

**Summary Minutes of the  
U.S. Environmental Protection Agency (EPA)  
Science Advisory Board (SAB) Asbestos Committee  
Public Meeting of July 21-22, 2008**

Committee Members: See Roster (Attachment A)

Date and Time: Monday, July 21, 2008, 9:00 AM – 6:00 PM  
Tuesday, July 22, 2008, 8:30 AM – 3:00 PM

Location: Embassy Suites Hotel (Consulate/Ambassador Room)  
1259 22<sup>nd</sup> Street, Washington, D.C.

Purpose: The purpose of this meeting was to conduct a consultation of the EPA's proposed interim approach for estimating cancer risks from inhalation exposure to asbestos at Superfund Sites. The *Federal Register* announcement of the meeting is in Attachment B and the meeting agenda is in Attachment C.

Participants: Dr. Agnes Kane, Chair  
Dr. Louis Anthony (Tony) Cox, Jr.  
Dr. Jeffrey Everitt  
Dr. Murray Finkelstein  
Dr. George Guthrie  
Mr. John Harris  
Dr. Karl Kelsey  
Dr. Paul Lioy  
Dr. Morton Lippmann  
Dr. Gary Marsh  
Dr. Gunter Oberdorster  
Dr. Luis Ortiz  
Dr. Julian Peto  
Dr. Christopher Portier  
Dr. Carol Rice  
Dr. Randal Southard  
Dr. Leslie Stayner  
Dr. David Veblen  
Dr. James Webber

Ms. Vivian Turner, Designated Federal Officer (DFO)  
Dr. Vanessa Vu, SAB Staff Office  
Mr. Barry Breen, Mr. Steven Foster, and Dr. William Sette, Office of Solid Waste and Emergency Response  
Dr. Timothy Barry, Office of Policy, Economics and Innovation  
Mr. William Brattin, EPA Consultant

Additional Attendees (see Attachment D)

July 21, 2008 Morning Session

Ms. Vivian Turner, the DFO for the SAB Asbestos Committee, welcomed the SAB Committee Members as well as the public. She noted that as required under the Federal Advisory Committee, the Committee's deliberations are held in public with advanced notice given in the *Federal Register*, and the meeting minutes will be made publicly available after the meeting. She also stated that the SAB Members are all subject to federal ethics regulations. She noted that EPA received twelve written comments, which have been made available to the Committee for their consideration and are posted on the SAB website. Ms. Turner noted that a Committee Member, Dr. Andrew Gelman could not be present at the meeting.

Dr. Vanessa Vu, SAB Staff Director, welcomed the members of the public as well as the distinguished members of the SAB Committee. She stated that the purpose of today's meeting was to conduct a consultation with EPA's Office of Solid Waste and Emergency Response (OSWER) on their proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos at Superfund sites. Dr. Vu indicated that public input is a vital part of the advisory process. She noted that as such, the SAB advisory committee will consider all comments from the public as they deliberate their responses to EPA's charge questions.

Mr. Barry Breen, Deputy Assistant Administrator, OSWER, discussed EPA's effort to develop a new method to quantify asbestos risk. This new approach was developed primarily in response to environmental asbestos exposure in Libby, Montana. The approach is based on the hypothesis that different asbestos minerals pose different risk according to their composition and dimensions. This approach may help to improve the accuracy of risk assessments. Mr. Breen stated that this proposal is just one component of a larger effort. Other efforts being made to address the asbestos issue included: animal toxicology studies and monitoring and assessment of exposed individuals in the Libby community. Exposure to complex mixtures of asbestos and other dusts is also a primary issue of concern.

Dr. Agnes Kane, SAB Committee Chair, asked the SAB Committee Members to briefly introduce themselves and provide their background and area of expertise. Dr. Kane then reviewed the agenda and asked EPA representatives to provide highlights of the Agency's proposed method.

Mr. Steven Foster, Science Advisor for OSWER, and Dr. Timothy Barry, Senior Scientist, Office of Policy Economics & Innovation, provided an overview of the proposed interim approach to estimating cancer potency factors (see their presentation in Attachment E). Mr. Foster stated that the purpose of today's meeting is to have a consultation with the panel to discuss whether the new approach is scientifically warranted and feasible and to gain insight into methods for improvement. If a consensus is reached and a modified approach is developed, the EPA will consult with the SAB again before implementing the approach.

Following several clarification questions from Committee members, Dr. Kane asked Ms. Turner to begin the public comment period.

### Public Comments

Ms. Turner stated that 17 individuals from the public wished to provide oral statements. She asked the public speakers to keep their statements to less than five minutes. Copies of the public speakers' oral statements were distributed to Committee Members and meeting attendees. The public speakers' oral statements are in Attachment F. Each of the public speakers made their statements in the following order:

1. Dr. David Egilman, Clinical Associate Professor, Brown University
2. Mr. Jonathan Ruckdeschel, Ruckdeschel Law Firm, LLC.
3. Mr. Rick Nemeroff, Nemeroff Law Firm, Dallas, TX.
4. Dr. Richard Lemen, former U.S. Assistant Surgeon General
5. Mr. Scott Frost, Water & Kraus, LLP, Dallas, TX
6. Ms. Linda Reinstein, Executive Director and Cofounder of the ADAO
7. Mr. Terry Lynch, International Vice President, Health Hazard Administrator, IAHSI and Allied work.
8. Ms. Randy Rabinowitz, on behalf of the American Association of Justice
9. Dr. Michael Silverstein, University of Washington School of Public Health
10. Ms. Laura Welch, Medical Director for the Center for Construction Research & Training (CPWR), MD
11. Dr. Franklin Mirer, Professor of Environmental and Occupational Health Sciences, Hunter College.
12. Dr. Michael Silverstein on behalf of Dr. Phil Landrigan, Mount Sinai Hospital, NY, NY.
13. Dr. William Cleveland, Professor of Statistics at Purdue University, Lafayette, IN.
14. Dr. Suresh Moolgavkar, Exponent Inc.
15. Mr. James Morris
16. Ms. Pat Girtin and Mr. Ed Houser
17. Dr. Barry Castleman

### **July 21, 2008 Afternoon Session**

The Committee reconvened after breaking for lunch. Dr. Kane asked the lead discussants to summarize their responses briefly to the charge questions, followed by additional comments from other Committee Members (see Attachment G for assigned lead discussants and Attachment H for EPA's charge questions).

EPA's first charge question posed to the Committee is whether there are sufficient data to support an effort in developing risk assessment method(s) to account for the potential

differences in cancer risk based on mineral type and size characteristics. Several members expressed that in their professional judgment there is scientific basis to support this hypothesis and there is a need for such an effort. Committee Members inquired EPA representatives about the Agency's current efforts in obtaining further data analyses from asbestos exposures at Libby, Montana. An EPA spokesperson indicated that EPA will make the Libby Action Plan available to the Committee. Several Members expressed the view that the Libby data could be used as a starting point to refine risk assessment techniques for superfund sites. Other Members, however, cautioned that the data from Libby are very different from almost of the other superfund sites. There was also a discussion of the importance of additional animal toxicology studies to help inform the potential differences in cancer risk among different fiber types and dimensions. Several members suggested there is a critical need for additional exposure analyses of epidemiologic studies as was conducted in the recently published Charleston, South Carolina textile cohort study. Dr. Kane acknowledged that there were divergent views on whether such an effort is warranted at this time and indicated that the Committee will revisit the first charge question at a later time.

Dr. Kane then asked the Committee to proceed on the next charge question. Charge question 2 refers to the adequacy of the background information as described in Sections 2 -5 of the EPA draft document as the scientific basis for the proposed dose-response assessment approach. Individual lead discussants had lengthy discussion on these sections. Overall, the lead discussants unanimously commented that all of these sections—physical and chemical characteristics of asbestos (section 2), toxicology (section 3), epidemiology (section 4), and mode of action (section 5)—are inadequate and incomplete. Mr. Foster pointed out the purpose of these sections is to provide a synopsis of the available science and not intended to be a comprehensive literature review. Many Members, however, expressed the view that it is essential that a thorough review of available literature in these areas be conducted as the scientific bases for any revised risk assessment methods.

The Committee then returned to the discussion of charge question 1 but did not come to closure on this question. In closing, Dr. Kane thanked everyone who was in attendance and stated that the Committee will reconvene in the morning.

### **July 22, 2008 Morning Session**

Dr. Kane reviewed the agenda for the day. Dr. William Sette of OSWER requested to make a short presentation. He remarked that while EPA fully acknowledged the need for a greater embellishment of sections 2-5, he reminded the Committee that the focus of this document is on developing an interim method which makes use of current TEM measurements at superfund sites to predict cancer risk for different exposures of mixtures of asbestos. Dr. Kane then asked the Committee to discuss the remaining charge questions.

The lead discussants and other Committee Members expressed their views that the use of EPA's 1986 risk models are reasonable starting points and recommended that the Agency

to investigate alternative models that reflect more recent data. Further consideration of the interaction between asbestos and smoking is recommended in light of more recent data (charge question 3). The Members, however, were divided regarding the choice of fitting the epidemiologic data to model risk using the data at either the level of individual studies or at the level of exposure groups (charge question 4). There was a suggestion that both types of fitting could be considered, recognizing that considerable uncertainties are associated with either choices.

Next, the lead discussants briefly summarized their responses to charge question 5 which relates to the characterization of the uncertainties of exposure data. These Members noted that while the EPA's draft document has identified many uncertainties, there is a need for quantitative sensitivity analyses to determine how all of these uncertainties will interact. With regard to charge question 6, these members generally supported the proposed methods to account for measurement error in the exposure data. The lead discussants were also generally supportive of EPA's proposed approach to derive study specific parameters to generate bin-specific cancer potency factors (charge question 7). Other Members, however, expressed concern about this approach because case control studies would be excluded since a value for alpha parameter would not be available for a number of these studies.

The lead discussants for charge question 8 were supportive of the use of multiple binning strategies on the basis of fiber type and dimensions. However, they have serious reservations concerning the proposed 20 binning categories due to a lack of TEM analytical data sets which link health outcomes from epidemiologic studies. Other members suggested that the binning strategies should also be based on animal data. The major caveat involved in this approach is how well the animal models reflect human biology.

### **July 22 Afternoon Session**

The Committee reconvened after lunch break and took on charge question 9 which concerns methods for characterizing goodness-of fit of different binning strategies. The lead discussants supported the use of Bayes Factors for initial comparison of different binning strategies but recommended additional evaluation methods including conditional independent tests and simulation-based validation. In regards to charge question 10, the lead discussants judged that the "what if" approach for evaluating sensitivity analysis is scientifically valid and useful. These members urged the Agency to plan ahead as to what will be done with the results of the sensitivity analysis. They suggested consideration of model cross-validation as an additional technique.

The lead discussants commented that the proposed three criteria for study selection for the modeling effort (charge question 11) are problematic because they are too restrictive and many studies would be excluded, particularly for malignant mesothelioma. In response to charge question 12, the lead discussants suggested the inclusion of additional studies (charge question 12).

Charge questions 13 and 14 involve the proposed approach for extrapolation from dust to PCM-based measures, and extrapolation from PCM measures to Bin-specific TEM measures. Overall, the lead discussants have serious reservations regarding the proposed method due to a lack of available data to estimate the TEM specific levels of exposure for the epidemiologic studies used in this type of analysis. The lead discussants did not have any suggested methods for estimating the uncertainty associated with calculated lifetime cancer risks (charge question 15).

The Committee returned to charge question 1. The Committee generally agreed to a straw statement for their consensus response to this critical question. The proposed statement to be conveyed in the letter to EPA would be along the lines of *“the SAB agrees that there is sufficient evidence to suggest these pursuits are worthwhile; however, the current proposed method is weak and the Agency should consider a broader range of alternatives”*.

Dr. Kane thanked everyone for their active participation and reminded the members to submit their written responses to Ms. Turner. Ms Turner then adjourned the meeting.

Certified as true

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Vivian Turner  
DFO

/S/

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Dr. Agnes Kane, Chair  
Asbestos Committee

#### Attachments

- A - Asbestos Committee Roster
- B - Federal Register Notice
- C - Agenda
- D - List of Attendees
- E - Presentation by Stiven Foster and Timothy Barry
- F - Presentations by Public Commenters
- G - Committee Assignment Leads to Respond to EPA’s Charge Questions
- H - List of Agency Charge Questions to the Committee

US EPA Science Advisory Board  
Asbestos Committee Roster

**Chair**

**Dr. Agnes Kane**, Brown University (RI)

**Members**

**Dr. Louis Anthony Cox, Jr.**, Cox Associates (CO)

**Dr. Jeffrey Everitt**, GlaxoSmithkline Pharmaceutical R&D (NC)

**Dr. Murray Finkelstein**, Ontario Ministry of Labour (Canada)

**Dr. Andrew Gelman**, Columbia University (NY)

**Dr. George Guthrie**, US Department of Energy (PA)

**Mr. John Harris**, LabCor Portland, Inc. (OR)

**Dr. Karl T. Kelsey**, Brown University (RI)

**Dr. Paul J. Liroy**, Robert Wood Johnson Medical School-UMDNJ &  
The Environmental and Occupational Health Sciences Institute (EOHSI)  
(NJ)

**Dr. Morton Lippmann**, New York University School of Medicine (NY)

**Dr. Gary Marsh**, University of Pittsburgh (PA)

**Dr. Gunter Oberdörster**, University of Rochester (NY)

**Dr. Luis Ortiz**, University of Pittsburgh (PA)

**Dr. Julian Peto**, London School of Hygiene and Tropical Medicine  
(London)

**Dr. Christopher Portier**, National Institute of Environmental Health  
Sciences (NC)

**Dr. Carol Rice**, University of Cincinnati (OH)

**Dr. Randal Southard**, University of California, Davis (CA)

**Dr. Leslie Stayner**, University of Illinois (IL)

**Dr. David Veblen**, Johns Hopkins University (MD)

**Dr. James Webber**, New York State Department of Health (NY)

Attachment B

# Science Advisory Board Staff Office; Notification of an Upcoming Meeting of the Science Advisory Board Asbestos Committee

[PDF Version](#) (2 pp, 71K, [About PDF](#))

[Federal Register: June 4, 2008 (Volume 73, Number 108)]

[Notices]

[Page 31865-31866]

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ENVIRONMENTAL PROTECTION AGENCY

[FRL-8575-6]

Science Advisory Board Staff Office; Notification of an  
Upcoming  
Meeting of the Science Advisory Board Asbestos  
Committee

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

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SUMMARY: The Environmental Protection Agency (EPA or Agency) Science Advisory Board (SAB) Staff Office announces a public meeting of the SAB Asbestos Committee to provide consultative advice on the Agency's proposed approach for the estimation of cancer potency factors for inhalation exposure to asbestos.

DATES: The meeting dates are Monday, July 21, 2008 from 9 a.m. to 5:30 p.m. through Tuesday, July 22, 2008 from 8:30 a.m. to 4 p.m. (Eastern Time).

ADDRESSES: The meeting will be held in the Embassy Suites Hotel, located at 1259 22nd Street, NW., Washington, DC.

FOR FURTHER INFORMATION CONTACT: Members of the public who wish to obtain further information about this consultation may contact Ms. Vivian Turner, Designated Federal Officer (DFO). Ms. Turner may be contacted at

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the EPA Science Advisory Board (1400F), U.S. Environmental Protection Agency, 1200 Pennsylvania Avenue, NW., Washington, DC 20460; or via telephone/voice mail, (202) 343-9697; fax (202) 233-0643; or e-mail at [turner.vivian@epa.gov](mailto:turner.vivian@epa.gov). General information about the EPA SAB, as well as any updates concerning the meeting announced in this notice, may be found on the SAB Web site at <http://www.epa.gov/sab>.

SUPPLEMENTARY INFORMATION: Pursuant to the Federal Advisory Committee Act, Public Law 92-463, notice is hereby given that the SAB Asbestos Committee will hold a public meeting to provide consultative advice on the Agency's proposed approach for the estimation of cancer potency factors for inhalation exposure to asbestos. The SAB was established by 42 U.S.C. 4365 to provide independent scientific and technical advice to the Administrator on the technical basis for Agency positions and regulations. The SAB is a Federal Advisory Committee chartered under the Federal Advisory Committee Act (FACA), as amended, 5 U.S.C., App. The SAB will comply with the provisions of FACA and all appropriate SAB Staff Office procedural policies.

Background: The EPA Office of Solid Waste and Emergency Response (OSWER) has developed a proposed approach for an incremental improvement to the current method that EPA employs for estimating cancer risk from inhalation exposure to asbestos at Superfund sites.

The proposed approach serves as an intermediate step in a larger Agency-wide review and update of its asbestos risk assessment. OSWER has requested the SAB provide consultative advice on its Proposed Approach for Estimation of Bin-Specific Cancer Potency Factors for Inhalation Exposure to Asbestos. After receiving advice from the SAB, OSWER plans to revise the proposed approach, and seek additional advice from SAB on the revised approach.

In response to OSWER's request, the SAB Staff Office announced that it was forming an Asbestos Committee in 71 FR no. 162 (pages 48926-48927) and 72 FR no. 207 (pages 60844-60845). The roster and biosketches of members of the Asbestos Committee are posted on the SAB Web site at <http://www.epa.gov/sab>.

Availability of Meeting Materials: The draft Proposed Approach for Estimation of Bin-Specific Cancer Potency Factors for Inhalation Exposure to Asbestos to be reviewed by the SAB Asbestos Committee will be posted on the OSWER Web site at <http://www.epa.gov/oswer/riskassessment/asbestos/2008>.

The EPA technical contact for this proposed approach is Mr. Stiven Foster, of EPA's Office of Solid Waste and Emergency Response. Mr. Foster may be contacted by telephone at (202) 566-1911 or via e-mail at [foster.stiven@epa.gov](mailto:foster.stiven@epa.gov). The agenda and other material for the upcoming public meeting will be posted on the SAB Web site at <http://www.epa.gov/sab>.

Procedures for Providing Public Input: Interested members of the public may submit relevant written or oral information for the SAB Committee to consider on the topics under review. Oral Statements: In general, individuals or groups requesting an oral presentation at a public meeting will be limited to five minutes per speaker, with no more than a total of one hour for all speakers. Interested parties should contact Ms. Turner, DFO, in writing (preferably via e-mail) at the contact information noted above, by July 7, 2008 to be placed on a list of public speakers for the meeting.

Written Statements: Written statements should be received in the SAB Staff Office by July 7, 2008 so that the information may be made available to the SAB Panel members for their consideration. Written

statements should be supplied to the DFO in the following formats: One hard copy with original signature, and one electronic copy via e-mail (acceptable file format: Adobe Acrobat PDF, WordPerfect, MS Word, MS PowerPoint, or Rich Text files in IBM-PC/Windows 98/2000/XP format).

Accessibility: For information on access or services for individuals with disabilities, please contact Ms. Turner at the phone number or e-mail address noted above, preferably at least ten days prior to the meeting to give EPA as much time as possible to process your request.

