

**MINUTES FROM THE EPA SCIENCE ADVISORY BOARD
SAB Arsenic Cancer Review Work Group
Public Meeting
April 6-7, 2010**

ATTENDANCE

SAB Work Group Members

Dr. Elaine Faustman (Chair)

Dr. Timothy Buckley

Dr. Thomas Burke

Dr. Deborah Cory-Slechta

Dr. George Daston

Dr. Nancy Kim

Dr. Jana Milford

Dr. Eileen Murphy

Dr. Steve Roberts

Dr. Agnes Kane, *(a member of the workgroup, was not in attendance but provided pre-meeting written comments for the workgroup discussion, see Attachment A)*

SAB Staff Office

Dr. Sue Shallal, Designated Federal Officers (DFO)

Dr. Vanessa Vu, Director

EPA Representatives

Dr. Peter Preuss

Dr. John Vandenberg

Dr. Reeder Sams

Dr. Santhini Ramasamy

Dr. Paul White

Other Participants

See Attachment B for the list of other participants including other EPA personnel and members of the public who were present at the meeting or participated by phone.

MEETING MATERIALS

The following meeting materials were available prior to or during the April 6-7, 2010 meeting and were available on the general SAB Web site, <http://www.epa.gov/sab>, and specifically at the following URL:

<http://yosemite.epa.gov/sab/sabproduct.nsf/MeetingCal/1A8B1D874ECECD45852576C0005DCF0B?OpenDocument>)

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- FEDERAL REGISTER NOTICE
- MEETING AGENDA
- WORK GROUP ROSTER
- CHARGE TO THE COMMITTEE
 - ORD NCEA Charge Questions with Memo dated February 26, 2010. (PDF, 4 pp., 78,338 bytes)
- AGENCY BRIEFING MATERIAL
 - Agency's Powerpoint Presentation on Inorganic Arsenic IRIS Assessment, 4-6-10. (PDF, 62 pp., 345,467 bytes)
- AGENCY-PROVIDED BACKGROUND MATERIAL
 - EPA Abernathy Memo 1989. (PDF, 14 pp., 877,053 bytes)
 - EPA Issue Paper: Inorganic Arsenic Cancer Slope Factor - July 23, 2005. (PDF, 38 pp., 441,271 bytes)
- PUBLIC COMMENTS
 - Oral Comments by Dr. Steve Lamm of Consultants in Epidemiology and Occupational Health, LLC.. (PDF, 3 pp., 57,304 bytes)
 - Oral Statement Presented by Dr. Samuel Cohen of the University of Nebraska Medical Center (PDF, 3 pp., 17,895 bytes)
 - Powerpoint Presentation by Dr. Barbara Beck on Inorganic Arsenic on Behalf of the Organic Arsenical Products Task Force (PDF, 7 pp., 42,617 bytes)
 - Powerpoint Presentation by Dr. Joyce Tsuji on behalf of Rio Tinto. (PDF, 8 pp., 2,466,371 bytes)
 - Powerpoint Presentation by Dr. Pamela Mink on behalf of the Wood Preservative Science Council. (PDF, 15 pp., 214,516 bytes)
 - Powerpoint Presentation by Dr. Samuel Cohen of the University of Nebraska Medical Center (PDF, 6 pp., 993,773 bytes)
 - Powerpoint Presentation from Dr. Lorenz Rhomberg on behalf of the North American Metals Council (PDF, 5 pp., 62,776 bytes)
 - A Letter from the Organic Arsenic Products Task Force, Rio Tinto Ltd., and the Wood Preservative Science Council, March 23, 2010. (PDF, 6 pp., 32,195 bytes)
 - Comments from Dr. Rosalind Schoof of Environ International Corp. (PDF, 13 pp., 92,094 bytes)
 - Comments from Dr. Steven Lamm and Others, March 29, 2010. (PDF, 25 pp., 756,079 bytes)
 - Comments from the Organic Arsenical Products Task Force by Gradient (PDF, 43 pp., 658,992 bytes)
 - Comments Submitted by Gary Kayajianian (PDF, 3 pp., 18,897 bytes)
 - Comments Submitted by Sharan Campleman of EPRI and Others. (PDF, 41 pp., 998,591 bytes)
 - E-mail Submission from Dr. Steve Lamm of CEOH, LLC, 4/7/2010. (PDF, 2 pp., 61,598 bytes)
 - JAWWA Article by Seidel et al Submitted by Steve Via. (PDF, 1 pp., 1,377,039 bytes)
 - Letter from Association of Metropolitan Water Agencies (AMWA) (PDF, 3 pp., 149,671 bytes)

