

**Summary Minutes of the Science Advisory Board
US Environmental Protection Agency
EPA Science Advisory Board
Arsenic Review Panel
Public Conference Call Meeting
Planning for the Arsenic Review**

**By Teleconference Only
Thursday, August 11, 2005
1:00 pm – 3:00 pm Eastern Time
Call 202-343-9999 for teleconference number and code**

ARP Members: See Roster –Attachment A

Date and Time: Thursday, August 11, 2005 (See Attachment B for the Federal Register notice for the meeting)

Location: Telephone Conference Meeting

Purpose: The purpose of this meeting was for the Board to receive a briefing on the arsenic issues, documents, and charge to the SAB and to plan for the Panel's September 12-13, 2005 advisory meeting.

Attendees: Panel Chair: Dr. Genevieve Matanoski (see Panel Roster in Attachment A)

Panel Members:

1. Dr. Genevieve Matanoski, Chair, Johns Hopkins University
2. Dr. H. Vasken Aposhian, University of Arizona
3. Dr. Aaron Barchowsky, University of Pittsburgh
4. Dr. David Brusick, Covance, Retired
5. Dr. Kenneth Cantor, National Cancer Institute
6. Dr. Jack Colford, University of California, Berkeley
7. Dr. Yvonne Dragan, National Center for Toxicological Research
8. Dr. Sidney Green, Howard University
9. Dr. Sioban Harlow, University of Michigan
10. Dr. Steven Heeringa, University of Michigan
11. Dr. Claudia Hopenhayn, University of Kentucky
12. Dr. James Klaunig, Indiana University
13. Dr. X. Chris Le, University of Alberta
14. Dr. Michelle Medinsky, Consultant
15. Dr. Kenneth Portier, University of Florida
16. Dr. Barry Rosen, Wayne State University
17. Dr. Toby Rossman, New York University
18. Dr. Justin Teegarden, Pacific Northwest National Laboratory
19. Dr. Miroslav Styblo, University of North Carolina
20. Dr. Michael Waalkes, National Cancer Institute
21. Dr. Janice Yager, Electric Power Research Institute

Others Participating in the Call:

1. EPA

a) Presenters:

- i) Dr. Ila Cote, EPA ORD
- ii) Dr. Edward Ohanian, EPA OW
- iii) Dr. Tony Maciorowski, EPA OSAB

b) Other: Reeder Sams, Elizabeth Doyle, Anna Lowit, Irene Dooley, TimMcMahon, Brenda Foos, Eric Burneson, David Cooper, Ila Cote, Vivian Turner, Larry Dorsey, Steve Knott, Nicole Pavlos, Doug Wolf, Johnathan Chen, Karl Baetcke, Diana Locke, Julian Preston, Dr. Kligman, Suzanne Ackerman, Vickie Dellarco, Chou Chen, Lance Wormel, Bill Wood, Rita Schoeny, Naju Kashha

2. Public

a) Public Commenters:

- i) Dr. Gary Kayajanian
- ii) Dr. Barbara Beck
- iii) Dr. Samuel Cohen
- iv) Dr. Joyce Tsuji
- v) Dr. Steve Lamm (last minute request)

b) Other: Pat Quinn, Has Shah, Bob Masters, Cameron Bowes, Chris Reimer, Neeraja Erraguntla, Richard Charron, Timothy Peschman, Gloria Post, Elizabeth Brown, Greg Blumenthal, Jennifer Sass, Others with names not identifiable on line

Meeting Summary

Thursday, August 11, 2005

The discussion followed the issues and general timing as presented in the meeting Agenda (Attachment C).

A. Tom Miller - Convene the Meeting: Mr. Thomas Miller, Designated Federal Officer for the SAB Arsenic Panel, convened the meeting and noted that this call was an open advisory meeting of the SAB under the auspices and requirements of the Federal Advisory Committee Act. This Panel is charged with considering and advising EPA on certain arsenic health issues described in EPA documents that are available on EPA's website:

- 1) http://epa.gov/oppsrrd1/reregistration/cacodylic_acid/
- 2) <http://epa.gov/waterscience/sab/>.

The specific charge questions which the panel will consider can also be found on the SAB website at (http://www.epa.gov/sab/panels/arsenic_review_panel.htm).