Dated: May 28, 2008.  
Vanessa T. Vu,  
Director, EPA Science Advisory Board Staff Office.  
[FR Doc. E8-12503 Filed 6-3-08; 8:45 am]

**US Environmental Protection Agency  
EPA Science Advisory Board  
Asbestos Committee**

**Consultation on the EPA's Proposed Approach for Estimation of Bin-Specific Cancer Potency Factors for Inhalation Exposure to Asbestos**

**July 21 - 22, 2008  
Embassy Suites Hotel  
1259 22<sup>nd</sup> Street, Washington, D.C.**

**AGENDA**

**Monday, July 21, 2008**

9:00 am	Convene the Consultation / Opening Remarks	Ms. Vivian Turner <i>Designated Federal Officer, SAB Staff Office</i>
9:05 am	Welcome Remarks	Dr. Vanessa Vu <i>Director, SAB Staff Office</i>
		Mr. Barry Breen, <i>Deputy Assistant Administrator, Office of Solid Waste and Emergency Response (OSWER)</i>
9:15 am	Introduction of Committee Members Purpose of Meeting and Review of the Agenda	Dr. Agnes Kane, <i>Committee Chair, and Members</i>
9:35 am	EPA's Remarks on Proposed Methods and Charge to the Committee	Mr. Stiven Foster, <i>Science Advisor, OSWER</i>
		Dr. Timothy Barry, <i>Senior Scientist, Office of Policy Economics &amp; Innovation</i>
10:30 am	Break	
10:45 am	Public Comments	(See the list of speakers)
12:00 pm	Lunch	
1:00 pm	Committee's Response to Charge # 2	Drs. Guthrie, Southard (section 2) Drs. Oberdorster, Ortiz (sections 3 & 5) Drs. Finkelstein, Marsh (section 4) Drs. Stayner, Webber

		(sections 6-7)
2:45 pm	Break	
3:00 pm	Committee's Response to Charge #1	Drs. Kelsey, Guthrie
3:45 pm	Committee's Response to Charge #8	Drs. Everitt, Harris
4:30 pm	Committee's response to Charge #3-4	Dr. Lippmann
5:30 pm	Summary of Day 1 and Plan for Day 2	Dr. Agnes Kane, <i>Chair</i>
6:00 pm	Adjourn for the Day	Ms. Turner, <i>DFO</i>

**Tuesday, July 22, 2008**

8:30 am	Reconvene the Consultation	Ms. Vivian Turner, <i>DFO</i>
8:35 am	Plan for the Day	Dr. Kane
8:45 am	Committee's Response to Charge # 5-7	Drs. Lioy, Portier
9:45 am	Committee's Response to Charge # 9-10	Drs. Portier, Cox
10:30 am	Break	
10:45 am	Committee's Response to Charge #11-12	Drs. Peto, Finkelstein, Stayner
12:00 pm	Lunch	
12:45 pm	Committee's Response to Charge #13-14	Drs. Harris, Veblan
1:30 pm	Committee's Response to Charge # 15	Drs. Cox, Rice
2:00 pm	Summary of Major Recommendations	Dr. Kane and Lead Discussants
2:45 pm	Next Steps and Action Items	Dr. Kane
3:00 pm	Adjourn the Consultation	Ms. Turner, <i>DFO</i>

Attachment D

List of Attendees  
SAB Meeting  
on the  
OSWER Interim Method to Assess Asbestos-Related Carcinogenic Risk  
**July 21, 2008**

<b>Name</b>	<b>Affiliation</b>
Robert Nolan	Cuny
Patricia A. Sullivan	NIOSH
B. Baifoe	Caplin & Drysdale
Danielle DeVoney	EPA
Morton Dubin	Orrich
Ed O'Brian	
Jean Fitzgibbon	EPA
Moses Boyd	TWGIFSG
Samar Chatterjee	EPA
Kurt Blasé	Nossaman
W. J. Brattin	Syracuse Research Corp
Frank Mirer	Hunter College
Richard Lemen	ADAO
Jim Knoz	EPA
Linda Birnbaum	EPA
Jonathan Ruckdeschel	Ruckdeschel Law Firm
Stiven Foster	EPA
Barry Breen	EPA
Randy Rabinowitz	AAJ
Scott Frost	
Michael Silverstein	UW
Terry Lynch	Asbestos Workers
Amaya Smith	AAJ
John Comerforol	Lipsitz & Ponterio
Rick Nemeroff	Nemeroff Law
Jay Turim	Exponent, Inc
Amber Bacon	Syracuse Research Corp.
Anna Belova	Abt Assoc, Inc
William S. Cleveland	Purdue Univ.
Lee Hofmann	EPA
Jim Morris	
Linda Reinstein	ADAO
Leonard K.	
John Flynn	
Pat Girton	

List of Attendees  
SAB Meeting  
on the  
OSWER Interim Method to Assess Asbestos-Related Carcinogenic Risk  
**July 21, 2008**

<b>Name</b>	<b>Affiliation</b>
Ben Hoser	
Christine Hoser	
Lisa Bradley	
Richard Naylor	
Thomas Bateson	EPA
Maria Hegstad	Inside EPA
Carolyn Collins	
Pat Rizzuto	BNA
Eileen Kuempel	NIOSH
Bob Pigg	AIA/NA
John Spinello	K& L Gates
Laura Welch	CPWR
Suresh Moolgavkar	Exponent
Mark Ellis	IMA-NA
Barry Castleman	
T C McNamara	The John McNarmara Foundation
B. Hostage	EPA
J. Michaud	EPA

List of Attendees  
SAB Meeting  
on the  
OSWER Interim Method to Assess Asbestos-Related Carcinogenic Risk  
**July 22, 2008**

<b>Name</b>	<b>Affiliation</b>
Bob Pigg	AIA/NA
J. Turim	Exponent
Lisa Bradley	EPA
Richard Naylor	Hinton & Williams
Samar Chatterjee	EPA
Carolyn Collins	
John Spinello	K& L Gates
Danielle DeVoney	EPA
P.A. Sullivan	NIOSH
Michael Silverstein	UW
Khin Cho Thaug	EPA
Janyne Michaud	EPA
Betsy Sutherlund	EPA
Linda Birnbaum	EPA
Maria Hegstad	Inside EPA
Doug Ammon	EPA

Attachment E

Presentation by Stiven Foster and Tim Barry



## Proposed Approach for Estimation of Bin Specific Cancer Potency Factors for Inhalation Exposure to Asbestos

*Timothy Barry, OPEI, Bill Brattin, SRC, Steven Foster, OSWER, Bill Sette, OSWER*



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RESEARCH REPORT



## Project Team

- US EPA
  - Timothy Barry, Office of Policy, Economics and Innovation (OPEI)
  - Steven Foster, Office of Solid Waste Emergency Response (OSWER)
  - William Sette, OSWER
- Contractor support
  - William Brattin, Syracuse Research Corporation (SRC)
  - Amber Bacom, SRC
  - Anna Belova, Abt Associates

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## Acknowledgements

- D. Wayne Berman, Aeolus Inc.
- Kenny Crump, Louisiana Tech University
- Marty Kanarek, University of Wisconsin – Madison
- Michael Lavine, Duke University
- Danielle DeVoney, USEPA, Office of Research and Development (ORD)
- Leonid Kopylev, USEPA, ORD
- Thomas Bateson, USEPA, ORD
- Glinda Cooper, USEPA, ORD

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## What is the Goal of the Proposed Approach?

- EPA's current approach to quantifying cancer risk treats all fibers counted by Phase Contrast Microscopy as equally potent.
- The proposed approach investigates whether a risk model that differentiates exposures by mineral type and particle size can improve the agreement between observed and predicted cases of lung cancer and mesothelioma.

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### Process for Development of this Approach

- We are seeking your advice at this early stage of development of this proposed approach about:
  - Whether it is scientifically and logically warranted;
  - Whether it is feasible;
  - And, if so, whether the proposed models, data, estimation methods, and evaluation approaches are cogent and reasoned;
  - And how they might be improved, or better addressed in other ways.
- If successfully developed, we plan to return to SAB for review of a draft final model, including results and a sensitivity analyses.



### Other Asbestos-Related Activities

- EPA's Integrated Risk Information System (IRIS) cancer and non-cancer assessments, and Libby amphibole assessment
- EPA's Libby Action Plan
  - A number of projects to improve our understanding of the toxicity of Libby Amphibole (LA) including:
    - a LA-specific reference concentration for non-cancer effects using occupational data;
    - a LA-specific inhalation unit risk (IUR) for cancer using occupational data (IRIS);
    - *In vivo* and *in vitro* studies of LA and other elongated mineral particles of concern
    - inhalation dosimetry models

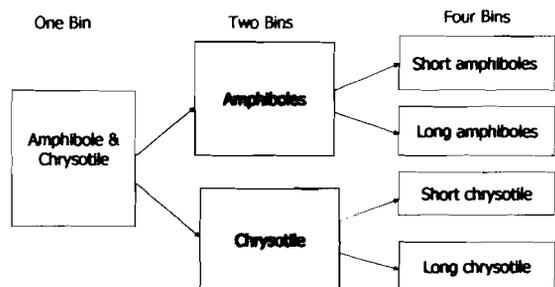


### Introductory Sections of the Proposal

- Overview of human studies – Many types of asbestos are known to cause both lung cancer and mesothelioma.
  - Some scientists see evidence that amphiboles may be a more potent inducer of mesothelioma and possibly lung cancer than chrysotile;
  - Others do not find that the data support this hypothesis.
- Overview of animal studies – Longer, thinner fibers appear to be more potent in causing carcinogenic effects
- Overview of mode of action data – additional effort is needed to determine the mode of action.



### Binning Strategy Concept



### Evaluating Different Binning Strategies

- If there are differences in potency among different bins, then agreement between observations and predictions should increase when bins are chosen that group particles of similar potency.
- Conceptually, many different binning strategies could be investigated.
- This proposal presents 20 binning strategies.

### Example Four-Bin Strategies

Designation	Length (um)	Width (um)
4A – amphibole, short	0-5	< 0.4
4A – chrysotile, short	0-5	< 0.4
4A – amphibole, long	> 5	< 0.4
4A – chrysotile, long	> 5	< 0.4
4E – amphibole, short	5-10	< 1.5
4E – chrysotile, short	5-10	< 1.5
4E – amphibole, long	> 10	< 1.5
4E – chrysotile, long	> 10	< 1.5

### Method for Estimating Bin-Specific Exposures

- Extrapolation from dust to PCM f/cc
- Extrapolation from PCM to bin-specific exposures using TEM data.
- Example: Bin 1 = PCM \* k(1)

Width (um)	Length (um)		
	< 5	5 - 10	> 10
< 0.25	0.13	0.06	0.04
0.25-0.5	0.15	0.12	0.06
0.5-1.0	0.08	0.13	0.05
1.0-1.5	0.04	0.04	0.04
> 1.5	0.02	0.01	0.01

PCME = 0.46  
(heavy line)

Bin 1 = 0.33  
(yellow shading)

$$k(1) = 0.33 / 0.46 = 0.72$$

### Asbestos Risk Models

- Starting Point: asbestos risk models adopted by EPA in 1986

- Relative risk model for lung cancer:

$$RR = \alpha(1 + CE_{10_p} * KL_p)$$

$\alpha$  = relative risk of lung cancer in absence of asbestos exposure

$CE_{10_p}$  = Cumulative exposure (PCM f/cc-yrs, lagged by 10 yrs)

$KL_p$  = Potency factor for lung cancer based on PCM (f/cc-yrs)<sup>-1</sup>

- Modified to account for multiple bins:

$$RR = \alpha(1 + \sum_{k \text{ bins}} CE_{10_k} * KL_k)$$

### Risk Models - Continued

- Starting Point: EPA 1986.
  - Absolute risk model for mesothelioma
 
$$Im = Q * C_p * KM_p$$
    - $C_p$  = Concentration (PCM f/cc)
    - $Q$  = Cumulative function (yrs<sup>3</sup>), which depends on time since first exposure and duration
    - $KM_p$  = Mesothelioma potency factor (PCM f/cc-yrs<sup>3</sup>)<sup>-1</sup>

- Modified to account for multiple bins:

$$Im = Q * \sum_{k \text{ bins}} (C_k * KM_k)$$

### Choice of Modeling Objectives

- Considered two alternatives:
  - Estimated and predicted *study-specific* potency values,
  - Observed and predicted number of cancer cases across each group of each study.
- The number of cases per group was selected because:
  - It allows fitting to occur in one-step;
  - Is based on observed data (number of cases);
  - Is more amenable to characterization of uncertainty.
  - Provides a logical basis for selecting probability model.

### Key Modeling Objectives

- Maximize agreement between observations (cancer cases) and modeled predictions
- Characterize uncertainty in key parameter estimates
- Evaluate different binning strategies
  - are the binning strategies significantly different?
  - how well does the model fit the observations?
  - are the estimates robust? Are the estimates sensitive to:
    - changes in modeling assumptions
    - changes in data?

### Complicating Factors

- Uncertainty in number of cases and significant uncertainties in exposure estimates complicate any modeling analyses.
- There are a number of statistical analysis techniques for considering uncertainties in explanatory variables
  - regression (*weighted, Monte Carlo simulation*)
  - maximum likelihood (*weighted, Monte Carlo simulation*)
  - measurement error methods (*regression calibration, simulation extrapolation*)
  - Bayesian Data Analysis Methods

### Selected Modeling Approach

- Bayesian data analysis is a powerful and general statistical technique to account for uncertainties in explanatory variables.
- Bayes-MCMC (Markov Chain Monte Carlo) employs Monte Carlo integration using Markov chains to perform the complex the integrations inherent in the Bayesian method.
- Key Elements of Bayesian Data Analysis (after Gelman et. al.)
  - Specifying a full probability model
  - Conditioning on the observed data
    - Calculating and interpreting the posterior distribution
  - Evaluating model fit
    - Does the model fit the data?
    - Are the substantive conclusions reasonable?
    - How sensitive are the findings to the modeling assumptions?

### Specification of the Probability Model

- Proposed that observed cases in an exposure group may be modeled as a Poisson random variable.
  - The basic unit is person-year of observation.
  - Observed outcome (death or not death) in each person-year may be characterized as a Bernoulli random variable.
  - The number of deaths in each group of binned person-years is the sum of a large number of Bernoulli random variables.
  - Sum is expected to approach a Poisson distribution.

### Specification of Priors

- Bayesian approach requires the specification of the prior distributions characterizing our state of knowledge about the model's parameters.
- Lung Cancer Priors
  - Study-specific Alphas
  - Bin-specific potency factors ( $KL_p$ )
  - Group-specific Exposures
- Mesothelioma Priors
  - Bin-specific potency factors ( $KM_p$ )
  - Group-specific Exposures
- General Approach for Specifying Priors
  - For  $(\alpha, KL, KM)$ , specify wide, flat, (relatively) noninformative priors
  - Use judgment-based priors for elements affecting exposures

### Characterizing Uncertainty in Exposure Data

Many factors contribute to uncertainty in cumulative exposure estimates based on PCM.

For example:

- Uncertainty in use of dust data rather than asbestos data.
- Potential un-representativeness of measured concentrations over space and time.
- Binning based on CE (not lagged by 10 years) rather than CE10 (lung cancer).
- Extrapolations or assumptions needed to estimate exposure parameters in mesothelioma studies.



## Characterizing Uncertainty in Exposure Data (continued)

Estimation of bin-specific concentrations adds more uncertainty because:

- PCM does not distinguish between amphibole and chrysotile, so the relative amounts of chrysotile and amphibole in workplace air must be estimated indirectly
- Extrapolation from PCM to size bins that are not identical to PCM requires data on the bi-variate length and width distributions of the fibers, but these data are usually not available for the workplace, so surrogate particle size data must be used.

Environmental Health Perspectives

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## Specifying and Combining Uncertainty in Exposure Data

- The uncertainty in the exposure data from each source may be characterized using judgment-based probability density functions.
- The combined uncertainty in exposure may be approximated by assuming each source of uncertainty is independent and multiplicative:

$$CE10 \sim CE10(\text{reported}) \cdot f(\theta_1) \cdot f(\theta_2) \cdot f(\theta_3) \dots$$

Environmental Health Perspectives

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## Comparison of Results for Different Binning Strategies

Based on Rank Ordering of Fits between Strategies:

- Proposal indicates Bayes Factor will be used
- Testing we have done since submitting the proposal indicates other approaches may be preferred:
  - Leave-One-Out Cross-validation (LOO-CV)
  - Deviance Information Criterion (DIC)

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## Evaluating Goodness of Fit

- For the several best binning strategies, we propose to evaluate the quality of fit using:
  - Scatter plots of observed vs. predicted
  - Residual plots
  - Comparison of observed vs. predicted study-specific potency factor

Environmental Health Perspectives

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### Sensitivity Analysis

- In order to determine the degree to which the data may influence the results:
  - Groups, studies, or groups of studies will be excluded;
  - Parameters or distributional form of one or more priors will be changed.

### Epidemiological study selection

- The study must be published in a refereed journal.
- The study must provide data that can be expressed in terms of the quantitative risk models for lung cancer and/or mesothelioma.
- The study cohort is reasonably assumed to have been exposed to approximately the same atmospheric composition of asbestos over time.

### Excluded Studies

- Unpublished Data:
  - Crocidolite miners in Wittenoom ;
  - Chrysotile miners in Quebec.
- Cohorts with Mixed Atmospheres:
  - Selikoff et al. (1979) and Selikoff and Seidman (1991).
- Studies with Other Limitations
- TEM analysis of South Carolina cohort (now available)

### Computing Lifetime Risk

- Bin-specific potency values are not cancer slope factors or unit risks.
- A life-table analysis is required to predict risk.
- How should uncertainty associated with potency factors be addressed?
  - Select a high end value for each factor,
  - Calculate bin-specific potency factor distributions for site-specific mixture.

## Summary

- Goal: Determine if improved agreement between observed and predicted cases can be achieved using a multi-bin approach compared to current 1-bin PCM approach.
- Risk models: Essentially the same adopted by USEPA in 1986, except adapted to multi-bin approach.
- Modeling objective: Comparison of observed and predicted number of cancer cases *in each group* of each study.
- Modeling approach: Bayes-MCMC
- Probability model: Poisson random variable

## Summary - Continued

- Data: Using published epidemiological studies that provide exposure response data in a form that can be used by the risk models
- Bin-Specific Concentrations: Estimate from reported data using bi-variate particle size data from workplace studies that used transmission electron microscopy (TEM) and estimates of the fraction of amphibole fibers.
- Comparison of results: considering different options

Attachment F

**Presentations made by Public Commenters at the Asbestos Committee Meeting  
July 21-22, 2008**

1. Dr. David Egilman, Clinical Associate Professor, Brown University
2. Mr. Jonathan Ruckdeschel, Ruckdeschel Law Firm, LLC. \*
3. Mr. Rick Nemeroff, Nemeroff Law Firm, Dallas, TX.
4. Dr. Richard Lemen, former U.S. Assistant Surgeon General
5. Mr. Scott Frost, Water & Kraus, LLP, Dallas, TX\*
6. Ms. Linda Reinstein, Executive Director and Cofounder of the ADAO
7. Mr. Terry Lynch, International Vice President, Health Hazard Administrator, IAHHI and Allied work.
8. Ms. Randy Rabinowitz, on behalf of the American Association of Justice \*
9. Dr. Michael Silverstein, University of Washington School of Public Health \*
10. Ms. Laura Welch, Medical Director for the Center for Construction Research & Training (CPWR), MD
11. Dr. Franklin Mirer, Professor of Environmental and Occupational Health \* Sciences, Hunter College.
12. Dr. Michael Silverstein on behalf of Dr. Phil Landrigan, Mount Sinai Hospital, NY, NY.\*
13. Dr. William Cleveland, Professor of Statistics at Purdue University, Lafayette, IN.
14. Dr. Suresh Moolgavkar, Exponent Inc.
15. Mr. James Morris
16. Mrs. Pat Girtin and Mr. Ed Houser
17. Dr. Barry Castleman

\* hard copy not available

**Garbage In → Gospel Out**

David Egilman MD, MPH  
Clinical Associate Professor Dept of Community Health  
Brown University  
degilman@egilman.com

1

**Particles do not convert to Fibers**

2

**Chrysotile causes Mesothelioma—Tremolite Contamination**

Churg, "Chrysotile, tremolite, and malignant mesothelioma: a reappraisal." *Ann NY Acad Sci* 1981; 357:1-12.