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- Letter from Dr. Janice Yager and Others, March 25, 2010. (PDF, 4 pp., 78,455 bytes)
- Letter from Dr. Samuel Cohen of the University of Nebraska Medical Center (PDF, 5 pp., 88,868 bytes)
- Letter from Mark Maslyn on Behalf of the American Farm Bureau Federation (AFBF) 3-29-10. (PDF, 2 pp., 1,079,012 bytes)
- Letter from Thomas Curtis on behalf of American Water Works Association (AWWA) and the Association of Metropolitan Water Agencies (AMWA) (PDF, 3 pp., 37,053 bytes)
- Submission from Dr. Richard Wilson of Harvard University (PDF, 5 pp., 28,314 bytes)
- Submission from Dr. Steven H. Lamm of Consultants in Epidemiology & Occupational Health, LLC (CEOH) 4-2-10 (PDF, 12 pp., 1,080,005 bytes)
- Submission from Mark S. Sanchez on behalf of the Albuquerque Bernalillo County Water Utility Authority (PDF, 12 pp., 4,715,387 bytes)
- Submission on Behalf of Rio Tinto and WPSC (PDF, 24 pp., 559,644 bytes)
- Submission on Behalf of the Wood Preservatives Science Council (PDF, 1 pp., 12,810 bytes)
- Request to Reschedule Meeting by Bergeson and Campbell on behalf of the Organic Arsenical Products Task Force (PDF, 5 pp., 51,051 bytes)
- SAB STAFF OFFICE
 - SAB Staff Office Response to Bergeson and Campbell Request (PDF, 1 pp., 21,311 bytes)

PURPOSE

The SAB Arsenic Cancer Review Work Group of the EPA Science Advisory Board (SAB) held a public meeting on April 6-7, 2010. The purpose of this meeting was to conduct a focused review of EPA's implementation of the 2007 SAB recommendations for the revision of the cancer risk assessment of inorganic arsenic.

LOCATION

The St Regis, 923 16th Streets, NW, Washington DC 20006

DATE AND TIME

The meeting was held on April 6, 2010 from 1:00 p.m. to 5:30 p.m. (Eastern Time) and April 7, 2010 from 8:30 a.m. to 2 p.m. (Eastern Time).

MEETING SUMMARY

The discussion generally followed the meeting agenda unless it was noted in the meeting summary below.

April 6, 2010

Convene the Meeting and Introductory Remarks

Dr. Suhair Shallal, Designated Federal Officer (DFO), opened the meeting at 1:00 PM. She presented background information on the SAB work group formation process and informed the audience that the SAB operates under the rules and regulations of FACA that required all meetings where discussions and deliberations take place must be held in public. She stated that none of the work group members required waivers as they did not have any conflict of interest or lack of impartiality issues.

Dr. Vanessa Vu thanked the Chair and members of SAB work group. She indicated that in response to EPA's request, the SAB Staff Office had assembled this workgroup of the chartered SAB to lead the focused review of the Agency's draft IRIS cancer assessment of inorganic arsenic. She stated that the work group was asked to determine the responsiveness of the Agency's implementation of the 2007 SAB recommendations regarding the revision of the cancer assessment of inorganic arsenic. She also asked the work group to consider public comments in their discussions and deliberations.

Review of Agenda

Dr. Faustman thanked the work group members and stated that the purpose of the meeting was to first and foremost respond to EPA's three charge questions. She also stated that any other issues may be addressed if time permitted. She then asked work group members to briefly introduce themselves. Afterwards, she asked EPA representatives to give their presentations and informed the work group members that they would have an opportunity to ask clarifying questions.

Agency Presentations (see EPA's power point presentations available on the SAB meeting web page identified above under "Meeting Materials").

