard Mortality Ratios (Bladder and Lung Cancer) vs. Southwest Taiwan Region for sub-groups of SW Taiwan Study Villages
- S. H. Lamm Comments for SAB Arsenic Teleconference (11/22/2010)
- S. H. Lamm Comments for SAB Arsenic Teleconference (11/22/2010) revised and resubmitted

Attachment A

Members of the Public Requesting Call-in Information for SAB Teleconference, November 22, 2010

William J. Adams
Kevin Archer
Nancy Beck
Norman Birchfield
Tawny A. Bridgeford
Bob Bukantis
Patricia Kablach Casano
Eric Dubé
P. Robinan Gentry
Peggy Hartness
David Harvey
Maria Hegstad
Katherine Kurtz
Jane C. Luxton
Rod McNeil
Mike Murphy
Resha M. Putzrath
Thornton L. Newlon
Santhini Ramasamy
Reeder Sams
Rosalind A. Schoof
J. Keith Tolson
Vera Wang
Brittany Westlake
George W. Wilson, Jr