Mr. Miller noted that the Arsenic Panel was formed using procedures which are generally described in the booklet entitled "Overview of the Panel Formation Process at the EPA Science Advisory Board." This document and a document concerning the formation of this Panel are also on the SAB website. A critical aspect of panel formation is the Staff Office's consideration of potential a) conflict-of-interest issues, and b) a person's perceived impartiality in performing official duties. Also considered are c) a person's breadth of expertise, knowledge and experience relative to the charge; and d) panel balance.

A portion of this issue was determined to be a particular matter. This means there may be financial interests that could be impacted by the issue and that there could be direct or predictable linkages between the issue and a person's financial interest. In regard to the Arsenic Review Panel, the Deputy Ethics Official for the SAB has determined that the legal criteria for making a conflict of interest, or an appearance of impartiality, finding is not met; therefore, waivers were not a consideration for these panel members.

Mr Miller stated that if any Panel Member, during their participation in this SAB activity, should discover an issue, or information, that might indicate a conflict or an appearance issue, that they should inform me immediately so that we can consider the need for and nature of any appropriate remedy. Panelists should also note when topics under discussion draw upon their own research.

Mr. Miller noted that is EPA and SAB policy to allow for public input to the SAB that is relevant to its deliberations. The Board allow for oral presentations when possible, however, we expect those comments to be focused and to summarize the major message that commenters are asked to make in advance in writing. He noted that **four** individuals had registered to make oral comments for this meeting and that their written comments have already been passed to the Panel members for information and three are located on the SAB website.

Then Mr. Miller asked those on the Panel to note their name and affiliation and they did so. He asked for others on the call who had not been acknowledged to announce their presence. No new persons did so.

Mr. Miller introduced Dr. Anthony Maciorowski, SAB Associate Director for Science, to make some introductory remarks.

B . Dr. Anthony Maciorowski welcomed everyone to the first teleconference of the Arsenic Review Panel. He thanked Dr. Matanoski, chair of the panel, and all of the panelists for agreeing to take on this important work. He stated that the quality and credibility of EPA science is dependent on advice and recommendations from external experts.

He also recognized the Agency representatives from the Office of Pesticide Programs, the Office of Water, and the Office of Research and Development who developed the materials that the Panel will be reviewing.

Dr. Maciorowski noted that the arsenic documents before the Panel will eventually be used to complete a final Agency risk assessment for organic and inorganic Arsenic and that the Charge questions to the SAB are focused wholly on the carcinogenic modes of action for organic and inorganic Arsenic.

Dr. Maciorowski noted that the Panel's advice will be transmitted to the EPA Administrator via the Chartered SAB who must review and approve all SAB subcommittee reports. In discharging its responsibility, the Board relies on this Panel for its specific expertise. The focus of the Board review of the draft report is on ensuring that the Agency charge questions are adequately addressed, and that advice and recommendations in the report are supported by information in the body of the report.

C. Dr. Genevieve Matanoski Comments

Dr. Matanoski welcomed the participants and thanked them for agreeing to help with this activity. She stated that the task for today's meeting was to make sure that Panel members understand the charge and that we have the documents needed to address the Charge's science issues. The Panel will not deliberate on the science today — that is for September's Panel meeting (See Attachment D for the draft agenda). She noted that she will be the Board member who ultimately must defend the Panel's draft report when it is reviewed by the Chartered SAB. She intends to deliver a draft report to the Board in November 2005 and get the final report to the Administrator in December.

D. Agency Presentations

Dr. Ila Cote, US EPA ORD, introduced the issue. She noted the importance of the assessments that the Panel is to review. The role of her office, NCEA, in this effort is to coordinate the agency's interaction with the SAB. The issue is complex and involves arsenical pesticides as well as inorganic arsenic. She noted the long Agency history of struggling with these issues and looks forward to the SAB's advice.

Dr. Edward Ohanian, US EPA Office of Water, gave an overview and background on the agency's arsenic Charge to the SAB. His full presentation is in Attachment E. Dr. Ohanian listed the review materials provided to the SAB for the review (charge, the OPP Science Issue Paper—including its Appendix E from ORD, the Draft Office of Water (OW) Toxicological Review of Ingested Inorganic Arsenic, and an issue paper on the inorganic arsenic cancer slope factor). He also noted the relevant statutory authorities that require EPA consideration of arsenic (e.g., the Safe Drinking Water Act, the Superfund and Resource Conservation and Recovery Act (RCRA) programs, the Clean Air Act, and the Food Quality Protection Act).