Dr. Peter Preuss, Director, National Center for Environmental Assessment (NCEA), presented an overview of the development of the IRIS Inorganic Arsenic Toxicological Review. He stated that there have been six opportunities for the public to comment on the Agency's revision of the cancer assessment of inorganic assessment. He explained that NCEA had implemented the 2007 SAB recommendations and was now seeking a focused review by the SAB work group to determine if they had satisfactorily implemented those recommendations.

Dr. Santhini Ramasamy (Office of Water) presented the history of the inorganic arsenic IRIS assessment. She stated that EPA's existing assessment was issued in 1988 and several groups had reviewed the available literature of inorganic arsenic including the two NRC reports published in 1999 and 2001. She also noted that EPA's 2010 draft assessment incorporated all the recommendations from previous advisory panels and that EPA's response to the 2007 SAB panel recommendations was provided in the appendix of the 2010 draft. Dr. Reeder Sams (NCEA) then provided a technical presentation regarding how the Agency had responded to the 2007 SAB recommendations.

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Work group members asked clarifying questions regarding model fitting, arsenic intake values and the definition of non-water intake. Agency representatives responded that, within the predictive range, the model used did not differ from the quadratic model that was recommended by the 2007 SAB panel. They also stated that NCEA had used the value of 10ug/day as the arsenic water intake value. EPA had relied on several references, both published and non-published internal agency memoranda, including a memorandum by Dr. Abernathy, formerly with EPA, to estimate the water intake value. Non-water arsenic intake from food and other sources, EPA representatives noted, was minimal and had little impact on the overall assessment.

In addition, work group members asked for clarification regarding the names of external peer reviewers listed in the introductory section of the 2010 draft assessment. They requested that the list be revised to indicate that the Science Advisory Board Arsenic Review Panel had reviewed the previous 2005 assessment not the current 2010 assessment. EPA representatives agreed to make the necessary changes.

Public Comments (See public speakers' presentations available on the SAB webpage identified under "Meeting Materials")

Dr. Faustman stated that there were seven registered public speakers. She asked each speaker to limit their oral presentation to five minutes to allow some additional times for clarifying questions from SAB work group members. The order of public presentations was as follows:

- Dr. Barbara Beck on behalf of the Organic Arsenical Products Task Force (APTF) focused on the mode of action of arsenic and its impact on the non-linear dose-response modeling.
- Dr. Lawrence Romberg on behalf of the North American Metals Council (NAMC) explained the importance of exploring and characterizing the Taiwanese reference population and to compare with the modeling results with using other human populations.
- Dr. Rosalind Schoof of Environ International Corp. provided her oral presentation by telephone. She focused her remarks on several issues related to the dietary intake of inorganic arsenic and water consumption rates.
- Dr. Joyce Tsuji on behalf of Rio Tinto presented additional information regarding the availability of new recent epidemiology and toxicology data to assess cancer risks of arsenic at low doses and the need to use the weight of scientific evidence in the Agency's risk assessment.
- Dr. Pamela Mink on behalf of the Wood Preservative Science Council (WPSC) elaborated further on the EPA's critical evaluation of the epidemiology studies. She stated that it was inadequate and offered some ways to improve it.
- Dr. Steven Lamm of Consultants in Epidemiology & Occupational Health, Inc. presented information regarding the Agency's low-dose modeling approach and suggested alternatives.
- Dr. Samuel Cohen of the University of Nebraska Medical Center focused on issues regarding the mode of action for the carcinogenicity of inorganic arsenic.

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Work group members asked clarifying questions throughout the public presentations pertaining to the reference population, exposure values, the endemic areas of Taiwan as well as the proposed mode of action. The public speakers offered further information and explanation of their presentations in response to members' questions. A map showing the villages that were included in the epidemiology studies was shown. The dietary differences of the Taiwanese and US population were also discussed.

Discussion of the Charge Questions

Dr. Faustman asked Dr. Thomas Burke to begin the discussion on the evaluation of the epidemiological data. Dr. Burke began his comments by stating that the EPA did a comprehensive review of epidemiological data. He indicated that the authors acknowledged the strengths and weaknesses of each of the studies. He expressed his support for EPA's selection of the Taiwanese studies (Wu 1989; Chen et al., 1988, 1992) which had a robust exposure data base. Other work group members expressed similar views. Dr. Burke noted that in 2007, the SAB specifically requested that EPA consider applying to each epidemiological study specific criteria to ensure systematic evaluation of all epidemiological studies. He pointed out that while these criteria were well covered in the narrative in Section 4 of the EPA draft report, the information provided in the tables of Appendix B was limited. Other work group members stated that more transparency and consistency were needed to help the reader understand why certain studies were excluded. Members further stated that additional information may also be needed on the statistical power of the studies and possible confounding factors (e.g., bias) and co-exposures to other agents. EPA representatives responded that evaluative criteria were used and acknowledged that they should have been better depicted in the summary tables.