7

**Chrysotile causes Mesothelioma—Tremolite Contamination**

Churg, "Chrysotile, tremolite, and malignant mesothelioma: a reappraisal." *Ann NY Acad Sci* 1981; 357:1-12.

8

**Junk Science From Junk Measurements**

- J.C. McDonald: "Can an fractured institution like the midget impingey (MI) give an accurate result?"
- Rosenfeld responded, "I have not had enough experience with the MI but it is the wrong instrument to which to base standards." (Shapiro 1979)

It is true that even a broken watch will tell the correct time twice a day.

3

**Fiber-Particle Count Relationship**  
*There is no relationship*

Dust (Asbestos plus dirt) Particles in MPPCF

4

**Chrysotile causes Mesothelioma—Tremolite Contamination**

Deposition of Dr. Graham Gibbs taken on December 16, 2000 in *Env. & Biol. Statist.* 24:43-50, pp. 44-45.

9

**Everyone is exposed to multiple fiber types**

Churg 1995

10

**QAMA-McGill Conclusion:**  
Asbestos PREVENTS Lung Cancer & Asbestosis?

**More Dust = Less Disease**

5

**Manipulation of Exposure Data**

"In all the conditional regression analyses of the full model, i.e. with 13 exposure measures, there was at least one negative regression coefficient, which taken at face value would imply a protective effect of exposure. Years in the highest relevant dust category were pooled with those in the adjacent category and the analysis was repeated. This process was iterated until either all coefficients had become positive, when it was terminated, or until the only negative coefficient was for category 1, in that circumstance, category 1 was eliminated from the model, which was equivalent to setting the coefficient to zero and the odds ratio to unity."

"Admittedly, *there was a degree of arbitrariness in some of the pooling carried out* but every effort was made to retain any 'significant' effects."

6

**Everyone is exposed to multiple fiber types**  
Chrysotile effect is synergistic with amphiboles.

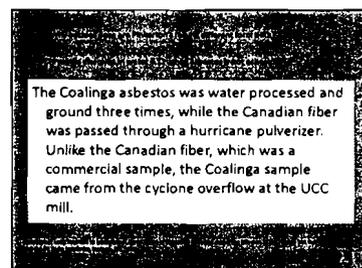
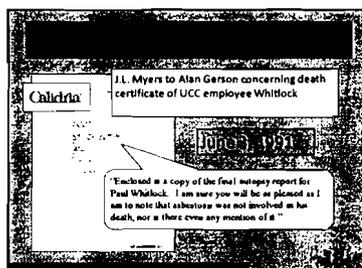
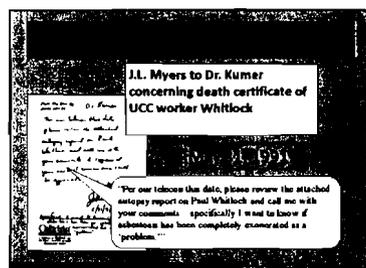
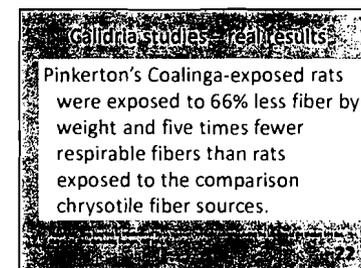
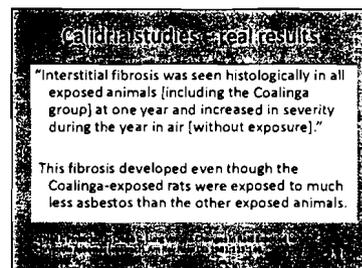
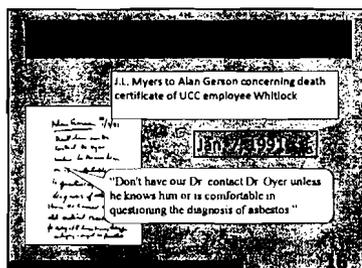
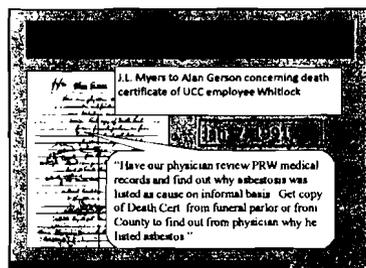
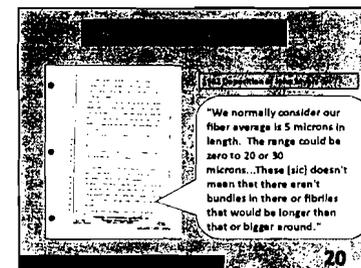
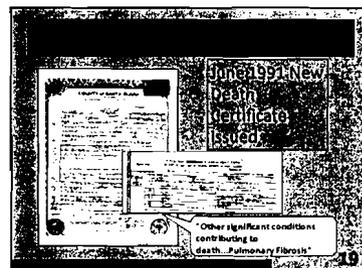
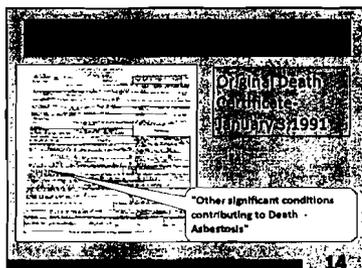
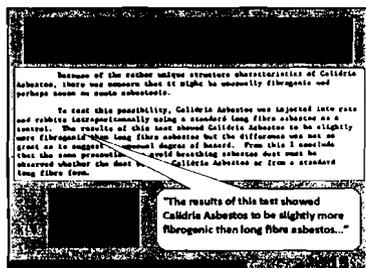
Churg 1995

11

**Asbestos Contamination - Special Report: The Fibrogenic Potential of Asbestos Products - July 1966**  
Not Published

"The results indicate that the asbestos products studied produced fibrosis: lesions of the visceral organs, and loss of fiber length. Of the 3 products, CMS-100 produces the most severe reaction."

12



Comments on Draft EPA Report:  
“Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos.”

**Rick Nemeroff**

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**Witnesses for Companies  
in Asbestos cases are not  
telling judges and juries  
the whole truth about  
the EPA's current position  
on asbestos.**



**EPA's SAB Asbestos  
Committee will be  
Misused, Misquoted and  
Misapplied by Witnesses  
for Companies in  
Asbestos cases**



**“Berman Crump”  
is being used  
against asbestos  
victims in  
Courtrooms  
around the  
country**

**2003**



**2008**

# Misused

**EPA's work is being  
used to determine  
occupational  
exposure risks**

# Misquoted

**Company witnesses fail to disclose that BC's work was a draft, has not been adopted, and does not reflect a change of EPA's position on asbestos.**

**Misapplied**

**Litigation use of  
your work will be  
to persuade juries  
to find NO  
causation and NO  
liability in  
occupational  
exposure settings**

**Lives are  
At Stake**

Comments on Draft EPA Report:

“Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos.”

Richard A. Lemen, Ph.D., MSPH

Assistant Surgeon General, USPHS (ret.)

&

Acting Director, NIOSH and Deputy Director,  
NIOSH (ret.)

**Warning: Risk Estimates are not just numbers they represent real humans and their families.**

## Uncertainties & Flaws

“Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos”

Dr. Greenberg –

“EPA is in danger of conveying the impression that the mathematical model takes precedence over biological plausibility”

“Attempts to derive a dose response relationship between inhaled asbestos and respiratory malignancy have required to be based on a gallimaufrey<sup>1</sup> of historic exposure data, and on end point data of varying quality.”

J A medley; any confused jumble of things; but strictly speaking, a hotch-potch made up of all the scraps of the larder.

**Warning:** Risk Estimates are not just numbers they represent real humans and their families.

7/20/2008

Dr. Richard A. Lemen, Assistant  
Surgeon General (ret.)

## Uncertainties & Flaws

“Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos”

### Dr. Dement –

“limitations of the available epidemiologic and fiber size data necessitate the use of many simplifying assumptions.”

“populations as worker cohorts studied to date have been predominately exposed to short fibers. Model fit statistics will not untangle this correlation, especially based on an ecological analysis using grouped rather than individual worker-specific data.”

“The rational for omission of the insulator worker studies by Selikoff and Seidman from the risk assessment seems very weak.”

**Warning: Risk Estimates are not just numbers they represent real humans and their families.**

7/20/2008

Dr. Richard A. Lemen, Assistant  
Surgeon General (ret.)

## Uncertainties & Flaws

“Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos”

### Collegium Ramazzini –

“We Consider the approach that is proposed in this document will have the effect of unjustifiably diminishing the regulatory level of concern that is directed to control of exposures to chrysotile asbestos.”

“The Collegium Ramazzini considers this document an affront to both good science and to morality.”

**Warning: Risk Estimates are not just numbers they represent real humans and their families.**

Dr. Richard A. Lemen, Assistant  
Surgeon General (ret.)

7/20/2008

## Uncertainties & Flaws

“Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos”

# NIOSH –

- Commenting on NIOSH proposed research framework and commenting in it on asbestos NIOSH says:

“Despite this body of research, several fundamental issues are not clearly understood and a broad systematic approach to further toxicological and epidemiological research would help to reduce remaining uncertainties.”

- The role of unregulated short (i.e., <5µm) fibers is not entirely clear
- It also remains unclear to what extent each of the various physiochemical parameter of asbestos fibers is responsible for respiratory disease outcomes (e.g., asbestosis, lung cancer, and mesothelioma) observed in asbestos-exposed individuals.
- Presently, little information exists on the mechanisms by which asbestos fibers ... produce lung cancer, mesothelioma, and non-malignant respiratory disease.

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7/20/2008

Dr. Richard A. Lemen, Assistant  
Surgeon General (ret.)

## Uncertainties & Flaws

“Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos”

### Canadian Studies –

Professor McDonald said in their attempt to convert particle to fiber measurements:

*“...more or less fizzling out..... We've been doing if for a good five or six years, and I think we know how unanswerable the problem is.”*

Yet he did it when McDonald & Liddell felt confident to equate 300 mppcf.y with 1,000 f/ml.y

**Warning:** Risk Estimates are not just numbers they represent real humans and their families.

## Uncertainties & Flaws

“Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos”

Dr. Berman –

“It be acknowledge[d] that the proposed work is premature and that the supporting database needs first to be improved and substantially expanded.”

“the severe pitfalls of conducting a meta analysis over a set of studies that are insufficiently rich to test the hypotheses of interest be highlighted”

**Warning: Risk Estimates are not just numbers they represent real humans and their families.**

7/20/2008

Dr. Richard A. Lemmen, Assistant  
Surgeon General (ret.)

## Uncertainties & Flaws

“Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos”

Most Cohorts included are mixed exposures

No pure chrysotile cohorts

Percentage of fiber type, in atmosphere sampled, does not equal to fibers captured in the sample

Short fibers missed with PCM

Chrysotile underestimated with PCM

No good correlation between sampling methods (mppcf and f/cc)

Historic sampling for developing TWA's vary by sampling time, sampling head, the sampler, counting protocol, and Quality Control (see Dr. Greenberg submittal)

Heterogeneity of cohorts preclude scientifically valid comparisons

**Warning: Risk Estimates are not just numbers they represent real humans and their families.**

7/20/2008

Dr. Richard A. Lemen, Assistant  
Surgeon General (ret.)

## Science vs. Faith

According to Immanuel Kant (1724-1804) there are two types of judgments, the analytical and the synthetic.

The analytical judgment is one where the truth can be determined within itself; that is, the definitions of the words within the statement of truth affirm the truth.

“All black houses are houses” Of course, a black house is a house.

The synthetic (judgment) truth needs to be determined by the action of looking at the house in question to see if it is indeed black

“The house is black”

**Warning: Risk Estimates are not just numbers they represent real humans and their families.**

7/20/2008

Dr. Richard A. Lemen, Assistant  
Surgeon General (ret.)

## Science vs. Faith

Applying Kant's "*Critique of Pure Reason*" to this exercise:

A particle measurement is a particle measurement,  
and  
A fiber count is a fiber count

Two more Points to the Kantian point-counterpoint:

A priori knowledge – it is a given and you just know  
it to be true

A posteriori knowledge – you need to observe it to  
ascertain its truthfulness

**Warning:** Risk Estimates are not just numbers they represent real humans and their families.

7/20/2008

Dr. Richard A. Lemen, Assistant  
Surgeon General (ret.)

## Science vs. Faith

Finally, let us note that Kant claims that indeed “perception is reality”

**Warning:** Risk Estimates are not just numbers they represent real humans and their families.

7/20/2008

Dr. Richard A. Lemen, Assistant  
Surgeon General (ret.)

# Bibliography

- Greenberg M, 2008. Comment on draft EPA Report: "Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos."
- Dement JM, 2008. Letter to Vivian Turner, EPA, July 16, Re: "Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos."
- Soffritti M, 2008. Letter to Office of Solid Waste and Emergency Response, EPA, 10 July, Collegium Ramazzini.
- Berman DW, 2008. Letter to Vivian Turner, EPA, July 3, Re: "Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos."
- NIOSH, 2008. Revised Draft NIOSH Current Intelligence Bulletin, Asbestos Fibers and Other Elongated Mineral Particles: State of the Science and Roadmap for Research. National Institute For Occupational Safety and Health, CDC, USPHS, DHHS, June.
- Mannion J, 2006. Philosophy Everything You Need to Understand the World's Greatest Thinkers, Adams Media Corporation, Avon, Massachusetts.



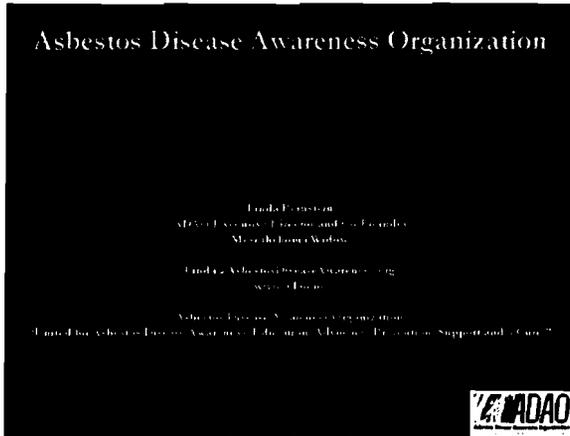
7/20/2008

Dr. Richard A. Lemen, Assistant  
Surgeon General (ret.)



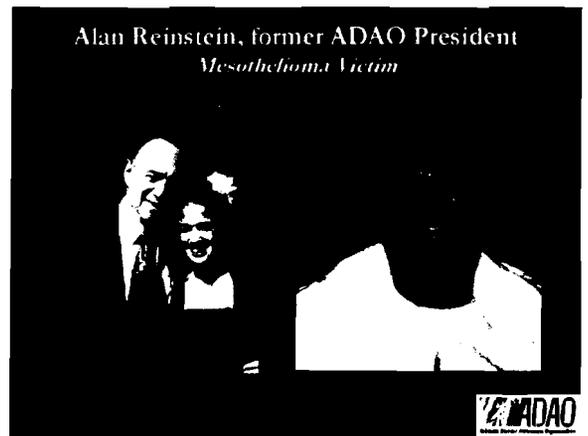
**Linda Reinstein, ADAO Executive Director and Co-Founder  
(OSWER) Interim Method to Assess Asbestos-Related Carcinogenic Risk**

**July 21, 2008**



I am Linda Reinstein, Executive Director and Co-Founder of the Asbestos Disease Awareness Organization and now a mesothelioma widow and single parent. There is a trail of tears from those exposed to asbestos, diagnosed with asbestos-related disease or who have died – and our families - that lead us to the facts that asbestos kills.

During the past five years, I have experienced first hand the disease, death and devastation caused from asbestos both personally and organizationally, as my late husband Alan lost his three year battle with mesothelioma, a fatal asbestos-caused cancer. The human toll from these preventable diseases is staggering.



This morning I dedicate my statement to Jill, who is undergoing her 5th surgery for mesothelioma in Texas while I am speaking. We call this death by a thousand cuts. Jill has been battling both pleural and peritoneal mesothelioma for 12 years and weighs only 82 pounds now.

“United for Asbestos Disease Awareness, Education, Advocacy, Prevention, Support and a Cure.”  
The Asbestos Disease Awareness Organization is a registered 501 (c) (3) nonprofit organization.  
1525 Aviation Boulevard, Suite 318 · Redondo Beach · California · 90278 · 310-437.3886  
[www.AsbestosDiseaseAwareness.org](http://www.AsbestosDiseaseAwareness.org)

**The EPA, WHO and ILO agree:**  
**Asbestos is a human carcinogen and there is no safe level of exposure.**



*YOUR JOB is becoming an asbestos problem because of the potential effects of asbestos fibers. It is your responsibility to protect your health and the health of others.*



The Environmental Protection Agency, (EPA) World Health Organization (WHO) and the International Labor Organization (ILO) agree asbestos is a human carcinogen and there is no safe level of exposure. OSWER's proposal to consider the potential of cancer potency differences between mineral groups (amphibole or chrysotile), particle size (length and width), under varied human exposure conditions, has a high disregard for public health. The EPA developed a risk assessment for asbestos, which has stood the test of time and corporate pressure for more than twenty years. You have the responsibility to uphold the science and promote public and political awareness

about the dangers of asbestos exposure both occupationally and non-occupationally and not minimize the carcinogenic risk of asbestos.

Penny slide you are looking at compares the nearly invisible deadly fibers just under President Lincoln's nose to grains of rice and human hair. As you know, these virtually invisible indestructible asbestos fibers can be 700 times smaller than human hair and remain suspended in air from seconds to days.

**How small is asbestos?**




**1976**

The International Agency for Research on Cancer (IARC) list asbestos as a human carcinogen and the National Institute for Occupational Safety and Health calls for a ban on asbestos in US workplaces.



It has been known since the nearly 100 years, asbestos kills. The International Agency for Research on Cancer (IARC) declared asbestos a human carcinogen 30 years ago. The adverse effects of asbestos exposure in humans have been documented in numerous EPA, IARC, WHO and ATSDR studies. Americans are growing intolerant of political and scientific discussions, as we believe our government has the power and responsibility to end this epidemic.

“United for Asbestos Disease Awareness, Education, Advocacy, Prevention, Support and a Cure.”  
 The Asbestos Disease Awareness Organization is a registered 501 (c) (3) nonprofit organization.  
 1525 Aviation Boulevard, Suite 318 · Redondo Beach · California · 90278 · 310-437.3886  
[www.AsbestosDiseaseAwareness.org](http://www.AsbestosDiseaseAwareness.org)

Think about people, not formulas.