Dr. Ohanian pointed out that arsenic issues have been the subject of two reviews by the National Research Council with reports being published on the issue during 1999 and 2001. He noted that since the 2001 NRC review, there have been new scientific data on the mode of carcinogenic action, metabolism and toxicokinetics for arsenic and its methylated species. Additionally, new epidemiological data on ingested inorganic arsenic have become available. The Agency has considered this new scientific information while conducting the hazard characterization required for tolerance assessment for DMA^V (and MMA^V), as described in the draft OPP Science Issue Paper and the ORD Issue Paper. The Agency has also developed a revised hazard and dose-response assessment & characterization for ingested inorganic arsenic which relies on the two NRC reviews (1999 and 2001).

Dr. Ohanian stated that the Agency is seeking comment and advice from the SAB on: (1) the scientific soundness of major conclusions drawn in these OW and OPP documents regarding the carcinogenic assessments of DMA^V and inorganic arsenic, and (2) the appropriateness of the Agency's application of its own 2005 Guidelines for Carcinogen Risk Assessment to health risk assessment/characterization for arsenicals.

Dr. Ohanian also summarized the Science and Assessment Issues for arsenic. For inorganic arsenic issues focus on the reanalysis of the slope factor for inorganic arsenic's carcinogenicity as recommended in the NRC arsenic reports. OW has implemented many of the NRC recommendations. Specifically, given the available scientific database, and recognizing that the carcinogenic mode of action of inorganic arsenic has not been fully established, the Agency uses linear low-dose extrapolation to estimate cancer risks from inorganic arsenic ingestion at low-dose.

For organic arsenic (Cacodylic acid or DMA^V) there are a number of challenging scientific issues, including the metabolic profile, the fact that DMA is a key urinary metabolite from exposure to inorganic arsenic, the absence of DMA epidemiology and the existence of rodent cancer bioassay data showing that dietary administration of DMA^V can result in bladder carcinogenesis in the rat.

The Draft OPP Science Issue Paper has addressed some of these scientific challenges. Since the scientific evidence indicates that inorganic arsenic and DMA^V have different pharmacokinetic and pharmacodynamic characteristics, OPP proposes to use the rat bioassay data on DMA^V to estimate its cancer risk. In addition, because the use of mode of action data in the assessment of potential carcinogens is a main focus of EPA's 2005 guidelines for carcinogen risk assessment, OPP is using the available mode of action data on DMA to guide the low-dose extrapolation. The ORD Issue Paper discusses these Mode of Action issues and perspective on the nexus between scientific issues for organic and inorganic arsenicals.

Dr. Ohanian noted that the Agency is asking for SAB comments and advice on key scientific issues concerning: (1) the metabolism and toxic effects of arsenic species, (2) the mode of action for carcinogenesis and implications on dose-response extrapolation for inorganic arsenic and DMA^V, (3) the selection of data for dose-response assessment,

(4) approaches to low-dose extrapolation; and (5) the implications of newer epidemiological data and the incorporation of the 2001 NRC recommendation on modeling the human cancer data for inorganic arsenic.

E. Public Comments

Dr. Matanoski then introduced the public comment session noting that each commenter would have 5 minutes to present their statements. Mr. Miller then noted that there would be 4 commenters.

Dr. Aposhian, a member of the review Panel, noted for the record that he had not realized that those representing the CCA issue would be participating in the meeting. He stated that he had done some work at one time on arsenic availability in the hamster for parties who had an interest in CCA pesticides. Because of the timing, he was not sure that he had included the information in the disclosures filed with the Staff Office previously. Mr. Miller, DFO, thanked Dr. Aposhian for raising the issue and stated that it would not be a problem for the day's meeting because no deliberations were to occur. He noted that he would follow up with Dr. Aposhian to obtain additional factual information on the situation so that a formal decision could be made on whether there was a conflict or appearance issue present for future meetings.

Then Mr. Miller introduced the public presenters in order.

- 1) **Dr. Gary Kayajanian, representing himself.** See Dr. Kayajanian's written comments on cancer risk estimation for inorganic arsenic are in Attachment F and G.
- 2) **Dr. Barbara Beck, Gradient Corporation, representing the MAA Research Task Force (MAATF).** See Dr. Beck's comments on the Agency's charge to the SAB in Attachment H.
- 3) **Dr. Samuel Cohen, University of Nebraska Medical Center, representing himself.** See Dr. Cohen's comments on the DMA-centric charge to the SAB in Attachment I.
- 4) **Dr. Joyce Tsuji, Exponent, representing the American Chemistry Council's Biocides Panel, Chromated Copper Arsenate Work Group.** See Dr. Tsuji's questions on dose response in Attachment J and comments on the charge to the SAB in Attachment K.
- 5) **Dr. Steven Lamm, representing himself.** Dr. Lamm interjected at the end of the comment period noting he had called late and left a message to request time on the agenda for a statement. See Dr. Lamm's written statement on a "two-factor" exposure model used to analyze arsenic carcinogenicity in Attachment L.