SAB work group members also noted that EPA's draft assessment included a review of epidemiological studies published through 2007. They recommended that EPA acknowledge the existence of epidemiologic studies published since 2007 and should provide an update of available studies that may have an impact on the cancer assessment.

Dr. Faustman summarized the work group's recommendations for Charge Question 1, as follows:

- Reformat Tables in Appendix B to improve clarity and readability.
- Include key information from previous reviews, including NRC (1999, 2001) to improve readability and clarity, and ensure retention of the conclusions and recommendations of previous reviews on the cancer assessment.
- Evaluate key studies published after 2007 to determine if they impact the cancer assessment.

Dr. Faustman then asked Dr. Daston to begin the discussion on the approach to dose-response modeling and sensitivity analysis. Dr. Daston began the discussion by stating that the EPA analyses were responsive to the previous SAB panel's recommendations in terms of dose-response modeling of cancer risks from exposure to inorganic arsenic. He also indicated that, in addition to the linear model, three non linear models, namely quadratic, linear exponential, and quadratic exponential, were evaluated. The excess cancer risk estimates predicted by the nonlinear models were found to be similar to the linear model.

Dr. Milford discussed her comments and offered ways to improve the sensitivity analysis and improve clarity. Her comments included the following:

- The report would benefit from a more detailed description of the Taiwanese datasets used in developing the risk model.
- More detailed discussion regarding the variability of well water arsenic concentrations across and within the 42 exposed villages.
- The SAB had previously suggested EPA to use the low and high percentile values for Monte Carlo analysis. EPA's analysis utilizing upper and lower limits was considered to be adequate but more information on the variability in the underlying water concentration data is needed to verify the results of the sensitivity analysis.
- EPA appeared to have responded to the SAB's recommendation by considering a dose-response model with an exponential quadratic dose-dependence, and three other model forms based on Morales et al. (2000) and NRC (2001). The results were described on p. 143, which concludes that "within the range of exposures covered by the epidemiological data, the alternative forms predict very similar risks." It would be very helpful if the results could be shown graphically (e.g., by showing the dose-response data and model dose-response curves for selected endpoints and age & gender classes).
- Has EPA published the data and parameter tables used in its modeling analysis? As requested by SAB in 2007, this would assist with transparency in the assessment.
- EPA has tested the sensitivity of the risk model to the choice of reference population (southwest Taiwan, all Taiwan, or no reference population) and to the value of non-water arsenic intake for both reference and exposed populations. Results indicate that the cancer incidence risks are fairly robust, with the exception of female bladder cancer risks. The sensitivity displayed for female bladder cancer risks seems to warrant further investigation and explanation; the result was described but not explained in the accompanying text (pp. 141-2). Additionally, EPA might consider whether any combinations of these parameter variations should be examined (e.g., using different non-water intake values in combination with a different reference population).

Work group members generally agreed that the draft assessment needs more information to improve clarity of the data input and the results sensitivity analysis.

Dr. Daston added that some form of a "reality check" in the sensitivity analysis may help inform the plausibility of the cancer estimates from exposure to low levels of arsenic. One example he cited was that of the U.S. historical bladder and lung cancer incidences based on the National Cancer Institute data. Members discussed the possibility of the theoretical estimates of these tumors from drinking water concentrations of 10µg/L and that they may exceed the historical national incidences. Members noted however that the historical national incidences are given as cases per year rather than being based on a lifetime exposure to inorganic arsenic. A reality check was suggested by comparing lung and bladder cancer rates in states known to have high arsenic exposures with those where exposure is lower. However, some members noted that this is difficult to do since actual exposure would not be feasible.