Lung Cancer:  $RR = \gamma \cdot I + \sum C_i \cdot 10^b \cdot K \cdot I^b$

Mesothelioma:  $Im = Q \cdot \sum C_i \cdot K \cdot M^b$

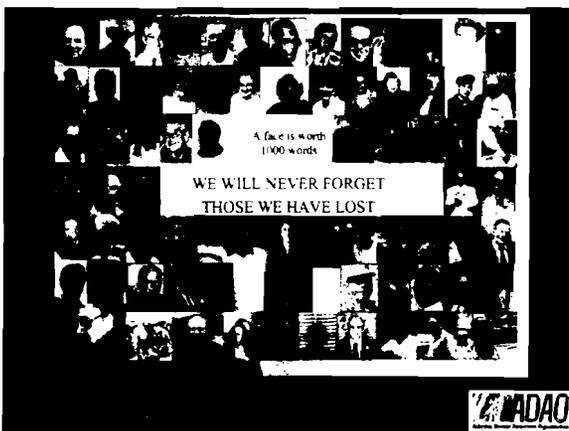


Think about people, not formulas. As a widow, I am appalled to see public health risk analysis translated to mathematical formulas. I doubt Hamilton Jordan, Steve McQueen, Warren Zevon, U.S. Capitol Tunnel Workers, John McNamara, Alan or Jill would approve of OSWER's *Interim Method to Assess Asbestos-Related Carcinogenic Risk* for lung cancer and mesothelioma. We all know asbestos kills.

Consider the rage of Americans, if we opened discussions about various types of tobacco leaves and their "cancer potency factors." This EPA public meeting today should focus on protecting public health rather than promoting industry. Science and technology has improved greatly and we should be discussing preventing exposure to these carcinogenic fibers and legislation to ban asbestos, not about new risk models that build a larger maze of confusion and deception.

*"The most efficient way to eliminate asbestos-related diseases is to stop using all types of asbestos."*

The World Health Organization



Victims are asking "Why is EPA falling prey to industry's requests?" I want Jill and her family to know you have heard our plea to prevent diseases by reaffirming that all asbestos fiber types and size cause disease. One life lost to asbestos disease is tragic, hundred of thousands of lives lost is unconscionable.

"United for Asbestos Disease Awareness, Education, Advocacy, Prevention, Support and a Cure."  
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**Statement of Terry Lynch  
EPA Hearing  
Monday July 21, 2008  
Washington, D.C.**

**My name is Terry Lynch. I am a third generation insulator and a Vice President with the International Association of Heat and Frost Insulators and Allied Workers, formerly the Asbestos Workers Union.**

**I understand that the EPA's scientific advisory board is trying to quantify the cancer risks of various asbestos fibers. I suppose there is some theoretical value to having such knowledge.**

**However, I believe there is greater value in the practical application of the scientific knowledge we already have.**

**Asbestos containing products have caused the largest man made public health catastrophe in our nation's history. Asbestos has killed our buddies, our children, and our spouses at alarming rates. Over 15% of our asbestos workers are dying of mesothelioma; and 30% of our members are dying of asbestos induced lung cancer. Countless others have asbestosis.**

**We are now told that 80-90% of the asbestos fibers that were in the products we worked with was chrysotile asbestos. So why the EPA would want to consider accepting Industry's assertion that chrysotile asbestos is safe is beyond comprehension.**

**Asbestos manufacturers in the 1950s, 1960s and 1970s advertised that their asbestos products, the ones we worked with, were "non-toxic and safe." The asbestos manufacturers knew that was false, as did our Federal Government.**

**This administration may have trouble with the saying "fool me once, shame on you, fool me twice, shame on me," but working people understand it pretty well.**

**Rather than focusing on how much of the poison it will take to kill us this second time around, an inquiry that only benefits the people who are still trying to mine and market asbestos products to American consumers, I think we should focus on banning the stuff.**

**As this board ponders how much poison the working people of this country have to inhale before they die a painful, horrific death, I'd like you to step out of the lab for a minute and into the living rooms of the real people who died from asbestos poisoning.**

### Bill Glynn

Brian Glynn is one of my buddies in Chicago. His dad, Bill, died from mesothelioma after working on countless projects that required him to use asbestos.

How would you feel if after this meeting today you brought home to your family a substance in this room that was lethal to your husband, wife, or children? How would you feel if you'd been assured it was safe?

### Charley and Cecelia Lynch

My father died from asbestosis and lung cancer. So did my mom. The decisions made in this room by this Agency have the power to kill thousands more; or they have the power to protect innocent workers and their families.

### Veronica O'Shea

Veronica O'Shea was the wife of Ed O'Shea, a Union buddy of my dad's who was a Chicago Asbestos worker.

Veronica was a volunteer school crossing guard and had children of her own. Her husband was a decorated veteran of World War II. These were the people who, literally, fought for our country's freedom, and then built it into the greatest industrial and economic force in the world. They were part of the Greatest Generation.

Veronica, like my mom and most women in the 1950's and 1960's, would wash her husband's clothes. After she died from mesothelioma, her autopsy showed that she had an asbestos exposure equivalent to an occupational exposure - - just from washing her husband's clothes.

So you'll forgive my skepticism when the agency responsible for protecting our environment convenes a panel to research again the deadliness of asbestos. We know it's deadly and we don't care if it's a little deadly or a lot.

My parents, the O'Sheas, and tens of thousands of innocent people like them are buried and we're still arguing about whether and how much and what kind of asbestos kills, and in whom.

Enough is enough.

Maybe if the same degree of interest were being put forth to ban asbestos, find a cure for mesothelioma, enforce workplace safety regulations, and provide health care to those who were intentionally poisoned, I'd feel differently.

**But Union members and working men and women know that if the EPA makes an official position that chrysotile is somehow safe (when we know it's not) we'll be right back where we were fifty years ago: manufacturers of chrysotile friction products, gaskets, packing, joint compounds, floor tiles, ceiling tiles, and every other manner of product will cite to the new "EPA science" as authority that it is safe.**

**And forty years later, we would be burying a whole new generation of victims.**

**You should exercise your authority wisely to prevent such carnage.**

**All Asbestos, including Chrysotile Asbestos, should be banned.**

**Thank you for your time and your consideration.**

**\*\*\*\*\***

# Comments on EPA Asbestos Risk Modeling and Analysis

William S. Cleveland

Shanti S. Gupta Distinguished Professor  
Statistics & Computer Science Departments  
Purdue University

1. Data of the EPA proposal are insufficient for the complex modeling being proposed.
2. Study goals are unachievable unless reliable, empirical information about measurement error can be determined.

## Two Displays of the Exposure-Incidence Study Data

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Square root incidence vs. square root exposure

- square roots bring error variances of counts closer to constant

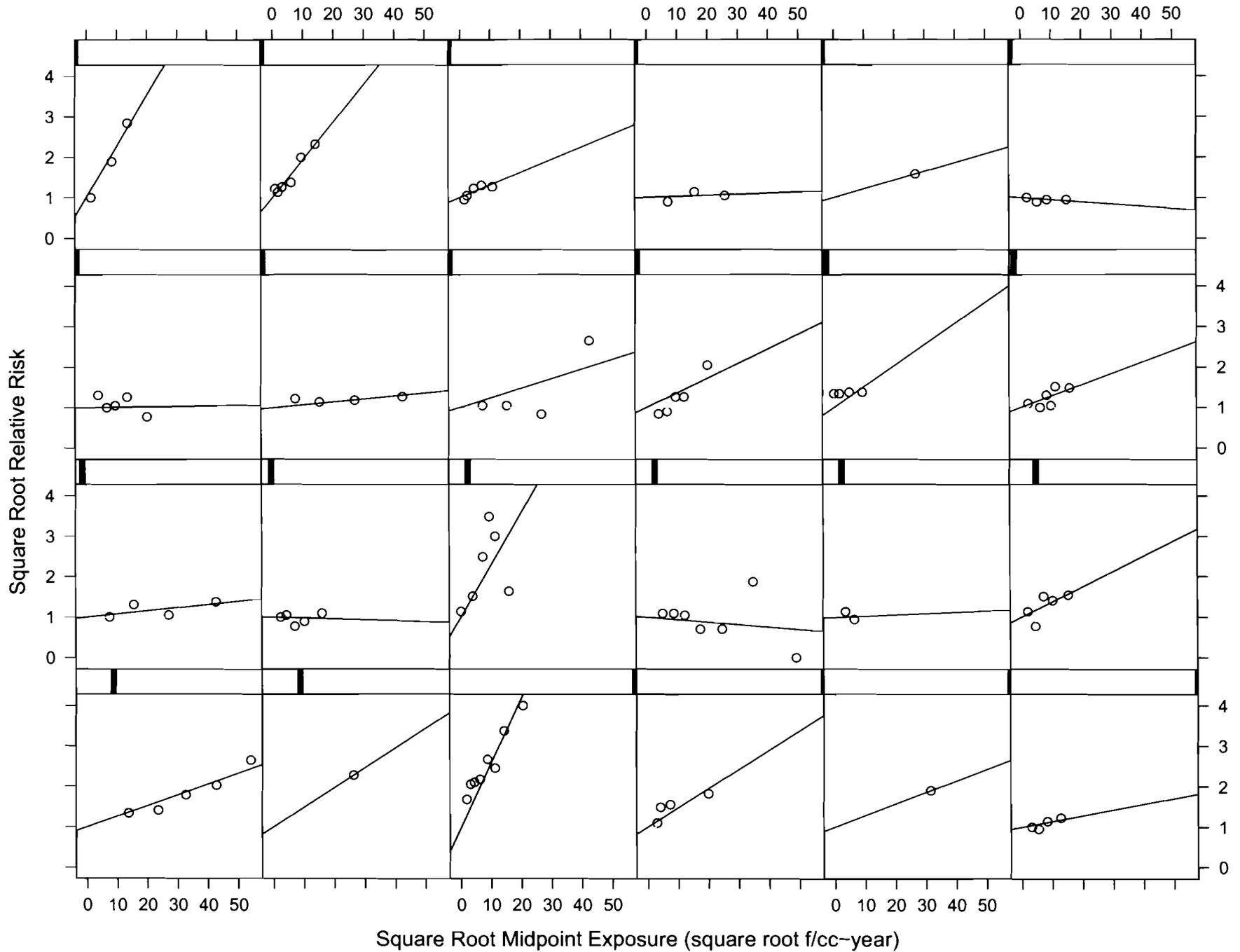
Lines fitted by least squares through “origins”

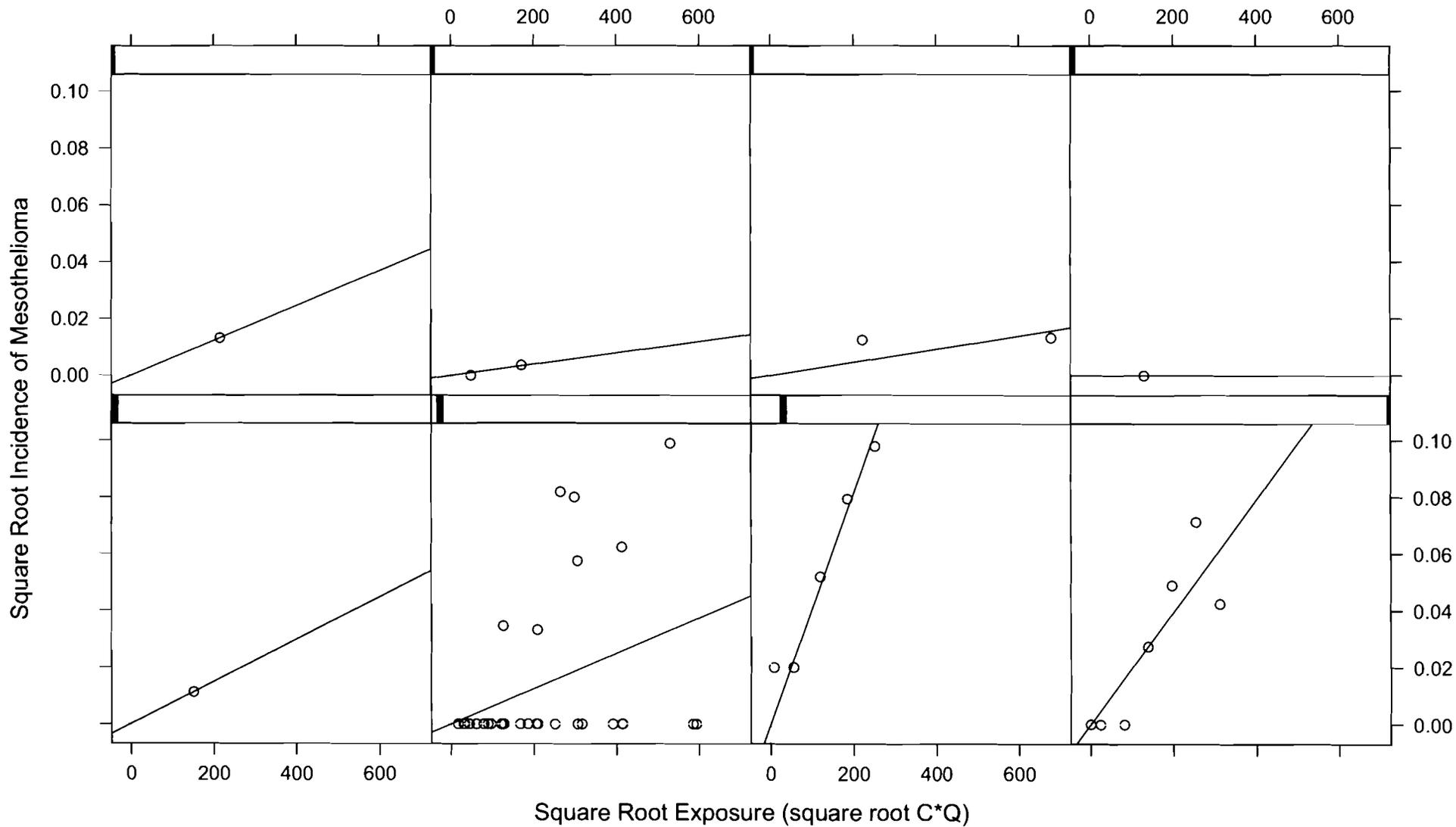
- lung: 0 exposure has incidence 1
- meso: 0 exposure has incidence 0

Panels are ordered, left to right and top to bottom by percent amphibole

- bar in strip label at the top of each panel shows percent amphibole, from 0% (left) to 100% (right)

# $\sqrt{\text{Lung}}$ vs. $\sqrt{\text{Exposure}}$ Ordered by Percent Amphibole (red bar)





## **What the Displays of the Data Show**

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Linearity of the relationship of disease and exposure

No evidence for a differential effect of mineral type: chrysotile and amphibole

Astonishingly small number of mesothelioma observations, and for the study with the largest number of bins, data and model are in strong disagreement

Large variability in risk coefficient estimates across studies

## Variability in Risk Coefficient Estimates

---

EPA Proposal: adding mineral type and particle size can account for variability

- "... cancer risk calculations that utilize the current PCM-based potency factors may either under-predict or over-predict risk, depending on the mineral type and size of asbestos particles that are present in the exposure setting that is being evaluated"

Exposure measurement error surely causes variability

- known to exist and vary across studies
- systematic over-estimation of exposures: under-prediction of risk coefficients
- systematic under-estimation of exposures: over-prediction of estimates of risk coefficients
- random over-estimation and under-estimation does not cancel out, but leads to underestimation of risk coefficients that increases with the magnitude of the errors

## Random Measurement Error: An Example to Illustrate

---

Conserve time by a dose-response example with a normally distributed dose instead of the binary response, death or not, of the asbestos data. The principles are the same in both cases.

The True Model: Linear Dependence of Response on Dose

$$\text{Response}_i = \text{Dose}_i + \text{Noise}_i, i = 1 \dots 400$$

$\text{Dose}_i$  is normal with mean 10 and variance 1

$\text{Noise}_i$  is normal with mean 0 and variance 0.75

Measurement Error: We Observe Dose + Error

$$\text{Observe}_i = \text{Dose}_i + \text{Error}_i$$

$\text{Error}_i$  is normal with mean 0 and  $\sigma^2$

What happens if we do not account for measurement error?

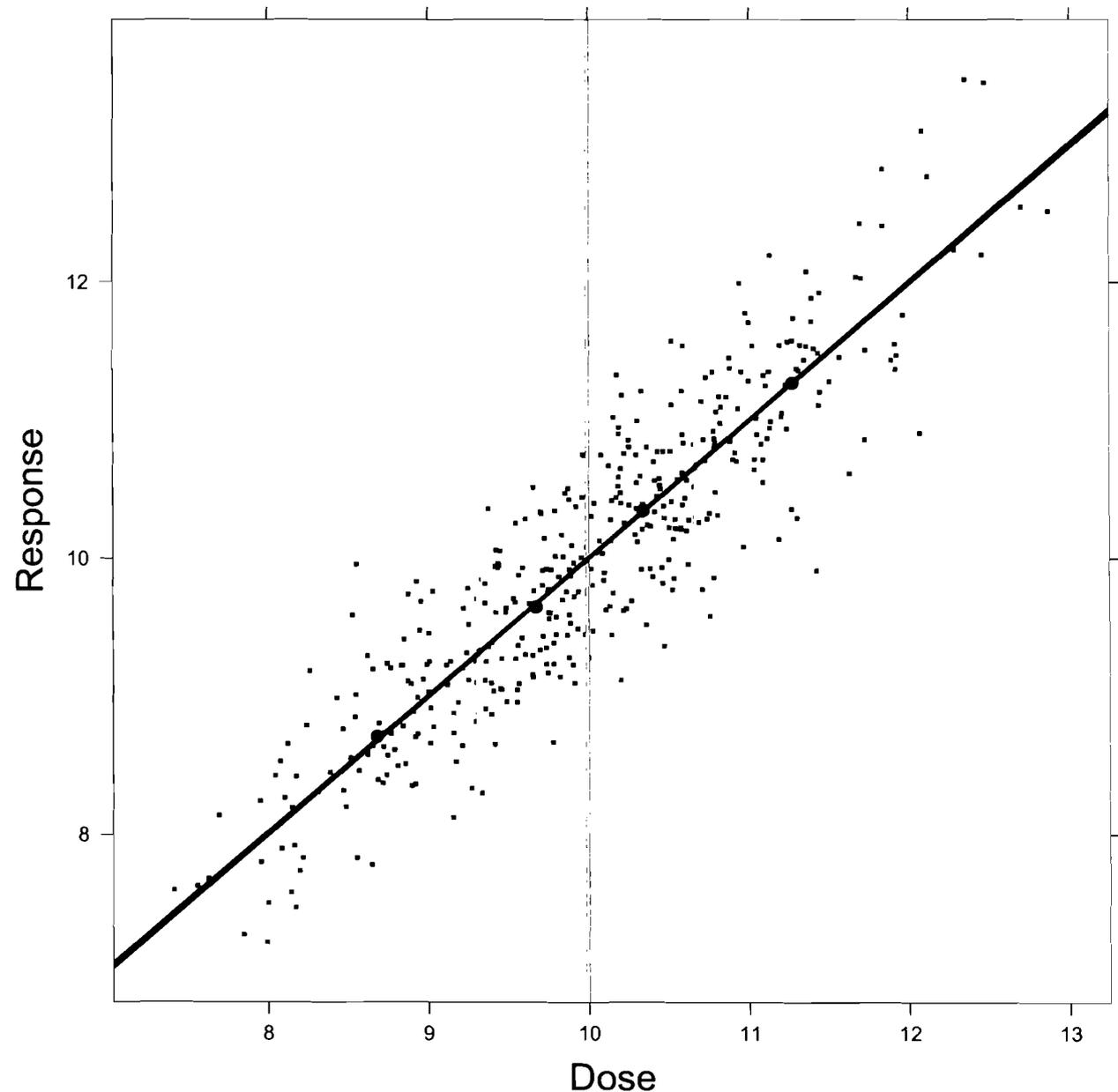
We will add errors with increasing  $\sigma^2$  to dose. Linear pattern will remain. Underestimation of risk will increase.

