

**U.S. Environmental Protection Agency
Science Advisory Board
Libby Amphibole Asbestos Review Panel**

**Public Teleconference
July 25, 2012**

Minutes of the Meeting

ATTENDANCE

SAB Panel Members (For full roster, see Attachment A)

Dr. Agnes Kane (Chair)	Dr. Michael Pennell
Dr. James Bonner	Dr. Julian Peto
Dr. Scott Ferson	Dr. Carrie Redlich
Dr. George Guthrie	Dr. Andrew Salmon
Mr. John Harris	Dr. Elizabeth (Lianne) Sheppard
Dr. Tom Hei	Dr. Randal Southard
Dr. David Kriebel	Dr. Katherine Walker
Dr. Morton Lippmann	Dr. James Webber
Dr. John Neuberger	Dr. Susan Woskie
Dr. Lee Newman	

SAB Staff Office

Dr. Vanessa Vu, Director
Dr. Diana Wong, Designated Federal Officer (DFO)

EPA's National Center for Environmental Assessment (NCEA)

David Bussard, Director, Washington Division

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

MEETING MATERIALS

The meeting materials available prior to or during the July 25, 2012 teleconference are available on the SAB web site at, <http://www.epa.gov/sab> and specifically at the following URL:

<http://yosemite.epa.gov/sab/sabproduct.nsf/MeetingCal/DE16F40DF2BE9271852579FB0054C2BF?OpenDocument>

PURPOSE

The SAB Libby Amphibole Asbestos (LAA) Review Panel held a public teleconference to discuss SAB Panel's 7/11/2012 draft review report on EPA's draft *Toxicological Review of Libby Amphibole Asbestos* (August, 2011).

DATE AND TIME

The teleconference was held on July 25, 2012, from 1:00 p.m. to 4:00 p.m. Eastern Time.

MEETING SUMMARY

Convene the Meeting and Welcoming Remarks

The teleconference was announced in the *Federal Register*¹ and generally followed the meeting agenda.² The teleconference is for the SAB Panel to discuss its 7/11/2012 draft review report on EPA's *Toxicological Review of Libby Amphibole Asbestos*. Dr. Diana Wong, Designated Federal Officer (DFO) took the roll call and opened the meeting at 1:00 p.m. She stated that the EPA Science Advisory Board (SAB) operates under the rules and regulations of the Federal Advisory Committee Act (FACA). Panel meetings are announced and open to the public, meeting minutes are prepared, all materials prepared for or by the panel are available to the public, and panel draft reports are reviewed and approved by the chartered SAB. She noted that the SAB Panel members were in compliance with federal conflict of interest and ethics requirements that apply to them. She then turned the meeting over to Dr. Agnes Kane, Chair of the LAA Review Panel.

Review of Agenda

Dr. Kane stated that the purpose of the meeting was to discuss the SAB Panel's July draft review report³ on EPA's draft *Toxicological Review of Libby Amphibole Asbestos* (August, 2011).⁴ (Comments from Panel members are available on the SAB website.^{5,6}) Dr. Kane also described the agenda of the meeting.

Remarks from EPA's National Center for Environmental Assessment (NCEA)

Mr. David Bussard, Director of the Washington division of NCEA, went over questions and requests for clarification on the SAB draft report.⁷

Public Comments

Dr. Kane informed the Panel and the teleconference attendees that the SAB had received four requests from the public to make oral comments at the teleconference. She stated that the list of registered public speakers⁸ and written public comments are available on the SAB website.⁹ Public speakers were provided an opportunity to present their comments by phone. Public commenters provided oral statements in the following order:

- Dr. Elizabeth Anderson, Exponent, Inc., commented on the choice of localized pleural thickening (LPT) as the critical endpoint for the derivation of the RfC, and that the proposed RfC in the draft assessment is below background levels as currently assessed using phase contrast microscopy (PCM).
- Dr. Suresh Moolgavkar, on behalf of W.R. Grace, commented on the issues arising in the derivation of the RfC and the IUR.
- Dr. David Hoel, Exponent, Inc., commented on whether pleural plaques are predictive of risk for other asbestos-related diseases, including asbestosis, mesothelioma, and lung cancer. He also commented on the modeling approach for the RfC.