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The work group discussed the current understanding of the mode of action (MOA) by which inorganic arsenic causes cancer. Members indicated that the working hypothesis of arsenic induced bladder cancer mediated by repeated cell injury, cell death, followed by compensatory cell proliferation was reasonable. However, the mode of action for arsenic induced lung cancer was not understood. Dr. Faustman read Dr. Agnes Kane's written comments on this subject: *"Due to multiple potential mechanisms for arsenic carcinogenicity and diversity of potential target tissues, it is very difficult to do a single risk assessment model. The complexity and limited understanding of the mode of action of arsenic should be openly acknowledged in the 2010 draft IRIS assessment."* Workgroup members expressed general agreement that based on available data, the MOA of arsenic carcinogenicity was not fully understood.

Dr. Faustman summarized the discussion and recommendations regarding Charge Question 2, as follows:

- Accept recommendations offered by Dr. Milford to improve the sensitivity analysis
- Dr. Kane's summary statement best characterized the work group overall position on the MOA for inorganic arsenic carcinogenicity.
- Further clarification was warranted on which Taiwanese villages were selected and which were used for the sensitivity analysis including subsets of data sets.
- Additional information or elaboration to improve transparency was needed regarding the reference populations (all of Taiwan vs. S.W. Taiwan) including exposure, geography, and the effect on risk

Dr. Faustman asked work group members and the rapporteurs for each charge question to summarize their comments and be ready to present their major recommendations on the following day. The meeting was adjourned approximately at 5:45 PM.

April 7, 2010

The meeting reconvened at 9:00 AM. Dr. Faustman began the meeting by reiterating the thoughts and concerns raised by work group members on the previous day. She provided the following listing of the requested revisions and documentation from EPA representatives:

- Clarify which information came from previous NRC reports, do not simply cite reports.
- Model approach and assumptions need further explanation.
- The EPA memorandum of Dr. Abernathy should be made publicly available or a summary of the information it contains. This information should be clarified in the EPA document.
- Uniformity of the Tables is needed
- Sources for exposure data should be clarified
- New Taiwan map to be provided showing areas of exposed population
- Female vs. male bladder cancer incidence difference should be explained

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Dr. Faustman then asked Dr. Buckley to begin the discussion of comments on sensitivity analysis for exposure estimates. Dr. Buckley commented that the Agency was responsive to the previous SAB recommendations but there was a need to improve clarity, including the assumptions made and rationale for selection of input values for the exposure modeling. In addition, members recommended maintaining consistency in the selection of the terms behind the exposure assumptions among US and Taiwanese populations (e.g., mean, upper, or lower bounding estimates, etc.). Another work group member emphasized the need for a clear rationale that explains why EPA did not do a sensitivity analysis for sensitive subpopulations. Another work group member indicated the need for an explanation of why food was considered the main non-water source of exposure. Other members suggested that inclusion of graphs in conjunction with Table 5-11 would be helpful.

Members stated that the water consumption rates were not well justified and more information regarding the sources of the assumptions should be added. Both information on the sources of the values used and a justification of why these values have been selected should be included in the assessment, members added. Other work group members also suggested that drinking water consumption data for the US population should be related to those of the Taiwanese population. Members noted that a justification for the non-water intake value used for the exposed and reference population was also needed.

Some members of the audience raised concerns during the morning break that that all public comments that were submitted to the ORD docket prior to the meeting had not been distributed to the SAB work group members. After the break, Dr. Vu explained that the SAB and ORD had different procedures for submitting comments by the public for consideration. She also explained that the majority of public comments that had been submitted to the ORD docket were also submitted to the SAB DFO and therefore had been distributed to the work group members prior to the face-to-face meeting. Other comments had been submitted to the ORD docket only; however, since the ORD comment period had not yet closed, a complete accounting of new comments was not available at the time of this meeting. Dr. Vu informed both the work group and the audience that all comments submitted to the ORD docket would be distributed to the work group for their consideration. EPA representatives said that they would compare the sets of public comments received via the ORD docket and those currently posted on the SAB website and would forward any comments that were not yet posted on the SAB website to Dr. Shallal so that she can distribute them to work group members.

Dr. Faustman then asked each rapporteur to present the major recommendations from their subgroups.