Oblique black line:  
true dose-response  
line.

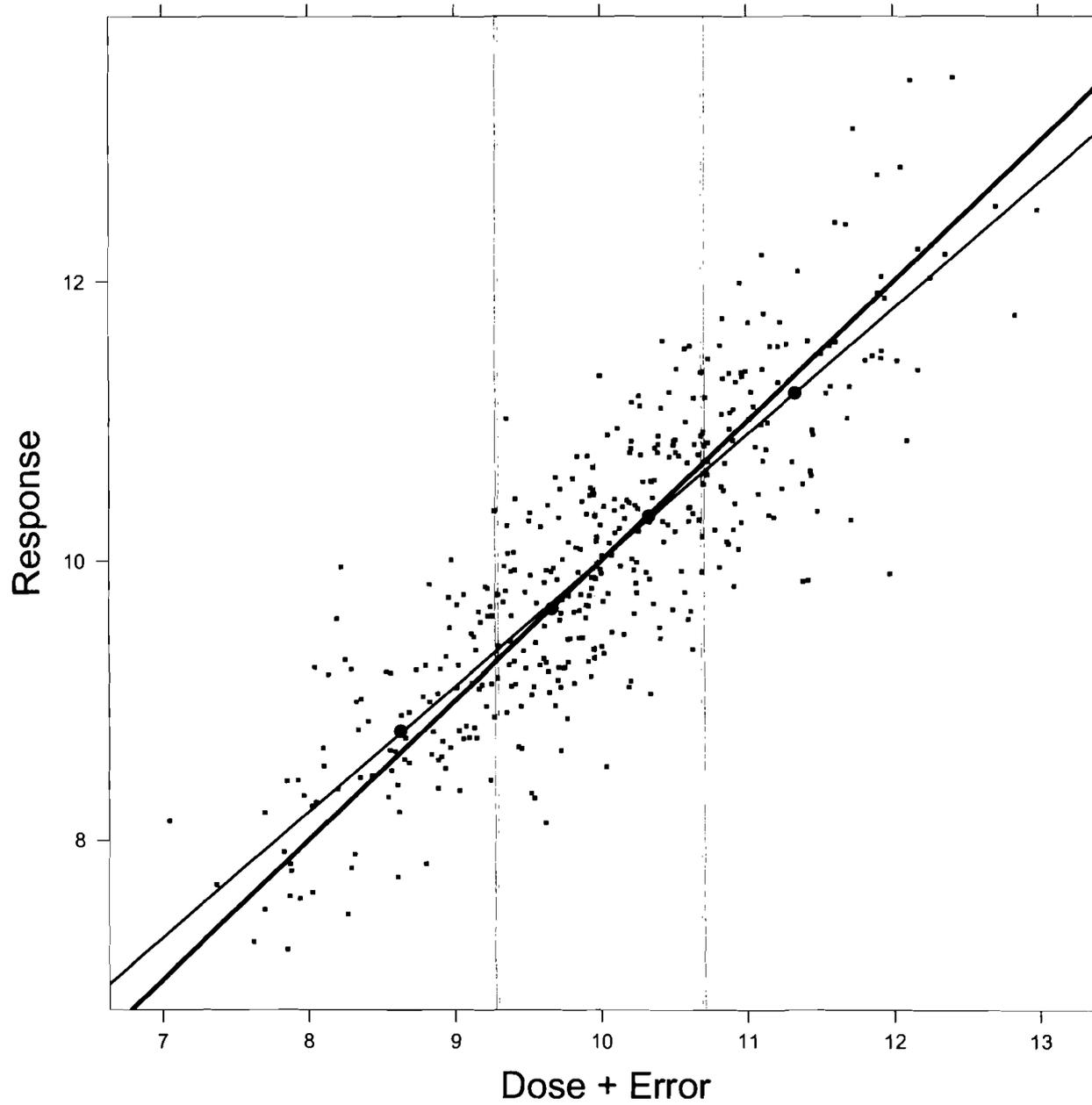
Vertical lines:  
divide the data into  
bins.

Red dots:  
dose and response  
bin means, as done  
in asbestos studies.

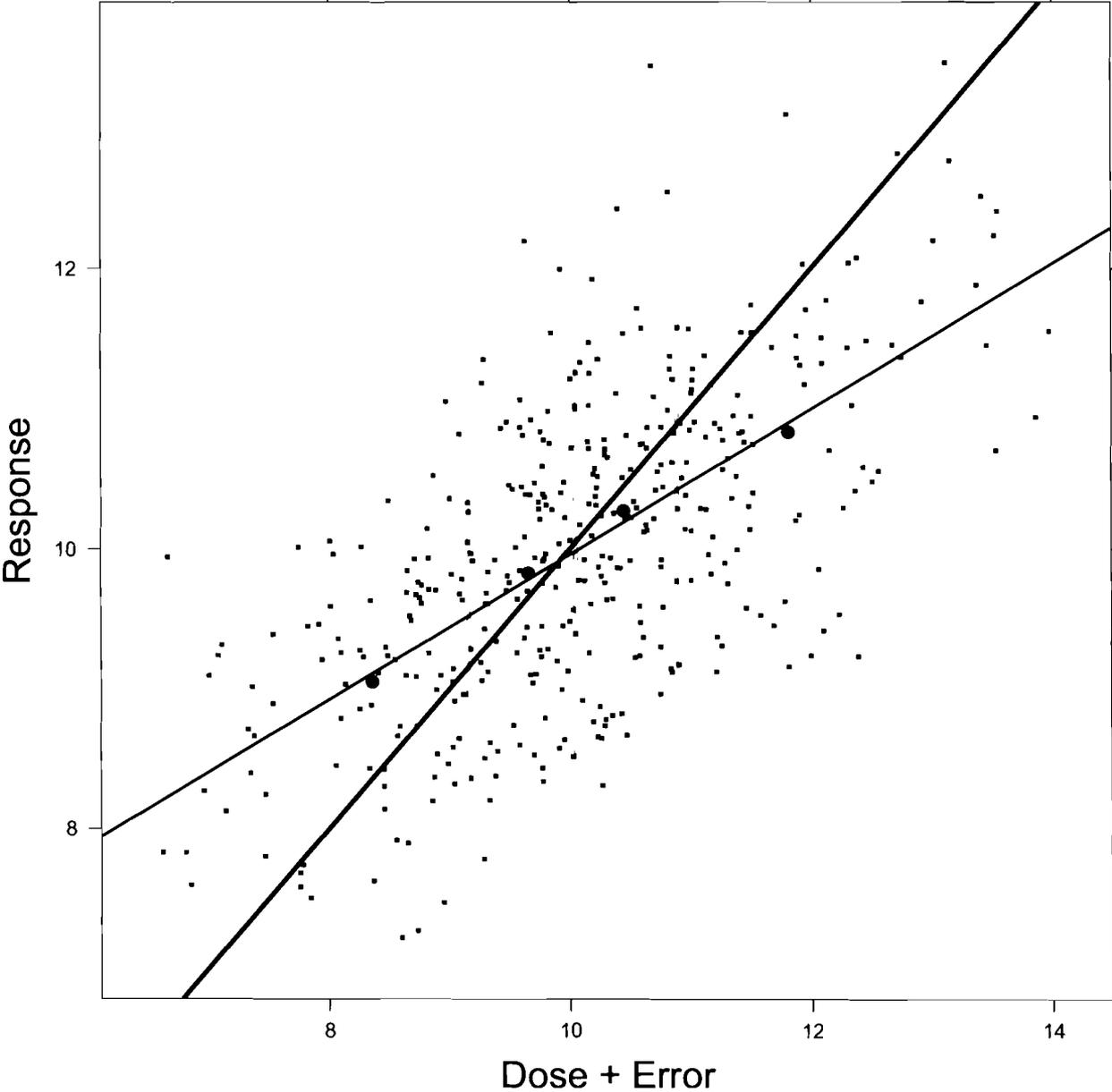
Red line:  
least squares fit to  
bin means.



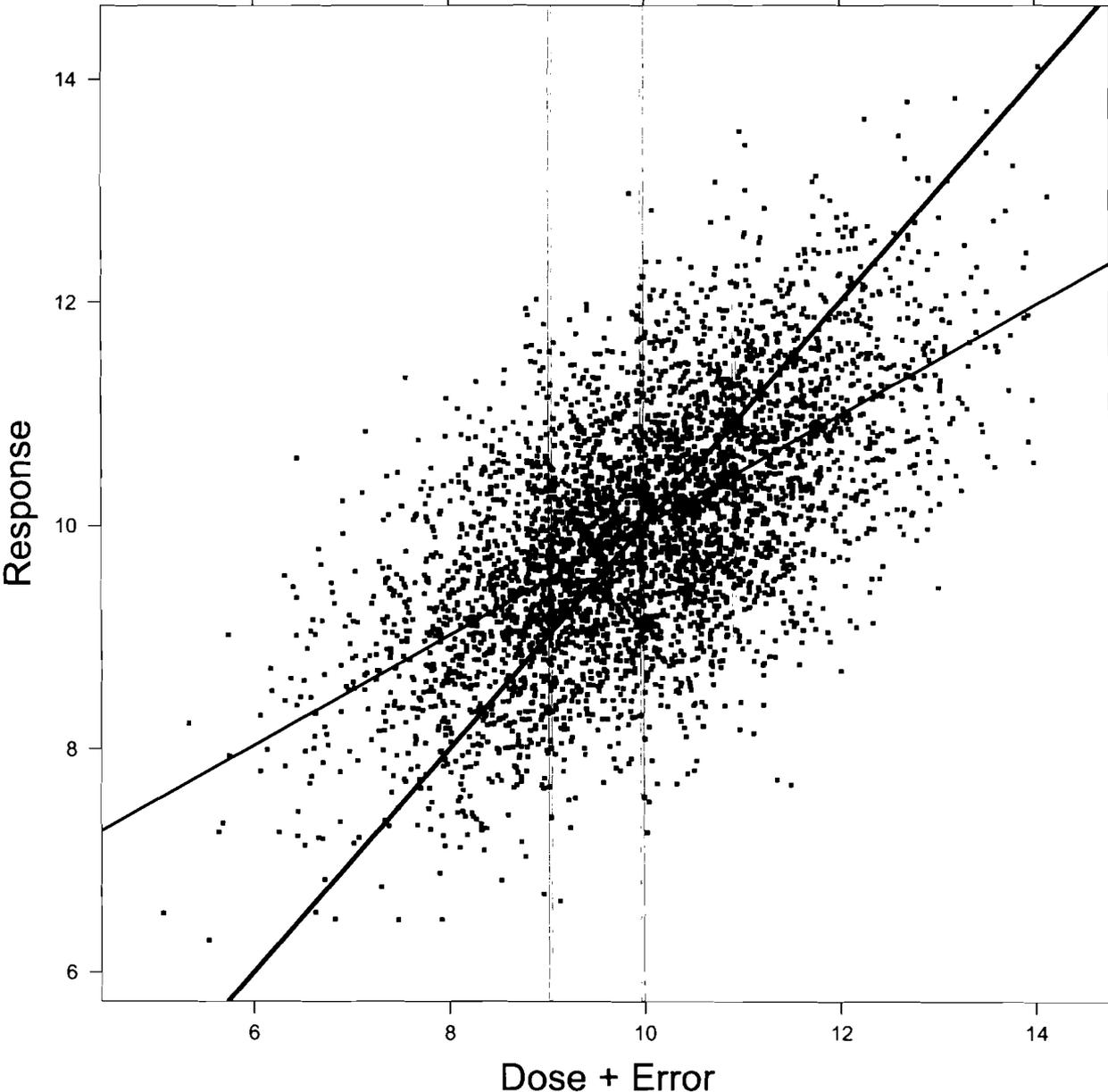
# Error Variance 10% of Dose Variance. Bias Evident.

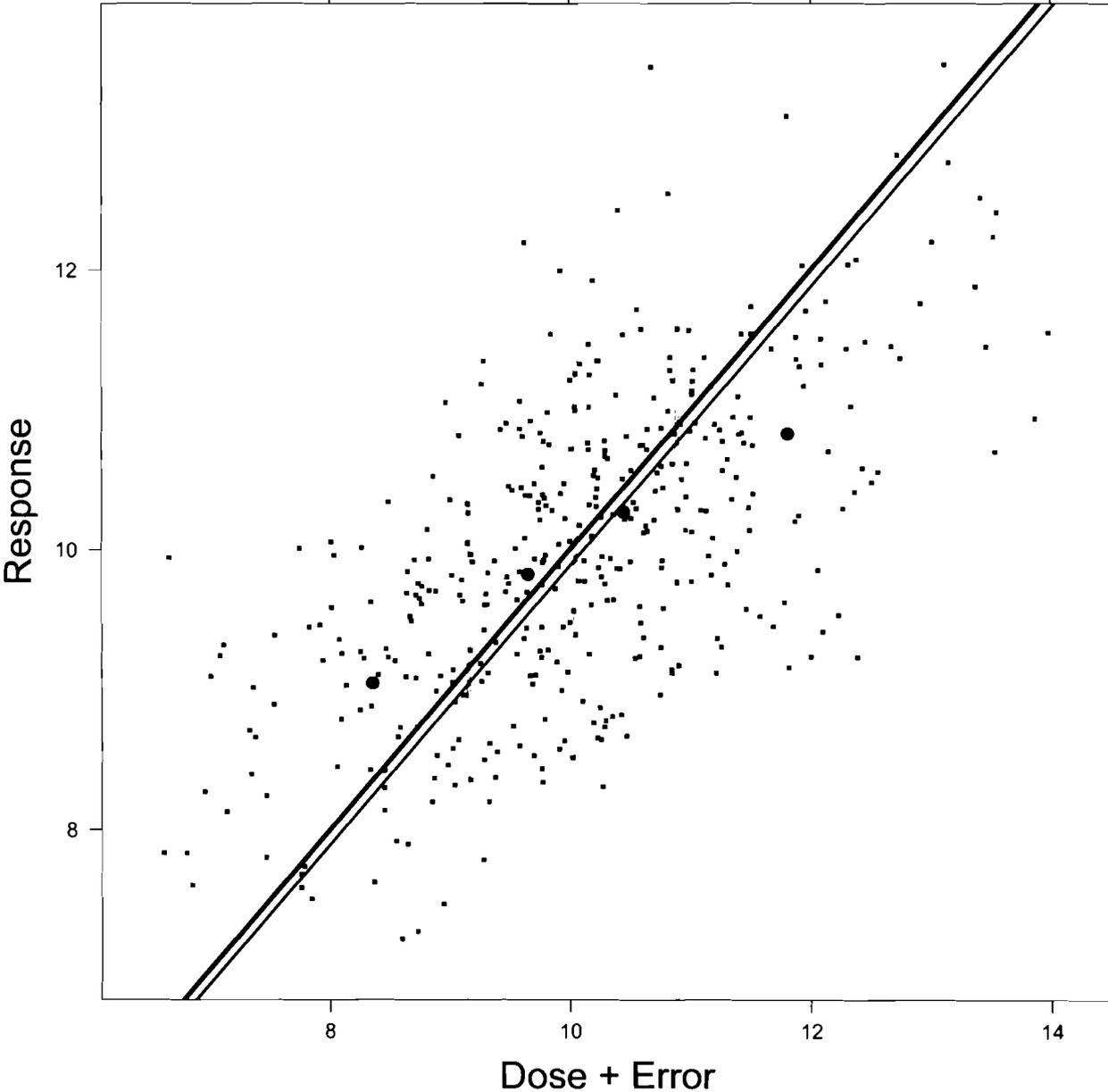


**Error Variance 100% of Dose Variance. Bias Increases With Error Variance.**<sup>11</sup>



**10× Sample Size = 4000 Observations: Bias Does Not Change**





## The Effect of Random Measurement Error

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### No Adjustment for Error

If we have two studies with the same true risk coefficients, the one with more random measurement error will tend to have a smaller estimated risk coefficient.

Impedes between-study inference since different studies can be expected to have different measurement error distributions

- e.g., if we have two studies, one amphibole and one chrysotile, we are at the mercy of measurement error if we do not adjust

Does not necessarily obscure everything

- e.g., linear relationships can remain linear
- e.g., positive risk coefficients can produce statistically significant positive estimates

### Adjustment for Error

Accurate estimation in the presence of measurement error can occur when there is reliable, empirical information about the error distribution.

Information put into a risk estimate from outside the data, like a fixed error variance, controls the estimate

EPA proposal relies on between-study accuracy to estimate particle size and mineral type effects, so measurement error is a critical matter.

Bayesian priors describe the exposure error distributions.

Information in the priors will control risk estimates and results of particle size and mineral type effects.

Further study of asbestos risk should have a strong scientific grounding.

This can only come through (1) study of "raw data" — exposures, death or not, demographic variables, smoking, etc. — for individuals, and (2) a concerted effort to characterize measurement error.

The approach is valid only if the priors are accurate descriptions of the actual error distributions.

Current information about error distributions appears insufficient.

**Comments on "Proposed Approach for Estimation of Bin-specific Cancer Potency Factors for Inhalation Exposure to Asbestos"**

**Suresh H. Moolgavkar, M.D., Ph.D.**

**Exponent, Inc.**

With more than 20 years having passed since the last EPA risk assessment for asbestos, it is about time to take a new look at the data and conduct a risk assessment that is based on the current state of knowledge of asbestos-induced disease, particularly the current state of knowledge regarding the dependence of risk on fiber type and fiber dimensions. It seems to me that the EPA has two choices here. One choice might be to acknowledge that risk assessments need to be easily understood and transparent, but that the science is complex and difficult to understand. Thus the EPA could choose to make a number of simplifying assumptions and arrive at estimates of risk that it believes to be protective of public health while acknowledging that these numbers do not represent outputs from the best possible analyses. The second choice, which the EPA appears to be making here, is to conduct the best possible analyses of the available data. If this is indeed the choice EPA has made, then it falls short, particularly in its choice of models for analyses.

There are three fundamental issues the EPA has to address here.

1. The choice of the appropriate bin-specific models for asbestos-induced lung cancer and mesothelioma (I will not discuss asbestosis here).
2. The appropriate methods to address exposure measurement error.
3. The appropriate methods for fitting the models to data and estimating the parameters.

