UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAR 2 8 2013

OFFICE OF THE
ADMINISTRATOR

David T. Allen, Ph.D.
Chairman
Science Advisory Board
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Dear Dr. Allen:

I want to thank you, Dr. Deborah L. Swackhamer and Dr. Agnes Kane for your January 30, 2013, letter providing the Science Advisory Board Libby Amphibole Asbestos Review Panel's comments on the U.S. Environmental Protection Agency's draft Integrated Risk Information System toxicological assessment of Libby amphibole asbestos, released for public comment and external peer review in August 2011. The EPA greatly appreciates the panel's thorough review and constructive comments.

It is useful to know that the SAB panel found the draft to be comprehensive and generally clear, logical and well-written and that the methods for conducting the exposure-response modeling were clearly described. It is also useful to know that the SAB panel:

- found that localized pleural thickening is an appropriate health endpoint for the derivation of the inhalation reference concentration;
- supported the derivation of an RfC for Libby amphibole asbestos based on radiographic evidence of localized pleural thickening in an occupationally exposed Marysville, Ohio, cohort;
- agreed with the agency's conclusion that Libby amphibole asbestos is carcinogenic to humans by the inhalation route of exposure;
- supported the selection of the Libby worker cohort for derivation of the inhalation unit risk; and
- agreed that the use of the subcohort hired post-1959 for quantification was reasonable due to the lack of exposure information for many workers in the earlier years.

Your letter also included several recommendations from the SAB review panel that will enhance the clarity of the draft toxicological assessment of Libby amphibole asbestos and strengthen the scientific basis for its conclusions.

It also identified critical research needs for epidemiological studies, mode-of-action analysis and measurement methods for Libby amphibole asbestos that will strengthen future assessments. The EPA is carefully considering and making revisions to the assessment that address these comments and recommendations as well as the comments received from the public.

Based on the panel's recommendations, some of the key revisions being incorporated into the draft toxicological assessment of Libby amphibole asbestos include:

- a more detailed review of the literature on localized pleural thickening to further support the appropriateness of that health endpoint for deriving the RfC;
- additional analyses of pleural abnormalities using recently published studies on two other Libby amphibole asbestos-exposed cohorts to the extent data permit;
- more justification for selecting the best model in the non-cancer exposure-response analysis;
- an examination of other exposure metrics besides simple cumulative exposure, such as time-weighting of exposures;
- more justification for selecting 10 percent extra risk as the benchmark response;
- a re-evaluation of a default database uncertainty factor of 10 as part of the consideration of additional new studies;
- a closer examination of the EPA's justification for selection of subchronic-to-chronic and LOAEL-to-NOAEL uncertainty factors;
- a formal mode-of-action analysis for carcinogenicity;
- increased discussion of the role of fiber determinants in toxicity;
- a closer examination of the implications of the subcohort selection on the inhalation unit risk;
- a more detailed discussion and justification of how the use of mortality data, rather than incidence data, might have resulted in an undercount of lung cancer and mesothelioma cases and any implications for IUR derivation;
- more support for the EPA's choice of statistical models for the exposure-response analysis;
- graphical display of the fit to data for both main models and for a broader range of models in the draft document;
- consideration of literature on epidemiological studies of other types of amphibole for dose-response assessment model selection; and
- a re-evaluation of model uncertainty.

I thank you once more for your thoughtful review of the EPA's draft IRIS toxicological assessment of Libby amphibole asbestos. Your independent critical review helps to ensure that the EPA uses the best science to fulfill our mission to protect human health and to safeguard our environment.

Sincerely,

Bob Perciasepe

Bob Perciasepe
Acting Administrator

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF THE
ADMINISTRATOR

Deborah L. Swackhamer, Ph.D.
Immediate Past Chairwoman
Science Advisory Board
U.S. Environmental Protection Agency
University of Minnesota
1985 Buford Avenue, 173 McNeal Hall
St. Paul, Minnesota 55108

Dear Dr. Swackhamer:

I want to thank you, Dr. David T. Allen and Dr. Agnes Kane for your January 30, 2013, letter providing the Science Advisory Board Libby Amphibole Asbestos Review Panel's comments on the U.S. Environmental Protection Agency's draft Integrated Risk Information System toxicological assessment of Libby amphibole asbestos, released for public comment and external peer review in August 2011. The EPA greatly appreciates the panel's thorough review and constructive comments.

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Sincerely,

Bob Perciasepe

Bob Perciasepe
Acting Administrator

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OFFICE OF THE
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Agnes Kane, Ph.D.
Chairwoman, Libby Amphibole Asbestos Review Panel
Science Advisory Board
U.S. Environmental Protection Agency
Brown University
Department of Pathology and Laboratory Medicine
70 Ship Street, Box G-E5
Providence, Rhode Island 02912

Dear Dr. Kane:

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