Dr. Burke presented on behalf of the members assigned to Charge Question 1. He stated that the work group supported the selection of the Taiwanese studies for dose-response analysis. He also noted that a thorough review of the other epidemiologic studies was needed and the rationale for not using them should be provided. Additionally, more uniformity in the presentation of information in the tables of Appendix B was also needed and the criteria that were used to evaluate epidemiological studies should be clearly presented. He continued and stated that a discussion of the statistical power of each study should be presented. Graphs would

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be useful for illustrative purposes, he said. Furthermore, bias to the null should be referenced and documented.

Dr. Daston presented on behalf of the members assigned to Charge Question #2. He stated that EPA has been responsive to the SAB panel's recommendations regarding modeling of inorganic arsenic cancer risks and corresponding sensitivity analyses. He continued that EPA followed the recommendation to use a linear model for low-dose risk estimation, and compared the results with three non-linear models, quadratic, quadratic exponential and linear exponential. The excess cancer risks from these three non-linear models were not wildly different from the linear model and therefore there was no basis for departing from default procedures. Dr. Daston reiterated the points offered by Dr. Milford regarding the sensitivity analysis discussed on the previous day. He suggested that it may be helpful to include a reality check in its assessment possibly by comparing data on cancer rates for individual states to see whether states with high arsenic levels have bladder and lung cancer rates that are more consistent with the excess risks estimated by the model. Other work group members clarified that the US incidence data is expressed as cases per year and not cases resulting from life-time exposure.

In addition, based on Dr. Kane's written comments, Dr. Daston stated that arsenic exposure produces epigenetic alterations, both global hypomethylation and hypermethylation, resulting in silencing of tumor suppressor genes. It also inhibits DNA repair and is a transplacental carcinogen. He continued explaining that since the mode of action of arsenic carcinogenicity was not fully understood, the group generally agreed with Dr. Kane's concluding statement which states, "*Due to multiple potential mechanisms for arsenic carcinogenicity and diversity of potential target tissues, it is very difficult to do a single risk assessment model. This complexity and limited understanding of the mode of action of arsenic should be openly acknowledged in the 2010 draft IRIS report.*"

During the lunch break, members of the public provided the DFO with additional comments for distribution to the work group members regarding the exposed Taiwanese population. Specifically this was in the form of a table showing tumor incidence and mortality ratios in endemic areas of Taiwan¹. Additional information was also provided by the Wood Preservative Science Council regarding the need for a reference population in the Agency's analysis and a discussion of the appropriateness of the selected population. Hard copies of the additional public comments were distributed to work group members for their consideration.

After the lunch break, Dr Faustman asked Dr. Buckley to summarize his subgroup's major recommendations for Charge Question #3. Dr. Buckley stated that EPA should clarify the goal, the basis of the assumptions and exposure values used in the sensitivity analysis. He added that the rationale from other documents should be brought forward into the current assessment. EPA should also provide a gender specific analysis related to water consumption rate along with a discussion of why there may be differences. Clarifications of what values were used (mean, upper mean, etc.) and the rationale for their use was needed.

¹ Table 2 from Tsai et al., 1999, Mortality for Certain Diseases in Areas with High Levels of Arsenic in Drinking Water., *Arch. of Enviro. Health.* 54(3):186-193

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After the workgroup discussion and deliberation ended, Dr. Shallal stated that she would ensure that all public comments were sent to work group members. She also asked work group members to notify her if they believed additional deliberations were necessary after receiving all public comments. Dr. Faustman reminded work group members to send their revised comments to their subgroup rapporteur. Dr. Shallal asked work group members to include her as a recipient on any correspondence among members. All final integrated comments were to be sent to Dr. Shallal by April 21, 2010.

The meeting adjourned at approximately 2:05 PM.

Respectfully Submitted:

_____/s/
Dr. Suhair Shallal
Designated Federal Officer,
EPA SAB Inorganic Arsenic Cancer Review Work Group

I certify that these minutes are accurate to the best of my knowledge:

_____/s/
Dr. Elaine Faustman
Chair,
EPA SAB Inorganic Arsenic Cancer Review Work Group

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.