The second and third issues are easily dealt with. So long as the exposure measurement error is Berksonian, which is a reasonable assumption, monte carlo methods can be used to integrate over the measurement error distribution even for complicated models for asbestos-induced cancer. See, for example Heidenreich et al. (2004) for an application to radon-induced lung cancer among miners. For parameter estimation, what EPA calls a Bayesian framework is nothing more than maximum likelihood estimation because of the assumption of flat priors. Markov chain monte carlo methods are simply convenient computational tools for maximum likelihood estimation and, more generally, for exploration of the likelihood surface.

The first issue, that of choice of bin-specific models, is much more problematic. Here the EPA has a real opportunity to explore models other than the ones used in 1986 and in the recent Aeolus report. The EPA also has the opportunity to investigate the interaction between asbestos and cigarette smoking in lung cancer. The situation here is more complex than the EPA acknowledges. I direct the EPA's attention to a recent paper by Wraith & Mengerson (2007).

The model for mesothelioma is the one originally developed by Professor Julian Peto and based loosely on ideas of multistage carcinogenesis. This model shows quite clearly that the hazard function for mesothelioma depends on intensity of exposure, duration of exposure and time since exposure stopped. While the hazard function is linear in intensity, it is a cubic function of duration of exposure and time since exposure stopped. Therefore, the hazard function for mesothelioma is not a well defined function of cumulative exposure, a fact that is not clear in the current EPA document. The EPA now has the opportunity to investigate whether other models, such as the two-stage clonal

expansion model, can describe the mesothelioma data. Particularly in view of the fact that clonal expansion is one of the postulated modes of action for asbestos, this model would appear to be particularly appropriate. One consequence of asbestos acting as a promoter is that the bin-specific hazard functions may not be simple multiples of each other as assumed by EPA..

The proposed model for lung cancer presents the greatest problems in my opinion. This is a linear excess relative risk model with the multiplicative fudge factor  $\alpha$  thrown in. In this model the risk depends strictly on cumulative exposure: intensity, duration and time since exposure stopped are not independently considered. We have considerable evidence that such a model flies in the face of biology. First, we know that it does not hold for many other lung carcinogens, including cigarette smoking. In fact, we know that the risk of lung cancer among ex-smokers depends in a complicated way on intensity of smoking, duration of smoking and time since smoking stopped. We know that the hazard function for asbestos-induced mesothelioma also depends on all three factors, as noted above. It is incumbent upon the EPA to develop better models for lung cancer, based on individual level exposure information. If such models can be developed for mesothelioma, as attested to by the Peto model, there is no reason that they cannot also be developed for lung cancer. Finally, as I have already pointed out above, a thorough investigation of the interaction of asbestos and smoking in lung cancer should also be undertaken.

I look forward to making these comments in person at the SAB meeting on July 21 and 22.

#### References

Heidenreich WF, Luebeck EG, Moolgavkar SH. Effects of exposure uncertainties in the TSCE model and application to the Colorado miners data. *Radiat Res* 2004; 161:72-81.

Wraith D, Mengersen K. Assessing the combined effect of asbestos exposure and smoking on lung cancer: A Bayesian approach. *Statist Med* 26:1150-1169, 2007.

# **Comments on EPA approach to risk assessment for asbestos – July, 2008**

**Suresh H. Moolgavkar, M.D., Ph.D.**

## General Comments

- **Agency is correct to revisit asbestos risk assessment in light of the new information developed over the last two decades.**
- **In particular, important to recognize the differences in toxicity by fiber type and fiber dimensions.**
- **The general approach adopted by the agency is appropriate.**
- **However, there are a number of problems that need to be addressed for successful implementation.**

## Exposure Assessments

- **Exposure assessments by fiber type is difficult but, I believe, possible. Particularly important to characterize accurately the mix of fibers in occupational cohorts (see examples below).**
- **Exposure by fiber dimension may be particularly problematic.**
- **Risk assessment by fiber type appears to be doable. Because of possible exposure assessment problems, more skeptical that it can be done by fiber dimension.**
- **Canadian cohorts cannot be considered to be pure chrysotile cohorts.**
- **Yano cohort is also not a pure chrysotile cohort.**

## Models & Analyses

- Real opportunity to take a fresh look at data.
- Exploitation of this opportunity requires that new models be considered, particularly for lung cancer, but also for mesothelioma.
- Models for lung cancer based on cumulative exposure are epidemiologic incarnations of Haber's law in toxicology.
- Such models are biologically untenable. Intensity of exposure, duration of exposure, time since exposure stopped are all important – cigarette smoke, arsenic, ionizing radiation (radon daughters) are all examples of these facts, as is asbestos-related mesothelioma.
- Interaction of asbestos and cigarette smoking in lung cancer should also be revisited.
- In view of possible promotional activity of asbestos and the differences in half-life of the different fiber types, assumption of proportionality of hazards (assumption of bin-specific constants  $K$  multiplying a common hazard function) made by OSWER may be problematic.

**Remarks of James P. Morris on July 21, 2008  
Science Advisory Board Meeting to Review the Proposed  
Approach for Estimation of Bin-Specific Cancer Potency  
Factors for Inhalation Exposure to Asbestos**

**Georgia Morris nee O'Shea**

**Born:** July 1, 1942

**Died:** April 4, 2008 in her 65<sup>th</sup> year

**Cause of Death:** Mesothelioma, acquired second hand by a loving and dutiful daughter from her father George, an asbestos worker.

As background, George and Rosemary had one child Georgia. George got his union card in 1937. Georgia lived with her mom and dad for her first 25 years. Until the 7<sup>th</sup> grade in her parents' rental apartment, so small that Georgia slept on a cot in the dining room. In the 8<sup>th</sup> grade, Georgia's parents bought a 2 bedroom house. Georgia finally had her bedroom! Her only time away from her parents was to attend college. She had two majors – English and Elementary Education. Her mother worked; consequently, Georgia, the loving and dutiful daughter, did the laundry in the basement including shaking out her father's work clothes. She also cleaned, vacuumed and changed linens. Every night she would hug, kiss and run her fingers through her father's hair on his return from covering pipe with asbestos. George died from asbestos. George's brother Ed became a pipe cover after serving as a tank commander under General Patton. Ed died from asbestos as did his wife Veronica two years later. Georgia's mom is still alive at 88 having buried her husband and her only child.

## **Georgia Morris nee O'Shea**

**Born:** July 1, 1942

**Died:** April 4, 2008 in her 65<sup>th</sup> year

**Cause of Death:** Mesothelioma, acquired second hand by a loving and dutiful daughter from her father George, an asbestos worker.

My name is Jim Morris. I hold BS and MBA degrees. I was a Naval Officer and served in Vietnam. I met Georgia less than a month after my discharge in 1966. We were married in February 1968. She gave me the 3 best children in the world. For the last 20 years I have worked for Export-Import Bank of the U.S., a U.S. government agency. Before mesothelioma Georgia was hospitalized only 4 times – for the births of our children and a hysterectomy. We put our children through good private colleges without scholarship help. Our debts finally paid, Georgia and I started enjoying the good life – travel, grandchildren, etc. Asbestos robbed us of 20 great years.

## **Georgia Morris nee O'Shea**

**Born:** July 1, 1942

**Died:** April 4, 2008 in her 65<sup>th</sup> year

**Cause of Death:** Mesothelioma, acquired second hand by a loving and dutiful daughter from her father George, an asbestos worker.

In January 2007 Georgia felt pain in the upper right hand part of her back. Her GP sent her to massage therapy. It didn't work! The pain persisted! Her GP turned her over to a neurologist whose preliminary testing showed the pain may be mesothelioma related. He

then turned her over to a pulmonologist who in early June confirmed that Georgia had mesothelioma.

### **Georgia Morris nee O'Shea**

**Born:** July 1, 1942

**Died:** April 4, 2008 in her 65<sup>th</sup> year

**Cause of Death:** Mesothelioma, acquired second hand by a loving and dutiful daughter from her father George, an asbestos worker.

Miami's medical community knows little about the treatment of this cancer. Georgia, our daughter and I immediately flew to Boston and to Harvard and met with Dr. David Sugarbaker, a world renowned thoracic surgeon specializing in mesothelioma treatment. He told us there is no cure for mesothelioma; however, he would be willing to perform surgery which removes the lung, the pleura surrounding the lung, part of the diaphragm and as much of the cancer that is naked to the microscope. After these removals, the next step is to insert a heated, chemo treated blanket into the void for about 20 minutes to hopefully kill any unspotted cancer, which if successful could prolong her life for 2 to 5 years and maybe even longer. Because of time demands he could not operate for 5 to 6 weeks. God, were we happy! When we returned, Dr. Sugarbaker cancelled the operation because it had become too dangerous, told us to go back home and get chemo which hopefully will reduce the cancer's size so he can operate more safely.

### **Georgia Morris nee O'Shea**

**Born:** July 1, 1942

**Died:** April 4, 2008 in her 65<sup>th</sup> year

**Cause of Death:** Mesothelioma, acquired second hand by a loving and dutiful daughter from her father George, an asbestos worker.

We were fighters and didn't give up. We went to the University of Chicago and met with Dr. Kindler, a world respected medical oncologist specializing in mesothelioma. Georgia was on chemo for the next 18 weeks. We returned to Chicago and learned that the cancer did not shrink and that Georgia's body could not endure anymore chemo.

### **Georgia Morris nee O'Shea**

**Born:** July 1, 1942

**Died:** April 4, 2008 in her 65<sup>th</sup> year

**Cause of Death:** Mesothelioma, acquired second hand by a loving and dutiful daughter from her father George, an asbestos worker.

I never left her side for 9 months. I bathed her, I fed her, she needed to keep her weight, so every day I made her a chocolate milk shake using Haagen Das and heavy whipping cream. I changed her adult diapers when she wet them. I dressed her. I moved her from our bed to her wheelchair. I took her outside and pushed her on long walks for the fresh air. Her pain was intense and became even worse with time. We saw pain doctors, to no avail! She just kept taking bigger and bigger doses of Oxycontin along with Ativan. She was on oxygen for 24 hours a day for over six months. All the pain killers led to constipation. She took medicine for this affliction. She would have a bowel movement every 3 days. I would have to turn her oxygen tank to its highest level because of the effort expended to have a BM. Over time all the medicines caused occasional non lucid moments. The only humorous moment I can recall is when I dozed off on the couch one

afternoon. I'm a golfer, as was Georgia. She managed to maneuver her wheelchair over to the stove and take out a frying pan. I heard this commotion, went to the stove, and asked her what she was doing. She told me she was scrambling golf balls for my breakfast!

Georgia died in our bed wearing her oxygen mask sometime before 6 a.m. on April 4, 2008. I was asleep at her side. At our marriage her wish to me was not to walk in front of her for she may not follow, not to walk behind her for she may not lead, but to walk beside her as friends. Ladies and gentlemen, I did! She was my best friend for over 40 years.

### **Georgia Morris nee O'Shea**

**Born:** July 1, 1942

**Died:** April 4, 2008 in her 65<sup>th</sup> year

**Cause of Death:** Mesothelioma, acquired second hand by a loving and dutiful daughter from her father George, an asbestos worker.

Statistics are misleading. The Internet tells me 1 in 1,000,000 Americans die of mesothelioma. It does not say what the probability of death is when the sample becomes people directly exposed to asbestos and their indirectly exposed spouses and children. It ain't a million to one!

Rather than having this meeting, we should somehow, firstly, find the spunk and gumption to ban asbestos from this country and secondly, find the money to cure this monster of a disease.

Thank you.

750 East Adams Street  
Syracuse, NY 13210

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## University Hospital

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November 6, 2007

John P. Comerford, Esq.  
Lipsitz & Ponterio  
135 Delaware Avenue, 5th Floor  
Buffalo, New York 14202

FAX (716) 849-0708

RE: James Girton  
JA07-295

Dear Mr. Comerford:

I have reviewed the records and pathology materials you sent related to Mr. Girton. According to the information provided Mr. Girton had exposure to asbestos from automotive brake and clutch materials. He was exposed to dust when brake linings were either hand sanded or resurfaced with an electric bench grinder. From 1954 to 1972 he worked at several car dealerships in New York and continued to do work at home on his own vehicles and for others from 1972 to 1979. He was around other mechanics as well when they did brake maintenance and removal.

The pathology materials I received correspond to the pathology from Lourdes Hospital (S07-5671) from Mr. Girton's right pleural and lung biopsies on June 11, 2007. The biopsy shows an invasive malignant tumor of the pleura diagnostic for malignant mesothelioma based on the immunohistochemical stains reported and provided for my review. These show the tumor cells positive for calretinin and CK5/6 and negative for BerEP4 and CEA. There is lung parenchyma contained within the lung biopsy and iron stained section revealed no asbestos bodies. The mesothelioma in the available biopsy sampling appears to be biphasic but predominantly epithelial. The diagnosis of mesothelioma was also confirmed by review at the Brigham & Women's Hospital.

To ascertain the lung burden of asbestos bodies and/or fibers, portions of the lung tissue from the paraffin blocks were digested using our standard sodium hypochlorite digestion, followed by collection of the residue on polycarbonate membrane filters for counting asbestos bodies by light microscopy or examining fibers using electron microscopy. There was insufficient tissue for determining the dry weight of the lung tissue.

The first analysis, by light microscopy, searched for asbestos bodies on a filter with a detection limit of 35 asbestos bodies per gram of wet lung tissue. No asbestos bodies were found in this analysis by light microscopy.

The first electron microscopic analysis used tissue from block A1 and analyzed all fibers at least 3 micrometers in length at a viewing magnification of 8,000 times in the electron microscope. In this analysis the detection limit was 18,700 fibers per gram wet lung. The types of asbestos fibers found included one tremolite fiber and one probable chrysotile fiber [undetectable magnesium], each representing 18,700 fibers per gram wet lung. The tremolite fiber was 9.8 micrometers by 1.6 micrometers and the probable chrysotile fiber was 16.9 by 0.16 micrometers. In addition to these fibers there were 3 fibers of probable talc detected ranging in length from 7.3 to 25.7 micrometers. No commercial amphibole fibers were detected in this analysis.

Page 2  
JA07-295  
Girton, J.

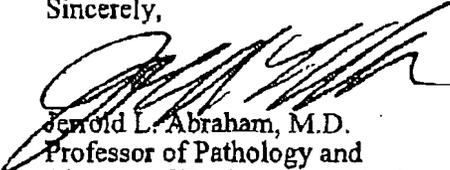
The second electron microscopic analysis analyzed fibers from block B1 at a viewing magnification of 4,000 times in the electron microscope. This analysis had a detection limit of 1,900 fibers per gram wet lung. In this analysis the concentration of asbestos was determined to be 38,700 fibers per gram wet lung. The types of asbestos fibers included chrysotile with partial depletion of magnesium at 21,000 fibers per gram wet lung, tremolite at 1,900 fibers per gram wet lung and additional probable chrysotile with complete depletion of magnesium at 15,500 fibers per gram dry lung. The length of the chrysotile fibers ranged from 4.9 to 61 micrometers; 10 of the 11 chrysotile fibers found were greater than 5 micrometers in length. The one tremolite fiber was 12.4 micrometers in length. The additional probable asbestos fibers ranged from 5.1 to 30.4 micrometers. In addition to the chrysotile and tremolite fibers 4 fibers of talc were found ranging from 5.3 to 29.9 micrometers in length. No commercial amphibole fibers were detected in this analysis.

In summary these lung fiber burden analyses confirm the absence of detectable commercial amphibole fibers within the detection limits of these analysis. The background range for commercial amphibole (amosite and/or crocidolite) would be up to 1,000 fibers per gram wet lung tissue. The background range for chrysotile fibers greater than 5 micrometers in length would be up to approximately 5,000 fibers per gram wet lung, and the concentrations of fibers greater than 10 micrometers in length for chrysotile in the general background population would be near 0. Therefore these findings confirm an elevated burden of chrysotile and related amphibole fibers in Mr. Girton's lung. This is consistent with his occupational history and independently determined from the history.

Asbestos exposure is well recognized to be the cause of nearly all malignant mesotheliomas. Mr. Girton had a history of asbestos exposure and developed a malignant mesothelioma. Therefore I can conclude to a reasonable degree of medical certainty that Mr. Girton's asbestos exposure was the cause of his malignant mesothelioma and will likely be the cause of his death.

Please let me know if you need additional information

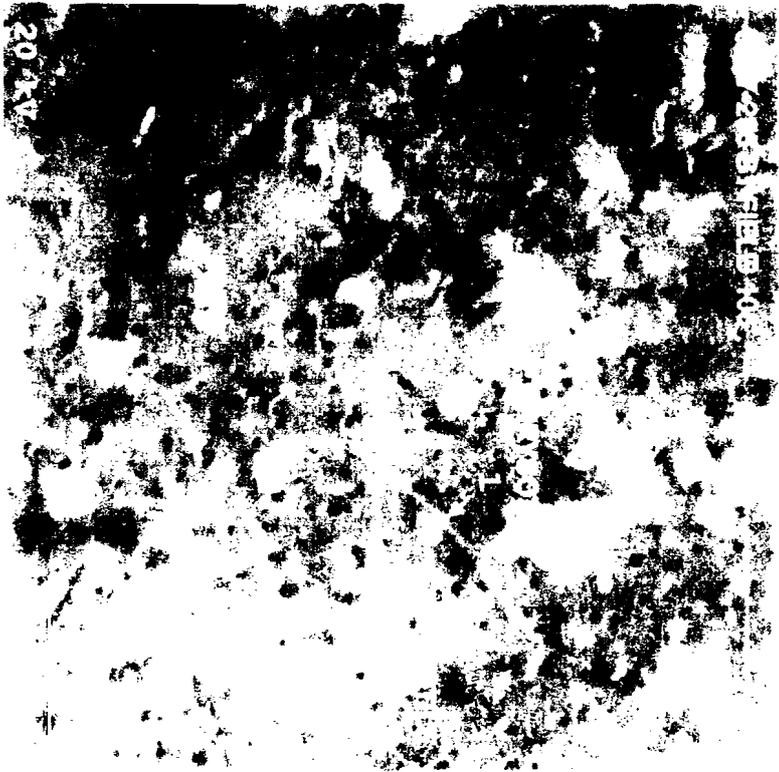
Sincerely,



Jerrold L. Abraham, M.D.  
Professor of Pathology and  
Director of Environmental and  
Occupational Pathology

P.S. The pathology materials are being returned under separate cover.  
JLA/hjg





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June 22, 2006

John Guinan, Esq.  
Levy, Phillips, and Konigsberg  
800 Third Ave.  
New York, NY 10022

Fax (212)605-6290

Re: Bennett Scott Hoser  
JA06-151

Dear Mr. Guinan:

As requested I have reviewed the records and pathology I received related to Mr. Hoser. My understanding from the information provided is that Mr. Hoser was diagnosed with mesothelioma at age 45 in October 2005. He had a radical pneumonectomy at Sloan Kettering in March 2006. His work history provided indicates he grew up on a dairy farm in New Jersey where he worked on various tractors. From at least 1975-1979 Mr. Hoser would personally sand the brake discs for the tractors (International Farmall Super MTA Tractors). He was also present as a young man when his father took a bench grinder to the brake discs, which created considerable airborne dust. Mr. Hoser also had exposure at Warren County Vocational Technical School in Broadway, NJ, in an auto mechanics class from 1977-1979, in which he worked on brakes, clutches, and gaskets. In 1978 he worked at Louie's Garage in Bloomsbury, NJ, and was present when multiple brake jobs were performed. He also worked at a Ford tractor dealership in Washington, NJ from February-July 1979, and worked on brakes, clutches, and gaskets on Ford tractors. Occasionally Mr. Hoser also performed brake jobs at his home. During the 1980's Mr. Hoser worked as a correctional officer in New Jersey and serviced numerous international harvester tractors at the site, with further exposure to asbestos-containing brakes and clutches. His testimony recorded March 3, 2006 goes into more detail on his work history.