- Dr. Jay Flynn, Libby Medical Program, commented on the use of pleural plaques as a non-cancer endpoint for the derivation of RfC.

Panel Discussion on the Use of LPT as the Critical Endpoint

The Panel chair asked the pulmonologists on the panel for their recommendations on the use of LPT as the critical endpoint. The pulmonologists agreed that LPT is an adverse effect appropriate for the derivation of RfC. It is an irreversible structural, pathological alteration of the pleura, and is associated with reduced lung function. Dr. Kane, who is a pathologist, stated that LPT is a pathological diagnosis. Another panel member stated that LPT is an adverse pathological change and is an adverse effect in its own right. Panel members agreed that on page 19, line 25 of the panel's draft report the statement that LPT itself is "predictive of" risk for other asbestos-related diseases" should be changed to "associated with", and the wording on page 19 will be clarified. One panel member asked if RfC can be based on cancer instead of LPT. Dr. Vanessa Vu explained that USEPA uses cancer endpoints for derivation of IUR and noncancer endpoints for derivation of RfC.

Panel Discussion of the SAB Draft Report

a. RfC Modeling:

The Panel discussed comment 4 in the July 24 memo⁷ from David Bussard where the Panel has recommended that EPA replace the Michaelis-Menten model with a dichotomous Hill model which allows the slope to be estimated and the inclusion of TSFE as a covariate. EPA also asked the Panel to clarify the recommendation that the Cumulative Normal Michaelis-Menten model should not be used. One panel member commented that SAB should not be too prescriptive on how EPA does the exposure-response modeling. The lead author of this subsection explained that Michaelis Menten and dichotomous Hill model are just logistic models. The Michaelis-Menten model is too restrictive; that is why the dichotomous Hill model was recommended. A panel member commented that the criterion for model selection is that the model fit the data well. The Panel is asking EPA to select the model with the best fit among representative plausible models. The lead author agreed that the language on page 29, line 18, can be revised to be less prescriptive. The Panel also discussed that the background and plateau can be fixed based on literature values because of the small dataset. In addition, the models are parametric models and it is valuable to estimate the plateau using literature values.

The Panel Chair assigned Drs. Sheppard and Salmon to revisit the recommendations on page 29, line 18 and page 31, line 1 and line 29-31, and provide less prescriptive wording.

The Panel discussed comment 5 in the July 24 memo on the evaluation of covariates. EPA asked SAB to clarify if the revised strategy is an alternative to the current method used in EPA's draft assessment. The lead author of the subsection responded that the current method is appropriate. The revised strategy is an alternative, not something that has to be done. EPA staff asked for clarification on how to use the risk score derived from fitting data from the full cohort to the subcohort. The lead author provided a reference, Gaylor et al. (1998), on how to apply this strategy.

b. IUR Interval Statistics:

The Panel discussed comment 6 in the July 24 memo. EPA asked if the Panel could offer references along with specific suggestion on how to apply interval statistics to the survival data. The lead author on interval statistics, Dr. Ferson, responded that he was not aware of references for survival outcome. He recognized that his recommendation may be difficult to implement.

c. IUR: Assumption of Independence:

The Panel discussed comment 7 in the July 24 memo. EPA asked the Panel to provide a reference that clarifies the specific application of the Fréchet inequality for disjunctions and for a bounding analysis of the independence assumption in combining risks of lung cancer and mesothelioma. The lead author of this recommendation acknowledged that this may be difficult for EPA to do.

d. Fiber Dimension Information for Study Description:

The Panel responded to comment 3 in the July 24 memo on the lack of fiber dimension information for study description. The Panel referred EPA to Berman (2011) and commented that fiber length is of critical importance in potency. Mr. Dave Bussard explained that EPA will look at the Berman paper and that the information on fiber characteristics was presented in Appendix D. The Panel suggested that EPA should move the information from the appendix to the body of the report.

e. Future Development of a TEM Method for PCM Equivalency:

Dr. Kane noted that Section 4.3 on development of a TEM method for PCM equivalency is added to Section 4, Long-Term Research Needs.

f. Executive Summary:

A panel member suggested that more text should be added in the executive summary on long-term research needs.

g. Cover Letter:

The Panel agreed that “predictive” on line 39 should be changed to “associated with”. A panel member volunteered to add one bullet to suggest future research needs on mechanistic studies. A panel member commented that on line 28, the phrase “However, there are many areas that need more consideration, and” should be added.

