

Asbestos: A Science-Based Examination of the Mode of Action of Asbestos and Related Mineral Fibers

DAY ONE -- Wednesday December 16, 2009

Pre-Workshop SESSION – Finalize documents by Original Teams

8:30am – 9:00am	Registration (Team members, Planning Committee & Reviewers ONLY)	<i>Venetian Foyer</i>
9:00am – 9:15am	Brief overview of morning activities <i>Maureen Gwinn, USEPA</i>	<i>Venetian Room</i>
9:15am – 12:00pm	Original Expert panels plus reviewers meet separately to finalize White Papers and prepare for presentation of key findings. Prepare PowerPoint presentation (15min max)	
	Pulmonary Toxicology	<i>Zurich</i>
	Pleural Toxicology	<i>Paris I</i>
	Non-pulmonary Toxicology	<i>Executive Boardroom</i>
	Genetic Toxicology	<i>Paris II</i>
	Susceptibility	<i>Vienna B</i>
	Environmental Exposure	<i>Brussels</i>

The specific charge to the panels is to come to conclusions concerning:

The strength of the published data on asbestos and related mineral fibers as reviewed in the white papers. Thus the breakout groups will assess the strength of the data on each of the areas covered by the white papers in their specific areas: pulmonary endpoints, pleural endpoints, non-pulmonary endpoints, Role of Mutagenicity in fiber-induced carcinogenicity, main factors that impact susceptibility to fiber-induced health effects and extrapolation of environmental exposure levels (low-dose, sporadic, high-dose) to health effects. Focus will be on the strength of the data, critical examination of conflicting data, data gaps and needs.

Each panel will develop a report that will put all the data from their specific area into sections:

1. Based on existing evidence we are confident of the following....
2. We consider the following to be likely but require confirmation....
3. Research on asbestos and related mineral fibers suggests several broad themes which we believe should be pursued on future investigations. These include...
4. Overall conclusion

12:00 – 1:00pm	LUNCH	<i>Shula's 347</i>
12:00 – 1:00pm	Public registration	<i>Venetian Foyer</i>

Public Workshop Begins

1:00pm – 1:05pm	Welcome <i>Claudia Thompson, NIEHS</i>	<i>Venetian</i>
1:05pm – 1:20pm	Opening Remarks <i>Linda Birnbaum, Director, NIEHS</i>	
1:20pm – 1:45pm	Workshop Background, Overview of Agenda and Planned Activities <i>Maureen Gwinn, USEPA and Claudia Thompson, NIEHS</i>	

SESSION I – Presentation of Key Points from Original Teams

1:45pm – 3:45pm	Plenary Presentations of Key Findings	<i>Venetian</i>
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Based on a mechanism/MOA, can the range of fibers or specific components that contribute to adverse health effects be determined, keeping in mind the role of different fibers in various disease endpoints. A key consideration will be how to express the dose metric corresponding to different effect endpoints, e.g., fiber burden (mg or surface area) normalized to lung tissue volume. During this session the results of the writing team’s efforts will be discussed for the following six endpoints.

1:45pm – 2:05pm	Pulmonary Endpoints (cancer and noncancer) <i>Brooke Mossman, University of Vermont</i>	
2:05pm – 2:25pm	Pleural Endpoints (cancer and noncancer) <i>Agnes Kane, Brown University</i>	
2:25pm – 2:45pm	Non-Pulmonary Endpoints (cancer and noncancer) <i>Andrij Holian, University of Montana</i>	
2:45pm – 3:05pm	Role of Mutagenicity in Fiber-Induced Carcinogenicity <i>Tom Hei, Columbia University</i>	
3:05pm – 3:25pm	Main factors that impact susceptibility to fiber-induced health effects <i>Joseph Testa, Fox Chase Cancer Center</i>	
3:25pm – 3:45pm	Extrapolation of Environmental Exposure levels (low-dose, sporadic, high-dose) to health Effects <i>Kent Pinkerton, University of California at Davis</i>	
3:45pm – 4:00pm	BREAK	

SESSION II – Overarching Questions

4:00pm – 4:15pm	Charge to breakout group tasks, overview of Overarching Questions	
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4:15pm – 6:00pm Four Concurrent Breakout Sessions

Group I	<i>Zurich</i>
Group II	<i>Paris I</i>
Group III	<i>Paris II</i>
Group IV	<i>Vienna B</i>

The breakout groups should examine the literature to come to conclusions on some overarching issues related to asbestos and related mineral fibers including:

Question 1. Physicochemical characteristics

What are the physico-chemical attributes (mineralogy, morphology, dimension) contributing to target organ deposition/clearance/response (durability, biopersistence and bioreactivity)? Are there qualitative and quantitative differences or similarities in dosimetry/toxicity and mode of action for different mineral fibers (pulmonary and pleural, cancer and non-cancer)?

Question 2. Mode of Action (MOA; Defined as a chemical's influence on the molecular, cellular and physiological functions in producing tumors or toxicity)

Do MOA/mechanisms findings from *in vitro* studies operate *in vivo* in laboratory animals? In humans at relevant exposure levels? What *in vivo* responses are not adequately explained by current understanding of the MOA or available *in vitro* findings?

Question 3. Genotoxicity

What is known about the direct and indirect mutagenicity of the various asbestos fiber types? What physicochemical attributes account for the differences/similarities in the genotoxic response to various fiber types? What role does this genotoxicity play in different clinical diseases? *In vitro*? Are there quantitative species differences?

Question 4. Extrapolation to Humans

What mechanistic studies *in vivo* or *in vitro* best bridge to current clinical outcome measures? Do we know what factors or mechanisms occur before inflammation following exposure to asbestos? What is the relationship between inflammation and fibrotic changes (e.g., on chest films or observed by other imaging) and mesothelioma? What data should be collected in epidemiological or other clinical surveys to enhance mechanistic understanding of the different dimensions of asbestos disease?

Question 5. Susceptibility

There is limited information on exposures in potentially susceptible populations (children, women, elderly, sick, etc). Would you expect there to be a dosimetry difference or susceptibility issue in any of these groups? If so, how best can this be determined?

The goal will be to reach a consensus on these questions/issues.

These questions will also be answered in the same framework as used for the white papers.

1. Based on existing evidence we are confident of the following....
2. We consider the following to be likely but require confirmation....
3. Research on asbestos and related mineral fibers suggests several broad themes which we believe should be pursued on future investigations. These include...

4. Rapid advances and critical recent advances
5. Summary of Overall conclusions

6:00pm - 6:15pm CLOSE – discussion of next day tasks

7:00pm **DINNER**

DAY TWO - Thursday December 17, 2009

Session II – Overarching Questions (continued)

8:00am – 8:15am Discussion of the day’s agenda *Venetian*

8:15am – 10:30am Breakout groups, continuation of discussion of questions

10:30am – 10:45am **BREAK**

10:45am – 11:30am Finalize PowerPoint presentation for Discussion

Session III – Plenary Presentation of Overarching Questions

11:30am – 12:30pm Presentation of Key Findings to Overarching Questions *Venetian*

11:30am – 12:00pm Group I

12:00pm – 12:30pm Group II

12:30 – 1:30pm **LUNCH** *Shula’s 347*

Session III – Plenary Presentation of Overarching Questions (CONTINUED)

1:30pm – 2:00pm Group 3

2:00pm – 2:30pm Group 4

2:30pm – 3:30pm Group Discussion

3:30pm – 4:00pm Summary presentation, next steps
Maureen Gwinn and, Claudia Thompson

4:00pm **END WORKSHOP**