The pathology materials I received correspond to the surgical pathology report S06-8961 from Memorial Hospital in New York. The sections of lung show some evidence of talc pleurodesis with foreign body reaction in sections 12 and 18. Section 21 from the right lower lobe and 20 from the right middle lobe show lung and 19 from the right upper lobe shows lung with tumor. The tumor was confirmed to be an epithelial malignant mesothelioma of the pleura, and there was also involvement of the peritoneum.

Portions of block 21 and 19 were digested using our standard sodium hypochlorite technique, with collection of the residue on nuclepore filters for counting of asbestos bodies by light microscopy and analysis of fibers using electron microscopy.

The first analysis, by light microscopy, used tissue from block 21 and had a detection limit of 181 asbestos bodies per gram dry lung or 54 asbestos bodies per gram wet lung. No asbestos bodies were detected in this analysis.

The first electron microscopic analysis used tissue from block 19 and analyzed all fibers at least 3 micrometers in length at a viewing magnification of 8000x in the electron microscope. In this analysis the detection limit was 20,000 fibers per gram wet lung or 93,000 fibers per gram dry lung. In this analysis the total concentration of asbestos was determined to be 1,213,000 fibers per gram dry lung (f/g-d). The predominant type of asbestos found was chrysotile at 466,000 fibers per gram dry lung followed by actinolite at 187,000 f/g-d and additional probable chrysotile from which magnesium had been completely depleted at 560,000 f/g-d. All of these chrysotile and probable chrysotile fibers were quite long, ranging in length from 5.1 up to 55.5 um and in diameter from 0.09 up to 0.23 um. The actinolite fibers were 2.6 and 6.0 um in length. This is certainly documentation of unusual chrysotile exposure, since the background concentration for such long chrysotile fibers would be extremely low in the general population, as discussed below.

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Hoser, B. S.

The second electron microscopic analysis used tissue from block 19 and analyzed all fibers at least 3  $\mu\text{m}$  in length at a lower magnification (4000x on the viewing screen of the electron microscope). In this analysis the detection limit was 52,000 f/g-d. A total concentration of asbestos fibers at 261,000 f/g-d was noted. In this analysis all of the fibers detected were either magnesium depleted chrysotile (104,000) or probable chrysotile with no detectable magnesium, ranging in length from 8.3 to 20.0  $\mu\text{m}$  and in diameter from 0.14 up to 0.28  $\mu\text{m}$ . No amphibole asbestos fibers were detected in this analysis.

The third electron microscopic analysis used tissue from block 21 and analyzed all fibers at least 3  $\mu\text{m}$  in length at a magnification of 8000x on the viewing screen of the electron microscope. In this analysis the detection limit was 108,000 f/g-d. No asbestos fibers were detected in this analysis.

The fourth electron microscopic analysis used tissue from block 21 and analyzed all fibers at least 3  $\mu\text{m}$  in length at a viewing magnification of 8000x on the viewing screen of the electron microscope. In this analysis the detection limit was 80,600 f/g-d. Asbestos fibers were detected at a concentration of 484,000 f/g-d. Chrysotile asbestos (partially magnesium depleted) and probable chrysotile asbestos (with no detectable magnesium) were detected at concentrations of 161,000 fibers per gram lung and 242,000 f/g-d, respectively. One actinolite fiber was detected representing a concentration of 80,600 f/g-d. The chrysotile fibers ranged in length from 6.9 to 22.6  $\mu\text{m}$  with diameters ranging from 0.14 to 0.18  $\mu\text{m}$ . The actinolite fiber was 12.3  $\mu\text{m}$  in length with a diameter of 0.8  $\mu\text{m}$ .

The last electron microscopic analysis used tissue from block 21 and analyzed fibers at least 3  $\mu\text{m}$  in length at a magnification of 4000x on the viewing screen of the electron microscope, searching specifically for fibers present at lower concentration than the detection limits of the other analyses. In this analysis the detection limit was 11,000 f/g-d. In this analysis chrysotile fibers were found at 45,000 f/g-d, ranging in length from 6.1 to 61.1  $\mu\text{m}$  and in diameter from 0.13 to 0.22  $\mu\text{m}$ . Actinolite fibers were found representing 22,000 f/g-d ranging in length from 4.0 to 10.8  $\mu\text{m}$  and in diameter from 0.47 to 0.63  $\mu\text{m}$ .

These findings are certainly consistent with Mr. Hoser's history of exposure predominantly to friction materials containing chrysotile asbestos fibers. There is no evidence of any commercial amphiboles in any of the analyses of his lung tissues. In the general background population, 95% of chrysotile fibers are shorter than 5  $\mu\text{m}$ , and calculations of the upper limits for chrysotile fibers longer than 5  $\mu\text{m}$  would result in a limit of approximately 50,000 f/g-d. For chrysotile fibers as long as most of those seen in Mr. Hoser's lung tissue, the upper limit of background would be much much lower than 50,000 f/g-d. Mr. Hoser's lung tissue contains greatly elevated concentrations of long chrysotile fibers.

These findings allow me to conclude to a reasonable degree of medical certainty that Mr. Hoser's asbestos exposure was the cause of his malignant mesothelioma and will likely be the cause of his death.

Please let me know if you need additional information.

Sincerely,

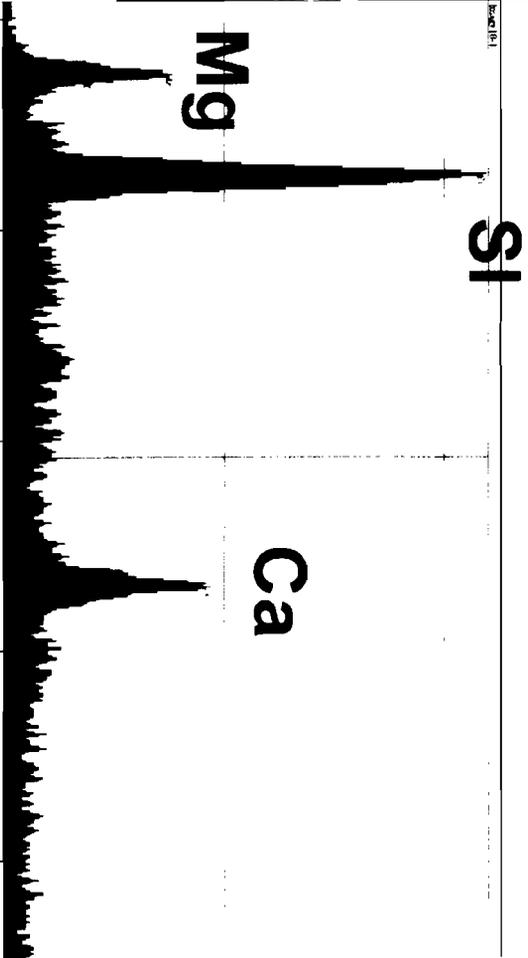
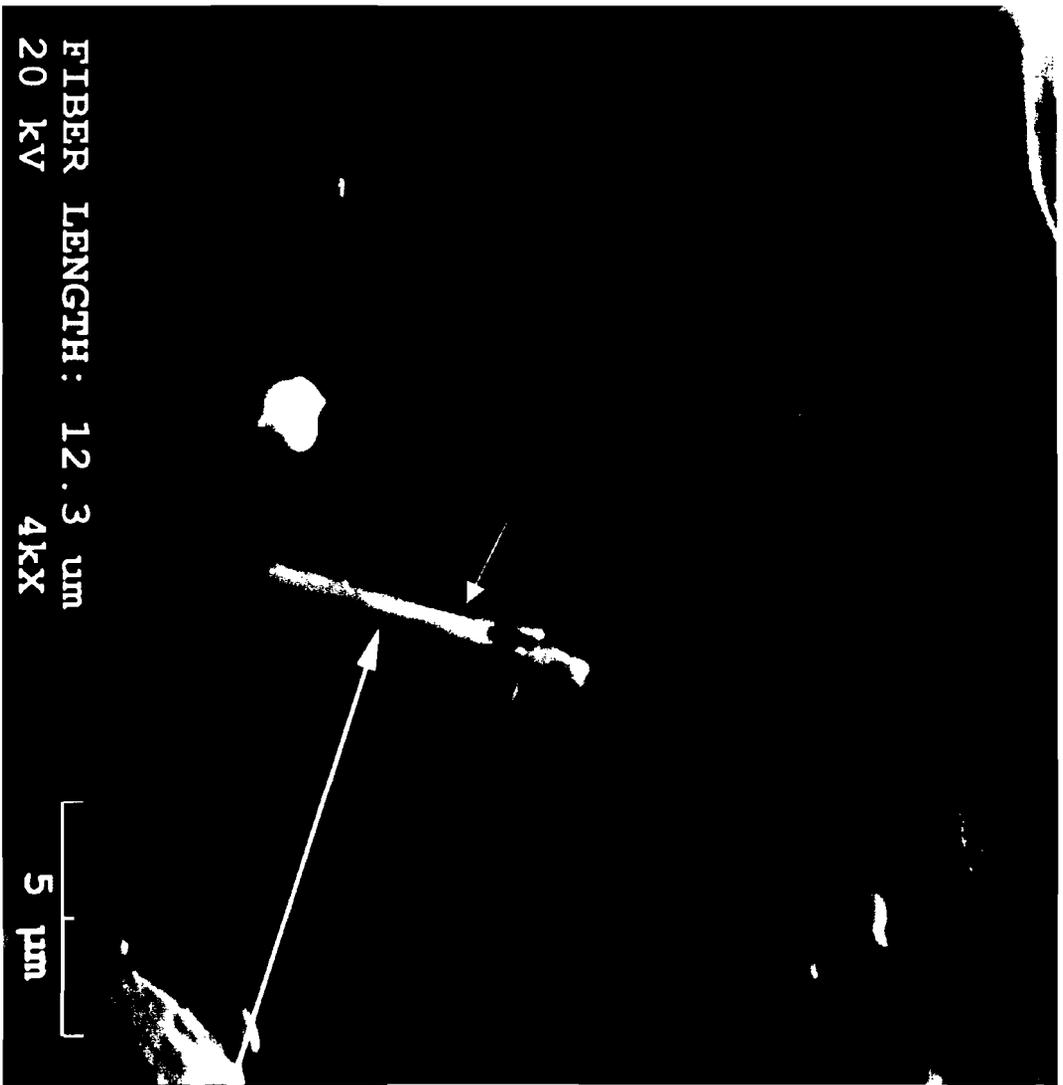


Jerold L. Abraham, M.D.  
Professor of Pathology and  
Director of Environmental and  
Occupational Pathology

p.s. The pathology materials are being returned under separate cover.  
JLA/ibp

**JAO6-151 HOSER  
SAMPLE C2  
4000X ANALYSIS**

**FIELD 77**



Original 05/31/97 14:08:00 - Backscattered Electron Image of Fiber  
View: 11C  
Detector: 0003 - 000300 - 000300



## **Comments to EPA Asbestos Panel, July 21, 2008**

Barry Castleman, ScD, Environmental Consultant    [barry.castleman@gmail.com](mailto:barry.castleman@gmail.com)

I have been involved in EPA and other government regulatory efforts involving asbestos and other toxic chemicals since the early 1970s, as an employee and consultant to environmental groups and as an independent public health worker. Much of my time today is spent working with others around the world to try to ban new use of asbestos products and bring exposures under better control in countries where asbestos continues to be used. In the past two months, I have participated at international conferences in Brazil and South Korea as part of this effort, at my own expense. I also testify regularly as an expert witness on the public health and corporate history of asbestos (the subject of my doctoral thesis), usually at the request of plaintiffs, in personal injury cases.

No one has paid me or agreed to pay for my preparation and appearance here today. The only organizations that have ever paid me for appearances before governmental bodies and panels were environmental groups such as the Natural Resources Defense Council and the Environmental Defense Fund. I have not been paid for any such work for the environmental groups since the 1980s, though I continue to work with NRDC.

Quantitative risk estimation is not my field, though I have been impressed by the large and irreducible uncertainties attendant upon making such extrapolations, given the limitations of the data and the simplifying assumptions that are inherent in the process. It is unclear to me what regulatory purpose EPA has in convening this panel.

I want to sound words of caution that other agendas will be involved, implicitly or explicitly, in the panel's work. The personal injury asbestos litigation in the US is projected to reach \$140-200 billion or more in the coming years, in addition to sums already paid. Defendant corporations have gone to extraordinary lengths to reshape the scientific literature to defend these cases, and I want to discuss that briefly.

### **Seeding the Literature**

The publication and promotion of scientific reviews was key to a brazen litigation defense strategy of General Motors, Ford, and DaimlerChrysler. Defendant corporations have been prevailed upon to disclose copies of the bills received for litigation services by Exponent and Chemrisk. The Exponent bill to the Big Three on Apr. 4, 2003, titled "Technical Support – Asbestos Litigation," has a line item, "Completion of Meta-Analysis." Additional charges for "Completion of Meta-Analysis" were billed on May 2, Aug. 1, and Aug. 29, and Oct. 31, 2003. On Jan. 2, 2004, there was a charge of \$19,500 for "Presentation of Mechanic Meta-analysis." In all, "Presentation at Conferences" was billed seven times between February and November, 2004 as "Technical Support – Asbestos Litigation." The "Finalization of 2 Submitted Manuscripts" (on garage mechanics epidemiology) was another item in bills for technical support in asbestos litigation to the Big Three (May 28 and July 1 and 30, 2004). Additional Exponent billings to the auto companies in 2004 were for writing responses to separate articles by Drs. Dodson, Lemen, and Egilman.

GM, Ford, and DaimlerChrysler have spent at least \$23 million between 2001 and spring of 2006, for the consulting and publishing services of Exponent and Chemrisk, and scientists including Dennis Paustenbach, Michael Goodman, David Garabrant, Mary Jane Teta, Patrick Hessel, Patrick Sheehan, Elizabeth Lu, Gregory Brorby, and Brent Finley. (D. S. Egilman and S. R. Bohme. "Scientific Method Questioned" *Int. J. Occ. Env. Health* 12: 292-293, 2006; and Exponent and Chemrisk bills produced by in Sept. 2006, in Rebekah Price v. DaimlerChrysler Corp. et al.). So, in addition to their technical shortcomings, such as selectivity in what was included in these reviews and what was not, the recent meta-analyses and commentaries of Exponent and Chemrisk authors should be read with it in mind that they were solicited for the purpose of fighting personal injury claims brought by mechanics and their family members. These publications were part of a strategy of corporate defense lawyers, approaching and generously supporting the scientist-authors, most of whom had previously published little or nothing on asbestos. These publications were created to provide evidence that mechanics' asbestos exposures do not cause asbestos diseases. They were to be published by the best scientists money could buy.

Additional papers have continued to be published by the Chemrisk and Exponent scientists, in such journals as *Critical Reviews in Toxicology*. One builds on the assumption that, since the chrysotile used in brake pads doesn't hurt mechanics, there must be a safe, non-zero threshold for worker exposure to chrysotile (1). Another argues that chrysotile, unaccompanied by amphibole exposures, does not cause mesothelioma, and laments, "Thus, decisions about risk of chrysotile for mesothelioma in most regulatory contexts reflect public policies, not the application of the scientific method as applied to epidemiological cohort studies." (2) This reflects a bizarre view of how public health and environmental policies are made, as if science, transparency, and the full participation by the affected industries was not fundamental to the process.

David Michaels' new book, *Doubt Is Their Product*, gives many examples of Chemrisk and Exponent scientists publishing "product defense" scientific papers and testifying as experts in opposition to regulation and compensation for toxic injuries in a wide array of industries. Supplying numerous examples in a chapter called, "The Enronization of Science," Dr. Michaels writes (p. 46):

Having cut their teeth manufacturing uncertainty for Big Tobacco, scientists at ChemRisk, the Weinberg Group, Exponent, Inc. and other consulting firms now battle the regulatory agencies on behalf of manufacturers of benzene, beryllium, chromium, methyl tertiary-butyl ether, perchlorates, phthalates, and virtually every other toxic chemical in the news today. Their business model is straightforward. They profit by helping corporations minimize public health and environmental protection and fight claims of injury and illness. In field after field, year after year, the same handful of individuals and companies comes up again and again.

I hope that if and when some of these versatile contributors to the literature appear here, you will prevail upon them to ask how they live with themselves, debasing and contaminating

science and the public health policies that necessarily have to be based on science. Maybe you can ask these authorities on the subject if there might be lengths to which scientists go in this product defense business that might justify criminal penalties, and how such laws might be drafted to guard the integrity of science and public health policy against the corruption of money.

Finally, to further acquaint you with the orientation of defendant corporations in asbestos litigation, I attach as an Appendix to my statement a presentation I gave at a conference on mesothelioma in Sao Paulo last month. This may be of use in understanding the underlying thrust of some of what you may be hearing during your deliberations.

1. Pierce JS, McKinley MA, Paustenbach DJ, and Finley, BL. An Evaluation of Reported No-Effect Chrysotile Asbestos Exposures for Lung Cancer and Mesothelioma. *Crit Rev Tox* 38: 91-214 (2008)
2. Yarborough C. Chrysotile as a Cause of Mesothelioma: An Assessment Based on Epidemiology. *Crit Rev Tox* 36: 165-187 (2006)

## APPENDIX

### The Denial of Liability for the US Epidemic of Asbestos Disease/ A Public Health Worker's Observations

The Four Dog Defense:

I don't have a dog.

OK, I have a dog but he didn't bite you.

My dog bit you but he didn't hurt you.

My dog bit you and hurt you, but it was your own fault.