Summary of Action Items:

The Panel Chair identified revisions to be made:

a. Cover Letter:

Line 28, line 2, add suggestion of future research on mechanistic studies.

b. Executive Summary:

- Page 3, line 36-40, add language that dimensions of administered fibers should be included in study description in the body of the document.
- Page 5, line 11,12, change sentence to “EPA should clarify the scientific basis for the use of time since first exposure(TSFE) in the models.”
- Page 9, add more write-up to long-term research needs.

c. Body of Draft Report:

- Page 18, line 11-14, Dr. Lippmann will revise text.
- Page 19, line 23-26, Dr. Redlich will revise text to separate issues more clearly with other endpoints.
- Page 29, recommendations, 2nd bullet, Drs. Sheppard and Salmon will revise the recommendation to be less prescriptive
- Page 31, recommendations, 2nd bullet, revise the recommendation on modeling.

- Page 36, check if additional references can be provided on interval statistics.

Concurrence on the Draft Report:

Dr. Kane asked panel members if they can give oral concurrence on the report, with recommendations from the panel deliberations incorporated. Panel members gave their oral concurrence. Dr. Kane announced that the Libby Asbestos Review Panel has completed its deliberative stage. The revised draft will be sent to the chartered SAB for review.

The DFO adjourned the meeting.

Respectfully Submitted:

Certified as Accurate:

/signed/

/signed/

Diana Wong, Ph.D., DABT
Designated Federal Officer

Agnes Kane, M.D. Ph.D.
Chair
SAB Libby Amphibole Asbestos
Review Panel

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by panel 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. Roster

**U.S. Environmental Protection Agency
Science Advisory Board
Libby Amphibole Asbestos Review Panel**

CHAIR

Dr. Agnes Kane, Professor and Chair, Department of Pathology and Laboratory Medicine, Brown University, Providence, RI

CONSULTANTS

Dr. John R. Balmes, Professor, Department of Medicine, Division of Occupational and Environmental Medicine, University of California, San Francisco, CA

Dr. James Bonner, Associate Professor, Toxicology, North Carolina State University, Raleigh, NC

Dr. Jeffrey Everitt, Director, Department of Laboratory Animal Science, GlaxoSmithKline Pharmaceuticals, Research Triangle Park, NC

Dr. Scott Ferson, Senior Scientist, Applied Biomathematics, Setauket, NY

Dr. George Guthrie, Focus Area Leader, Geological and Environmental Sciences, National Energy Technology Laboratory, US Department of Energy, Pittsburgh, PA

Mr John Harris, Principal, LabCor Portland, Inc, Portland, OR

Dr. Tom Hei, Professor and Vice-Chairman, Radiation Oncology, College of Physicians and Surgeons, Columbia University Medical Center, New York, NY

Dr. David Kriebel, Professor and Chair, Dept.of Work Environment, School of Health & Environment, University of Massachusetts Lowell, Lowell, MA

Dr. Morton Lippmann, Professor, Nelson Institute of Environmental Medicine, New York University School of Medicine, Tuxedo, NY

Dr. John Neuberger, Professor, Preventive Medicine and Public Health, School of Medicine, University of Kansas , Kansas City, KS

Dr. Lee Newman, Professor of Medicine, Div Env and Occup Health Sciences, School of Public Health, University of Colorado, Aurora, CO

Dr. Michael Pennell, Assistant Professor, Division of Biostatistics, College of Public Health, Ohio State University, Columbus, OH

Dr. Julian Peto, Professor, Department of Epidemiology and Population Health , London School of Hygiene and Tropical Medicine, London, , UK

Dr. Carrie Redlich, Professor of Medicine, Internal Medicine, School of Medicine, Yale University, New Haven, CT

Dr. Andrew G. Salmon, Senior Toxicologist, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Oakland, CA

Dr. Elizabeth A. (Lianne) Sheppard, Professor, Biostatistics and Environmental & Occupational Health Sciences, School of Public Health, University of Washington, Seattle, WA