F. Discussion of Charge and Review Materials

Dr. Matanoski asked the Panelists if they believed the charge questions were clear and answerable and if there was a need for additional data. Members comments in the ensuing discussion included:

1) Some members feel there is room to broaden the charge, somewhat, and asked if the Panel could address questions in a broader way than is asked by the agency?

Dr. Matanoski noted that the Panel must answer the specific question asked at a minimum. However, it can also go beyond that if the information is relevant to the issue raised in the question. Members should provide Tom Miller with any suggestions for changes to the charge as soon as possible.

2) EPA should provide the Panel (via the DFO) with reports from two citations on page 91 of the OW document. These are:

(USEPA 2004a) ORD Response for critical reviews of Manuscripts cited in AX-030820. April 2004.

(US EPA 2004b) Arsenic Drinking Water Health Advisory. OW July 2004.

3) EPA should better identify what it means by “Mode of Action”. The term has different meanings to different persons.

EPA intends to present information to the Panel at the September meeting (orally) and earlier (in writing) on the 2005 Cancer Guidelines and MOA.

4) Additional data has recently been published on arsenic in a number of areas. Can this be made available to the Panel (e.g., examples mentioned by members included: new mode of action studies (Dr. Green), reproductive and developmental effects- Drs. Waalkes, Hopenhayn, and Harlow, and selenium issues -Dr. Rossman). This issue was raised by Members and by the public as well.

The Chair noted that as Panelists consider various charge questions and issues, they may use new data as they find it to be available. This is part of Member’s background and experience and it comes to the table as information you judge to be important during your deliberations. Some of this may be published, some accepted for publication, etc. Thus, this can be part of a Member’s personal use information as they do their work in deriving advice to the Agency.

5) The charge focus for inorganic arsenicals is on low dose extrapolation for DMA. Can we consider other arsenical pesticides?

EPA would prefer the Panel to focus on the charge itself. However, as in item “1)” above, the Panel can go more broadly if there is reason to do so.

6) Question D1 focuses on DMA. Should there be an analogous question for inorganic arsenic?

This is actually covered in question B3. No action is needed regarding changes to the charge.

7) Members thought that Dr. Le should present information on his research into arsenic speciation.

Presentations by Dr. Chris Le (or any panel member) will be recognized as part of the panel’s deliberations and are appropriate

G. Assignments

1) Assignments to Questions:

Members discussed the appropriateness of their assignments. Some changes were made. See Attachment M.

2) Pre-Meeting Written Submissions:

Members discussed their pre-meeting assignments. They are to read the documents and prepare written, “first-thoughts” on the charge questions. These reflections will be compiled by the DFO and provided to members and placed on the SAB website for public information prior to the meeting. These statements should not be construed as final polished statements of Panel. They will be used to initiate the discussion among members and lead to the Panel’s advice once deliberations are complete. These comments are due to Tom Miller (miller.tom@epa.gov) by close of business on Thursday, September 1, 2005. Members noted a desire to have small Charge Question group interactions prior to the September meeting. Staff will explore the possibility of doing this and if they are to be done they will be arranged and participated in by the DFO so that a formal record can be kept.

H. Action Items

1) The Office of Water will provide the two citations mentioned by Dr. Tsuji in her comments (health advisory on arsenic, comments on a paper—the advisory may not really exist) [**Requested**]

- 2) Public Commenter Dr. Steven Lamm will provide synopsis of his comments and citations he noted
- 3) Panel Members will provide their suggestions for Charge question revisions to Tom Miller and Vivian Turner
- 4) Correct the Roster entry for Dr. Portier.
- 5) Work with EPA to ensure they deliver written explanatory information on how they view Mode of Action. Work with Dr. Bill Wood to ensure that his presentation on the 2005 cancer guidelines focuses on Mode of Action.
- 6) Work out issues of providing additional papers on things like, transplacental exposure from reproductive/developmental studies, rat toxicology studies by Dr. Waalkes, other studies by Dr. Hopenhyn, studies in EHP and Tox. Sciences (81(1) cited by Dr. Green.
- 7) Clarify whether studies in press are acceptable for background information and how these and other new studies can be used in the Panel's review.
- 8) Clarify how to focus on iAs MOA. Do we need to modify D2, or the issue. Is it covered in other questions?
- 9) Remind members of the need to provide their written reflections (bullets) on the charge questions by September 1.
- 10) Clarify with Vanessa that the Staff Office will not be able to set up pre-September 12 meetings with charge question groups.
- 11) Decide if we will ask Dr. Chris Le of the Panel to present on the arsenic species analytical state of the art.