ATTACHMENT A

Deliberative, DO NOT CITE OR QUOTE Preliminary Comments from Dr. Agnes Kane

Charge Question #1: Evaluation of the Epidemiological and Toxicological Data

In general, this 2010 draft IRIS report is comprehensive, well-organized, and clear. The EPA's responses to the SAB comments are appropriate and the summary evaluations of the epidemiology studies are excellent. A major issue in interpretation of these studies is the multiple other risk factors that contribute to development of skin, lung, and bladder cancers. This should be stated clearly and the possibility that arsenic could act as a co-carcinogen with cigarette smoking, ultraviolet light, and perhaps other chemicals at one or more of these sites should be acknowledged at the beginning of the report. The 2010 draft IRIS report does include a comprehensive discussion of susceptible populations and nutritional status, especially in regard to arsenic metabolism. The problems associated with risk assessment at low dose exposures in drinking water and background levels of arsenic in food and soil are discussed. A major limitation in the existing literature is the paucity of information on the range of arsenic body burden in different populations worldwide.

On the basis of the extensive toxicological data summarized by EPA in the IRIS document, multiple mechanisms may contribute to the carcinogenicity of arsenic. There is some support for each of these mechanisms based on animal bioassays and in vitro cellular assays, in addition to a limited number of epidemiology studies. It is unclear whether arsenic exposure contributes to development by skin, lung and bladder cancer through the same mechanistic pathway or whether there is tissue specificity. Three mechanisms are especially important in considering the mode of action of arsenic:

1. Arsenic exposure procedures epigenetic alterations, both global hypomethylation and hypermethylation resulting in silencing of tumor suppressor genes.
2. Arsenic can inhibit DNA repair and this mechanism may explain its co-carcinogenicity with ultraviolet light in skin cancer and with cigarette smoking and bladder cancer.
3. In rodents, arsenic is a transplacental carcinogen. This is a major concern for human exposure during pregnancy and has not been adequately studied.

Due to multiple potential mechanisms for arsenic carcinogenicity and diversity of potential target tissues, it is very difficult to do a single risk assessment model. This complexity and limited understanding of the mode of action of arsenic should be openly acknowledged in the 2010 draft IRIS report.

ATTACHMENT B

List of Attendees with their affiliations as entered on the sign-in sheets:

April 6, 2010

Patrick Quinn	The Accord Group
Raj Sharma	Arch Chemicals
Joyce Tsuji	Exponent
John Vandenberg	EPA
Resha Putzrath	Navy (NMCPHC)
Samuel Cohen	UNMC
Elizabeth Brown	Steptoe & Johnson
Seth Goldberg	Steptoe & Johnson
Lorenz Rhomberg	Gradient
Paul White	EPA
Burleson Smith	Policy Navigation Group
Barbara Beck	Gradient
Pamela Mink	Emory University
Eric Dube	Steptoe & Johnson
Steve Via	AWWA
Ross Nolard	Senate Ag Cmt.
Roy W Olson	Drexel Chem Co
Yvette Lowney	Exponent
Irene Dooley	USEPA
Michal Elden	OAPTF
Sharan Campleman	EPRI
Maria Hegstad	Inside EPA
Elizabeth Doyle	EPA
Edward Ohanian	EPA
William Mendez	ICF
Alan Kovski	BNA
Steve Hensley	USA Rice Fed
Nancy Beck	OMB
Marc Rigas	EPA
Chao Chen	EPA
Illegible	Private Citizen
Lalita Abhyankar	Private Citizen
Erica Brown	AMWA
Betsy Natz	ICI
Kevin Archer	Viance
Kevin Bromberg	SBA

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John Vandenberg	EPA
William Mendez	ICF
Resha Putzrath	
Reece Langley	USA Rice Fed
Shannon Meade	U.S. Camber of Commerce
Nancy Beck	OMB
Jim Collins	Tetra Tech
Elizabeth Brown	Steptoe & Johnson
J.W. Goodrich-Mahoney	EPRI
Lorenz Rhomberg	Gradient
S.M. Cohen	UNMC
Eric Dube	Steptoe & Johnson
Mari Hegstad	Inside EPA
Yvette Lowney	Exponent
Barbara Beck	Gradient
Michal Elden	OHPTF
Alan Kovski	BNA
Jeff Frithsen	EPA
Craig Segall	Sierra Club
Marc Regas	EPA
Ian Talby	
Herman Gibb	TetraTech

List of Participants Requesting access to the teleconference:

Dr. Helen Goeden of the Minnesota Department of Health
Dr. Rosalind Schoof of ENVIRON International Corporation