

Comments on the EPA Document, “Draft Toxicological Review of Libby Amphibole Asbestos” (EPA/635/r/002a)

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IRIS

- Originally intended simply to serve as a central database that would ensure the consistency of EPA health and risk assessments
- Now primary source for information concerning the weight of evidence (hazard identification) and quantitative risk information
- IRIS program and many draft toxicological assessments have come under close scrutiny
- Greatest focus has been on the quality of the science
- Recurring scientific deficiencies have been noted in recent EPA draft health assessments
- Need to restore the public's perception of the scientific quality of IRIS
- Potential enormous impact on the national and international communities.

Previous IRIS Health Assessments

- Increasingly, the NAS/NRC has been asked to provide the needed objective scientific review
 - Formaldehyde
 - Dioxin
 - Trichloroethylene
 - Tetrachloroethylene
 - Inorganic arsenic
- Delay in the review and finalization of IRIS toxicological reviews of these substances
- Many recurring and overlapping themes

General NAS recommendations

“Reframing the Development of the IRIS Assessment”

- Use of available evidence and understanding of mode of action to select outcomes
- Use of standard protocols
- Use of standardized approaches for study and weight-of-evidence descriptors
- Establish protocols for reviewing major types of studies
- Implement and standardize the approach to using existing weight-of-evidence guidelines
- Develop uniform language to describe strength of evidence for noncancer effects
- Harmonize the approach for characterizing uncertainty and variability
- Consolidate the outcomes around common modes of action

General NAS recommendations (cont.)

“Reframing the Development of the IRIS Assessment”

- Establish clear guidelines for study selection
- Balance strengths and weaknesses
- Human vs. experiment evidence
- Consider combining estimates among studies
- Carefully consider and explain models used
- Justify statistical and biological model, and describe fit to the data
- Determine points of departure
- Assess analyses that underlie the points of departure
- Provide range of estimates and describe effect of uncertainty factors on the estimates
- Establish adequacy of documentation to support conclusions and estimates

EPA Charge to SAB Reflects NAS Themes

- Cancer/IUR
 - Selection of study population
 - Exposure-response modeling
 - Determination of POD
 - Justify approaches used for confounding
 - Approach for calculating the IUR
 - Adequacy of descriptions of uncertainties and limitations

EPA Charge to SAB Reflects NAS Themes

- Non-cancer/RfC
 - Selection of study population
 - Selection of the critical endpoint and mode of action
 - Methods for exposure reconstruction and development of exposure estimates
 - Selection of exposure-response model
 - Selection of model for point of departure (POD)
 - Appropriateness of uncertainty factors

Federal Agency Reviews

- The Agency for Toxic Substances and Disease Registry (ATSDR)/Center for Disease Control and Prevention (CDC)
- Department of Defense (DOD)
- The National Institute of Environmental Health Sciences (NIEHS)
- The National Institute for Occupational Safety and Health (NIOSH)
- Office of Management and Budget (OMB)

Agency and Scientist Comments Echo NAS Themes: Cancer

- Use of data from a subcohort (unpublished), rather than evaluation of the entire Libby miners cohort [NIEHS, OMB, Moolgavkar, S.H. (2011)]
- Choice of statistical models (e.g., Poisson model used, rather than traditional Peto model previously used by EPA) and methods [ATSDR, Moolgavkar, S.H.]
- Treatment of lag time [DOD, OMB, Moolgavkar, S.H.]
- Consideration of mode of action and possibility of non-linearity [OMB, DOD, NIEHS]
- Treatment of confounding factors such as smoking [OMB, NIEHS]
- Treatment of uncertainties [ATSDR, NIEHS, Moolgavkar, S.H.]

Agency and Scientist Comments Echo NAS Themes: Noncancer

- Use of truncated cohort instead of the full Marysville cohort [NIEHS, OMB, Moolgavkar, S.H.]
- Choice of critical endpoint, pleural thickening, and treatment of confounders [ATSDR, OMB, Moolgavkar, S.H.]
- Characterization of exposure for selected Marysville cohort (e.g., attributing all disease to Libby Amphibole when some workers were exposed to other sources at other locations) [NIOSH]
- Choice of statistical methods for exposure-response characterization [Moolgavkar, S.H.]
- Justification of magnitude of uncertainty factors (10 and 10) for RfC derivation [DOD, OMB, ATSDR]
- Treatment of uncertainties [ATSDR, NIEHS, Moolgavkar, S.H.]

Agency and Scientist Comments Echo NAS Themes: Noncancer (cont.)

- Hazard identification and exposure-response characterization must be critically reviewed
- Human studies, as opposed to animal experiments, present challenges for the choice of a critical endpoint that is clearly associated with the agent in question
- Exposure characterization
- Choice of modeling approaches and uncertainty factors for derivation of the RfC

Practical Considerations: Proposed RfC < Background

- RfC, 0.00002 f/cc, is below most estimates of background concentrations in the US (ATSDR 2001)
- Not just Libby but nationwide, including areas of the country with naturally occurring amphibole in soils
- Eldorado Hills, CA, where the amphibole background level (about 0.0008 f/cc) is about 40 times higher than the proposed RfC (U.S. EPA 2011b).

Practical Considerations: Serious Challenges for Data Collection

- Current and historical sampling data from Libby and elsewhere would be not meet with the required sensitivity level for noncancer hazard evaluation.
 - EPA ambient air sampling at Libby, MT, does not cover the RfC.
 - Analytical sensitivities for EPA's activity-based sampling program are 10 to 100 times above the levels needed to evaluate a hazard quotient of 1 using the proposed RfC.
- Cost of analyzing samples down to this unprecedented low level would be several thousand to tens of thousands of dollars per sample.

Summary

- EPA has acknowledged that this document is the frontier of amphibole asbestos science (Jackson 2009).
- First effort to establish a safe level of exposure for noncancer for any form of asbestos
- Enormous implications; particular attention needs to be focused on this entire approach
- A thorough review by this committee, taking into consideration the recommendations from many groups, particularly the NAS/NRC, will strongly support EPA's efforts to reestablish the scientific credibility of the IRIS program and further the advancement of science and public health protection in the US
- A thorough review will also prevent a protracted period of review that has characterized recent assessments.