Members concluded their deliberations and the meeting adjourned.

Respectfully Submitted:

/ Signed /

Thomas O. Miller
Designated Federal Officer

Certified as True:

/ Signed /

Dr. Genevieve Matanoski
Chair, EPA Science Advisory Board
Arsenic Review Panel

ATTACHMENTS (available in hard copy)

Attachment A:	Panel Roster
Attachment B:	FR Announcement of Meeting (70FR43144, July 26, 2005)
Attachment C:	Agenda August 11, 2005
Attachment D:	Draft Agenda, September 12-13, 2005
Attachment E:	Dr. Ohanian's Remarks
Attachment F:	Public Comment: Dr. G. Kayajanian
Attachment G:	Public Comment: Dr. G. Kayajanian
Attachment H:	Public Comment: Dr. B. Beck
Attachment I:	Public Comment: Dr. S. Cohen
Attachment J:	Public Comment: Dr. J. Tsuji
Attachment K:	Public Comment: Dr. J. Tsuji
Attachment L:	Public Comment: Dr. S. Lamm
Attachment M:	Panel Assignment Table – Rev. 8/24/2005

**Attachment M (revised on 8/24/05):
SAB and SAB Staff Office Assignments to Goal-Specific Teams**

Charge Issue	Charge Question	Member Assigned
Issue A: Metabolism and Toxic Responses of Arsenic Species	Question A1: Metabolism and Pharmacokinetics	Dr. Aposhian Dr. Medinsky Dr. Le Dr. Rosen Dr. Styblo Dr. Hopenhayn
	Question A2: Response to mixtures of metabolites	Dr. Aposhian Dr. Medinsky Dr. Le Dr. Rosen Dr. Styblo Dr. Hopenhayn
Issue B: Modes of Carcinogenic Action for DMA and iAs	Question B1: Mode of Action of DMA ^V	Dr. Barchowsky Dr. Brusick Dr. Dragan Dr. Klaunig Dr. Rossman Dr. Styblo Dr. Waalkes
	Question B2: Human relevance of animal DMA ^V MOA	Dr. Barchowsky Dr. Brusick Dr. Dragan Dr. Klaunig Dr. Rossman Dr. Styblo Dr. Waalkes
	Question B3: Modes of carcinogenic action from exposure to inorganic arsenic	Dr. Barchowsky Dr. Brusick Dr. Dragan Dr. Klaunig Dr. Rossman Dr. Waalkes
Issue C: Selection of Data for Dose-Response Assessment	Question C1: Use of animal data for DMA ^V	Dr. Cantor Dr. Green Dr. Medinsky Dr. Teeguarden Dr. Waalkes Dr. Yager
	Question C2: Use of human epidemiological data from direct iAs exposure	Dr. Cantor Dr. Colford Dr. Harlow Dr. Hopenhayn Dr. Rosen Dr. Rossman Dr. Yager
Issue D: Approaches to Low-Dose Extrapolation for iAs and DMA^V	Question D1: Mode of Carcinogenic action understanding for DMA ^{V/III} and implications for dose response extrapolation to estimate human cancer risk	Dr. Cantor Dr. Colford Dr. Green Dr. Klaunig Dr. Medinsky Dr. Teeguarden Dr. Waalkes

	Question D2: Implementation of the recommendations of the NRC (2001)	Dr. Colford Dr. Harlow Dr. Hopenhayn Dr. Heeringa Dr. Portier Dr. Rosen Dr. Rossman
	Question D3: EPA re-implementation of the NRC (2001) model in language R and Excel spreadsheet.	Dr. Heeringa Dr. Portier Dr. Teeguarden
	Question D4: Literature describing drinking water consumption rates for the southwestern Taiwanese study population	Dr. Barchowsky Dr. Harlow Dr. Colford Dr. Yager
	Question D5: Selection of an estimate for dietary intake of arsenic	Dr. Aposhian Dr. Barchowsky Dr. Harlow Dr. Styblo Dr. Yager