Chrysotile does not cause mesothelioma

Chrysotile does not cause peritoneal mesothelioma

Brake repair does not cause any asbestos disease, especially mesothelioma

- Manufacturers delayed OSHA warnings put on products in 1970s and 1980s, and only applied them to comply with regulations (not because the products were really admitted to be harmful)
  - NCI website sentence in summary of asbestos is authoritative, not the more detailed EPA (2007) and OSHA (2006) notices on brake asbestos hazards
  - Only the recent literature on brake workers, paid for by the auto companies, is reliable
- No published literature (or unpublished, usually) on asbestos disease from our product  
No medical reports of asbestos disease specifically attributable to our product  
No epidemiology studies showing our product causes asbestos disease  
Existing epidemiology literature shows our product does *not* cause mesothelioma (brakes)  
Exposure to our product was below the TLV (and that's why we thought it was safe and used no warning labels or product literature that would warn people about asbestos exposure)  
After OSHA standards published June 1972, our product was "encapsulated" (and that's why

we thought it was safe and used no warning labels or product literature that would warn people about asbestos exposure from grinding, sanding, sawing, or wire-brushing it)  
OSHA required labels we applied to our products after 1972 didn't include the words "danger" and "cancer" -- just "caution" and "may cause serious bodily harm" (reason for no cancer warnings on product labels before OSHA asbestos regulations of 1986)  
We protected our workers in factories making asbestos products but did not think that product users were in danger (so no warnings to them)  
The mesothelioma may have been caused by exposure to natural background asbestos in the air  
The unions knew all about asbestos, it was their fault if a union member wasn't aware of the risk  
The government didn't require warnings before 1972 (OSHA didn't exist until 1971)  
If the worker was exposed during employment in the US Navy, it was the Navy's job to protect him and the Navy's fault if he got mesothelioma from our products or services performed for the Navy  
Military specifications required us to use asbestos in the products we sold the Navy without warning labels (also known as "The Devil made me do it" defense)  
The government's bureau of standards published guidelines in 1934 approving of asbestos use in our product (asbestos tape and paper in making dental tooth "crowns")  
The mesothelioma was caused by polio vaccine  
The plaintiff kept smoking after there were warnings on cigarettes, so he probably would have disregarded warnings on asbestos products, too, if they had been put on our product  
We had to use asbestos in our product, it was irreplaceable at the time  
The asbestos mining companies didn't tell us asbestos was dangerous  
Our company didn't have doctors, industrial hygienists, or safety specialists who knew asbestos was dangerous  
Our company never had workers' compensation claims for asbestos diseases, so there must not have been any cases  
If our company has to pay too many large jury awards, we'll go bankrupt and workers will lose their jobs

One of my favorites:

Brazilian chrysotile asbestos is safe (Eternit doctor, *Estado de Sao Paulo*, October, 1998)

Attachment G

US EPA Science Advisory Board  
Asbestos Committee

Consultation on EPA's Proposed Approach for Estimation of Bin-Specific Cancer Potency  
Factors for Inhalation Exposure to Asbestos

Committee Assignment Leads to Respond to EPA's Charge Questions

<b>Charge Question(s)</b>	<b>Lead Reviewers</b>
1	Drs. Kelsey, Gutherie
2- section 2 (physical/chemical characteristics)	Drs. Gutherie, Southard
2- section 3 (toxicology) & section 5 (mode of action)	Drs. Oberdorster, Ortiz
2- section 4 (epidemiology)	Drs. Finkelstein, Marsh
2- sections 6 & 7 (risk assessment methods)	Drs. Stayner, Webber
3 and 4	Dr. Lippmann
5, 6, 7	Drs. Liroy, Portier
8	Drs. Everett, Harris
9, 10	Drs. Cox, Portier
11,12	Drs. Peto, Finkelstein, Stayner
13,14	Drs. Harris, Veblan
15	Drs. Cox, Rice

Attachment H

**PROPOSED APPROACH FOR ESTIMATION OF BIN-SPECIFIC CANCER POTENCY  
FACTORS FOR INHALATION EXPOSURE TO ASBESTOS**

**CHARGE QUESTIONS TO THE EPA SCIENCE ADVISORY BOARD**

**OVERVIEW**

At present, EPA uses an approach developed in 1986 for quantifying cancer risk from asbestos exposure based on phase contrast microscopy as the measure of asbestos exposure. The 1986 method used existing epidemiological data from cohorts of workers exposed to asbestos in a variety of mining and manufacturing settings to select quantitative risk models and estimate potency factors for lung cancer and mesothelioma. EPA's Office of Solid Waste and Emergency Response (OSWER) is proposing an interim approach to account for the potential differences of cancer potency between different mineral types and particle size distributions at different human exposure conditions. The document submitted for review describes a "multi-bin" mathematical approach to estimate cancer risk according to mineral groups (amphibole or chrysotile) and particle size (length and width) based on transmission electron microscopy. There are a number of issues regarding the statistical methods to be used in the fitting (these are discussed in Section 8), as well as a number of issues regarding the epidemiological and exposure data used (these issues are discussed in Sections 9 and 10). The purpose of the following charge questions is to identify the key issues that OSWER has encountered and to seek input from the SAB on the proposed approaches for addressing these issues, what changes to the proposed approaches may be needed, and what alternatives should be considered .

**CHARGE QUESTIONS**

The proposed approach is based on the hypothesis that there may be significant difference in potency for lung cancer and/or mesothelioma as a function of asbestos mineral type and particle dimensions.

***Charge Question 1:***

1. Do you agree that the data are sufficient to indicate that such differences may exist and that an effort of this type is warranted?

**SECTIONS 2-7**

Sections 2-5 of the document provide a synopsis on the physical and chemical characteristics of asbestos, toxicology, epidemiology, and mode of action. An overview of EPA's 1986 dose-response method is described in section 6, and initial EPA efforts to develop bin-specific cancer potencies are described in section 7

***Charge Question 2:***

2. Please comment on the adequacy of these sections which serve as the scientific bases for the proposed dose-response assessment approach.

**SECTION 8**

Section 8 of the document describes the statistical approach that OSWER is proposing for use in fitting risk models to the available data. Detailed charge questions related to the proposed fitting process are provided below.

**Section 8.2 – Risk Models**

OSWER reviewed work done by others in which the adequacy of the risk models for lung cancer and mesothelioma were assessed. OSWER concluded that the existing risk models (i.e., the same models developed by USEPA 1986) were adequate for use in this effort.

***Charge Questions 3a-3c:***

- 3a. Do you agree that the lung cancer and mesothelioma risk models that are proposed are a scientifically valid basis for this fitting effort?
- 3b. Should additional model forms be investigated? If so, what model forms are recommended for investigation, and what is the basis for concluding that these forms warrant evaluation?
- 3c. For lung cancer, the current risk model is multiplicative with the risk from smoking and other causes of lung cancer. Should the nature of the interaction between asbestos and smoking be investigated further? If so, how should this be done? Do you think the model would be sensitive to additional quantification of the interaction between smoking and asbestos?

**Section 8.3 – Fitting Metric**

Fitting of the risk models to the data may occur either at the level of individual studies, or at the level of individual exposure groups. OSWER is proposing that fitting occur at the level of exposure groups.

***Charge Questions 4a-4b:***

- 4a. Is fitting at the group level (based on the number of cancer cases observed) preferred to fitting at the study level (based on the study-specific KL or KM values)? What are the advantages and disadvantages of this approach?
- 4b. If so, is it scientifically justifiable to use a Poisson likelihood model for the observed number of cases in each group? Please comment on any other models that should be considered.

**Sections 8.4 – Characterizing Uncertainty In Exposure Data**

In most cases, there are multiple sources of uncertainty in the measures of exposure reported in published epidemiological studies. Section 8.4 provides an overview of how OSWER proposes to characterize these uncertainties, and the details of the approach are provided in Appendix C. Application of the proposed methods to each epidemiological study are presented in Appendix A.

***Charge Questions 5a-5d:***

5a. Have all of the important sources of uncertainty in cumulative exposure matrices been identified? If not, what other sources should be accounted for?

5b. Is it appropriate to characterize the uncertainty from each source in terms of an independent probability density estimated using professional judgment? If not, what alternative approach is suggested?

5c. Are the general strategies for selecting distributional forms and parameter values described in Appendix C (and applied in Appendix A) appropriate for characterizing uncertainty in exposure metrics? If not, what alternative strategies are recommended?

5d. Based on the assumption that each of the sources of error is independent, OSWER is proposing an approach where the errors combine in a multiplicative fashion. Please comment on the scientific validity of this approach and provide detailed suggestions for other approaches OSWER should consider.

**Section 8.5. Fitting Approach**

OSWER considered a wide range of strategies for fitting the epidemiological data to the risk models, including simple minimization of squared errors, weighted regression, maximum likelihood methods, measurement error models, Monte Carlo simulation, and Bayes-MCMC. Based on the recognition that there is substantial error in both the independent variable (observed number of cases in an exposure group) and the dependent variable (metric of cumulative exposure for the group), OSWER is proposing Bayes-MCMC as the most robust statistical approach for fitting the data.

***Charge Questions 6a-6b:***

6a. Is it appropriate to account for measurement error in the exposure data by using “measurement error” models (weighted regression methods)? If so, how would the weights assigned to each exposure value be assigned?

6b. Is the assignment of a PDF for data quality sufficient or should data quality be factored into a weighted likelihood analysis?

6c. Do you think that the proposed strategy of fitting the risk models to the available epidemiological data using Bayes-MCMC is scientifically justifiable? If not, what alternative strategy do you suggest, and why?

**Section 8.6.2 –Specification of Priors**

Assuming that Bayes-MCMC is the method that will be used, it is necessary to specify prior uncertainty distributions for each of the fitted parameters, including  $\alpha$  (the vector of study-

specific relative risks of lung cancer at zero exposure),  $\mathbf{KL}_b$  (the vector of bin-specific potency factors for lung cancer), and  $\mathbf{KM}_b$  (the vector of bin-specific potency factors for mesothelioma).

**Charge Question 7:**

7. Are the priors proposed in Section 8.6.2 for  $\alpha_s$ ,  $\mathbf{KL}_b$ , and  $\mathbf{KM}_b$  consistent with available knowledge? If not, what alternative priors should be considered, and why?

**Section 8.7 – Comparing Results For Different Binning Strategies**

OSWER is proposing an approach in which the best binning strategy is determined empirically (by finding the strategy that yields the best fit with the data), rather than specifying a binning strategy *a priori* that is expected to be optimal based on information from other sources. Conceptually, an infinite number of binning strategies might be considered. The choice of the size cutoffs for length and width are judgmental, and are also limited by the availability of particle size distribution data (see Section 10). OSWER is proposing 20 different binning strategies for evaluation. Length bins proposed for use include <5, 5-10, and >10  $\mu\text{m}$ . Width bins proposed for use are <0.4 and 0.4 to 1.5  $\mu\text{m}$ .

**Charge Questions 8a-8d:**

8a. Do you agree that multiple binning strategies should be evaluated, or do you believe that a physiological basis exists that can be used to identify a particular set of length and width cutoffs that should be assessed? If so, what would those length and width cutoffs be, and can these bins be implemented considering the limitations in the available TEM particles size data sets? (see Section 10)

8b. Are there any of these strategies that you feel do not warrant evaluation? If so, why? Are there any additional strategies that you recommend for inclusion? If so, why?

8c. Assuming that fitting is performed using Bayes-MCMC, OSWER is proposing that a comparison of goodness of fit between different binning strategies be based on the Bayes Factor. Do you agree that this is a statistically valid method for comparing binning strategies? Are there any other comparison methods you would recommend? If so, why?

8d. Is it important to account for differences in the number of fitting parameters (bin-specific potency factors) when comparing 1-bin, 2-bin, and 4-bin strategies to each other? If so, how should that be done?

**Section 8.8 – Other Methods For Characterizing Goodness-of-Fit**

OSWER is proposing that the initial evaluation of goodness-of-fit of different binning strategies be based on the Bayes Factor, but is also proposing a number of additional evaluations to assess both relative and absolute goodness-of-fit. These are described in Section 8.8.

### ***Charge Questions 9a-9e:***

9a. What method(s) is (are) preferred for characterizing the absolute goodness-of-fit of any selected binning strategy? Should any of these methods be used to supplement the relative comparisons based on the Bayes Factor? If so, how?

9b. If different measures of goodness of fit do not yield results that agree, which method should be preferred, and why?

9c. What methodological options do you recommend for validating the results of the modeling efforts? What are the strengths and limitations of these options compared to others that might be available?

9d. In lung cancer studies, it is expected that the value of  $\alpha_s$  should be relatively close to 1.0. If the fitted value of any particular value of  $\alpha_s$  is substantially higher or lower than 1.0, should this be taken to reflect that the data set giving rise to the value are somehow flawed or are too uncertain for use, and should be excluded? If so, what criteria would you suggest for recognizing values that warrant concern?

9e. Is an examination performed of the residuals from the meta-analysis a rigorous and scientifically valid assessment of homogeneity?

### **Section 8.9 – Sensitivity Analysis**

OSWER is proposing an approach for evaluating the sensitivity of the results to the various assumptions and choices used in the effort that is based on series of “what if” tests. For example, this may include excluding all or some of the data from one or more of the studies, and assessing how those exclusions impact the results. Likewise, one or more of the PDFs used to characterize uncertain input data may be changed to evaluate if/how the results are altered.

### ***Charge Questions 10a-10b:***

10a. Is this “what if” approach for evaluating sensitivity scientifically valid and useful?

10b. Are there other techniques that you recommend for characterizing the sensitivity of the outcome to the data and methods that are used? If so, what?

## **SECTION 9. EPIDEMIOLOGICAL DATA PROPOSED FOR USE**

Section 9 of the document describes the methods that are proposed for selecting studies for use in the effort, along with a list of studies that are proposed for inclusion. Detailed charge questions related to Section 9 are provided below.

### **Section 9.1 – Criteria For Study Selection**

OSWER has reviewed the published literature and identified studies that include sufficient exposure-response data to allow the study to be included in the model fitting effort for lung cancer and/or mesothelioma. These rules are as follows:

- The study must be published in a refereed journal.

- The study must provide data that can be expressed in terms of the quantitative risk models for lung cancer and/or mesothelioma
- The study cohort must consist of individuals who were exposed to approximately the same atmospheric composition of asbestos.

Some members of the 2003 Peer Consultation panel recommended that a minimum set of data quality requirements be imposed as part of the study selection procedure, while other members favored inclusion of all studies and the use of uncertainty factors to account for differences in data quality. OSWER considered these peer consultation recommendations, and is proposing that no data quality requirement be imposed because a) formulation of the data quality rules would be very difficult, and b) the method for characterizing uncertainty in the data from each study ensures that data from strong studies has more influence on the results than data from weak studies.

***Charge Questions 11a-11e:***

11a. Are the study-specific selection rules proposed above scientifically valid for the intended uses? Should any additional selection rules be added?

11b. Is it appropriate to assume that all workers in a cohort are exposed to the an atmosphere with a constant composition (i.e., the mixture of asbestos types and sizes is constant) unless the authors report information to the contrary? If this is not an appropriate assumption, what alternative strategy would be available?

11c. Should a set of minimal data quality requirements (other than those above) be established for inclusion of a study in the analysis? If so, what elements of data quality should be considered, and how should those data quality rules be established?

11d. For lung cancer, OSWER's approach requires that there be at least two exposure groups per study in order impose some constraint on the value of the study specific value of  $\alpha$ . However, OSWER is proposing to use data from three cohorts described by Henderson and Enterline (1979), even though there is only one dose group for each cohort. This is because a reliable estimate of  $\alpha$  for the combined cohort can be derived from the data of Enterline et al. (1987). Is this approach appropriate and scientifically justifiable? If not, can you suggest an alternative strategy for retaining the data from this important study or should this study be excluded?

11e. One key assumption in any meta-analysis is that the data sets included in the analysis are homogeneous. How should the assumption of homogeneity be assessed prior to combining the data from the studies or groups? If you recommend statistical testing, please provide guidance on the reliability of a decision based solely on the test statistic. If testing produces evidence of heterogeneity between some studies, what steps can be recommended?

**Sections 9.2 and 9.3. Studies Proposed for Use and Studies Excluded**

Section 9.2 lists each of the lung cancer and/or mesothelioma studies that OSWER has identified as being sufficient for inclusion in the data fitting effort. There are a number of studies where cumulative exposure was not reported in the units needed for modeling. In order to utilize these studies, it was necessary to use the data provided to estimate cumulative exposure in the needed units (e.g., Yano et al. 2001, McDonald et al. 1982, 1983, 1984). Section 9.3 identifies several studies that were considered for use, and the reasons why they are proposed for exclusion.

***Charge Questions 12a-12c:***

12a. Are you aware of any studies that should be included in the model fitting effort that are currently excluded or omitted? If so, what are these studies, and do they meet the requirements for study inclusion?

12b. Are there any studies that are currently proposed for inclusion in the analysis that you believe should be excluded? If so, why?

12c. In cases where the epidemiological data are not reported in the form needed for use in the fitting effort, are the methods used to estimate the exposures scientifically sound, and are the methods used for characterizing the uncertainty in the estimates appropriate?

**SECTION 10. METHOD PROPOSED FOR ESTIMATING BIN-SPECIFIC EXPOSURES**

One of the largest problems with this effort is that none of the published studies included bin-specific exposure estimates. Therefore, the effort is contingent upon methods for estimating bin-specific exposures based on the data provided. Specific charge questions related to this process are provided below.

**Section 10.2 – Extrapolation from Dust to PCM-Based Measures**

A number of studies reported exposure in terms of dust rather than asbestos. In some cases, data are available to extrapolate from dust to asbestos levels. In other cases, no data are provided. OSWER is proposing to use an "average" extrapolation factor in this case.

***Charge Questions 13a-13b:***

13a. Is it scientifically justifiable to employ a default dust-to-PCM conversion factor when there are no site-specific data available?

13b. Are the uncertainty distributions specified in Appendix A to characterize the uncertainty in this extrapolation consistent with available information and are they statistically appropriate?

**Section 10.3 – Extrapolation from PCM to Bin-Specific Measures**

The process of extrapolating from PCM-based measures of exposure to bin-specific measures of exposure requires two types of data: 1) the fraction of the atmosphere that is chrysotile and the fraction that is amphibole, and 2) particle size data for both the chrysotile and the amphibole components. In the absence of reliable study-specific data, OSWER is proposing to use published TEM particle size data from similar workplaces as the basis of the particle size data needed for step 2.

***Charge Questions 14a-14i:***

14a. Are the point estimates and uncertainty distributions for the fraction amphibole term proposed for each study scientifically valid?

14b. Is it scientifically valid to use surrogate TEM data to estimate bin-specific concentrations and exposure values in studies where these data are not reported? If not, what alternative approach could be followed, or what additional data would be helpful?

14c. Are there any additional bi-variate TEM data sets available that would be useful in this analysis?

14d. Are the point estimates and uncertainty distributions for the fraction amphibole term scientifically valid?

14e. Can you suggest any ways to improve the process used to identify select the best available matching TEM data set(s) to a workplace? How sensitive would the model output be to these changes?

14f. Would the model benefit by establishing a common lower cut-point in diameter to normalize the lower detection limit across studies?

14g. Do the studies included in the model have surrogate data of sufficient quality and similarity to expected exposure conditions to support the model? If not, what alternative approach could be followed?

14h. Are the PDFs described in Appendix C to characterize the uncertainty in the extrapolation of TEM particle size data from one location to another sufficient and helpful in understanding the implications of the method used?

14i. Are the extrapolation techniques used on the raw TEM data sets to meet the bin definitions (e.g., 0.4 um diameter) transparent, objectively presented and scientifically valid? Are there alternative techniques that you would recommend?

## **SECTION 11 – UTILIZING POTENCY FACTORS TO COMPUTE LIFETIME RISK**

Assuming that it is possible to derive a set of bin-specific potency factors, it is expected that these will be used to evaluate lifetime risk of cancer to an individual with a specified exposure history using the same basic life-table approach used by EPA (1986). However, each bin-specific potency factor will be uncertain. Therefore, it is important to specify the uncertainty in the risk predictions that arise from the uncertainty in the potency factors.

### ***Charge Questions 15a-15b:***

15a. What method is best for estimating the uncertainty in lifetime cancer risk predictions that are associated with the uncertainty in the bin-specific potency factors?

15b. Assuming that estimates of exposure at Superfund sites will also have uncertainty, how should the overall uncertainty in risk predictions be characterized?