Dr. Randal Southard, Professor of Soils, AES Dean's Office, University of California at Davis, Davis, CA

Dr Katherine Walker, Senior Staff Scientist, Health Effects Institute, Boston, MA

Dr. James Webber, Research Scientist, Wadsworth Center, New York State Department of Health, Albany, NY

Dr. Susan Woskie, Professor, Work Environment, Health and Environment, University of Massachusetts Lowell, Lowell, MA

SCIENCE ADVISORY BOARD STAFF

Dr. Diana Wong, Designated Federal Officer, U.S. Environmental Protection Agency.

Attachment B. The following individuals requested the teleconference call-in number. Their affiliations are as entered on the registration request.

Danielle DeVoney, EPA
Thomas Bateson, EPA
Deborah McKean, EPA
Bob Benson, EPA
Malcolm Field, EPA
Charles Ris, EPA
Gina Perovich, EPA
Krista Christensen, EPA
Elizabeth Anderson, Exponent
Suresh Moolgavkar, Exponent
David Hoel, Exponent
Jay Flynn, Libby Medical Program
Nancy Beck, American Chemistry Council
Leonid Kopelev, EPA
Pam Marks, Beveridge & Diamond
Bob Sonawane, EPA
Maureen Gwinn, EPA
Vince Cogliano, EPA
Glinda Cooper, EPA
Samantha Jones, EPA
Karen Hogan, EPA
Paul White, EPA
Louis D'Amico, EPA
David Berry, EPA
Helen Dawson, EPA
Les Szabo, EPA
Julie Wroble, EPA Region 10
Karl Bourdeau, Beveridge & Diamond
William Concoran, Beveridge & Diamond
Holli Feichko, W.R. Grace
Lydin Duff, WR Grace
Jenny Hopkinson, Inside EPA
Jim Rollins, PNG
Randy Rabinowitz
Resha Putzrah, Navy and Marine Corps Public
Health Center
Thomas Hale-Kupiec, George Washington
University
Linda Wilson, New York State Office of
Attorney General
Clint Woods, House Committee on Science,
Space, and Technology
Dale Drysdale, National Stone and Gravel
Association

Matthew Brown, Associated Press
Correspondent
Steve Minshall, Ash Grove Cement Company
Rice Shane, USEC
James Millette, MVA Scientific Consultants
Jason Broshear, Geotechnical Environmental
Water Resources
Mark Ellis, Industrial Mineral Association
Thomas Smith, Trihydro
Sean Fitzgerald, Scientific Analytical Institute
Johnathan Thornburg, RTI International
Ed Cahill, EMSL
Robyn Denton, EMSL
Ron Mahoney, EMSL
Joe Centifonti, EMSL
Brendan Tully, Levy, Phillips, Konigsberg
Joshua Dischinger, Levy, Phillips, Konigsberg

Materials Cited

The following meeting materials are available on the SAB Web site, <http://www.epa.gov/sab>, at the [July 25, 2012, Libby Amphibole Asbestos Review Panel Meeting](#) page.

¹ Federal Register Notice Announcing the Meeting (77 FR 18808)

² Meeting Agenda, Libby Amphibole Asbestos Review Panel, July 25, 2012

³ SAB Libby Amphibole Asbestos Review Panel Draft Report (7/11/12) on EPA's draft Toxicological Review of Libby Amphibole Asbestos (August 2011)

⁴ Draft IRIS Toxicological Review of Libby Amphibole Asbestos (August 2011)

⁵ Comments from Dr. Mort Lippmann In Response To Memo from David Bussard, 7/24/2012.

⁶ Compilation of Panel Members' Comments, 7/20/2012

⁷ Agency Comments

- Memo from David Bussard, dated July 24, 2012, on Questions and Clarifications related to SAB July Draft Report.

⁸ List of Public Speakers

⁹ Public Comments

- Public Comments from Dr. David Hoel, Exponent, Inc.
- Public Comments from Dr. Suresh Molgavkar, Exponent Inc, on behalf of WR Grace
- Public Comments submitted by Karl Bourdeau of Beveridge & Diamond on June 25, 2012.