UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460
NOVEMBER 23, 1983

OFFICE OF
THE ADMINISTRATOR

Mr. William D. Ruckelshaus
Administrator
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Dear Mr. Ruckelshaus:

The Environmental Health Committee of the Science Advisory Board has reviewed the EPA Draft Health Assessment Document for Inorganic Arsenic (June 1983) at a public meeting in Washington, D.C. on September 22, 1983. The document was previously distributed to individual Committee members and consultants for their evaluation. At the meeting, Agency staff recounted the process for preparing the document and summarized for the Committee the salient points raised during the public comment period. In addition, representatives of various organizations presented comments directly to the Committee. With this information in hand, the Committee presented its own independent evaluation of the scientific adequacy of the document. Agency staff responded to Committee comments and answered questions posed to them.

The major conclusion of the document is stated on page 5-150. It reads: "Skin cancer and lung cancer have been shown by numerous epidemiologic studies to have an association with arsenic exposure. Arsenic has not been found to be a carcinogen in animal studies, however. In applying the IARC [International Agency for Research on Cancer] criteria for evaluating a substance as to the weight of evidence for human carcinogenicity, arsenic would be placed in group 1, which IARC characterizes as "carcinogenic to humans'." The Committee concurs with this conclusion.

The Committee made additional comments on the scientific adequacy of the document, particularly the discussion on the use of mathematical models, and expressed certain reservations about the document in its present form. These comments are included in the attached report. Agency staff provided assurances to the Committee that most of its comments would be

readily incorporated into a final document. On the basis of this review the Committee would unanimously consider the Health Assessment Document for Inorganic Arsenic to be scientifically adequate as a source document for Agency-wide use in making regulatory decisions, if appropriately modified.

Sincerely,

Herschel E. Griffin
Chairman
Environmental Health Committee
Science Advisory Board

Attachment

cc: Mr. Alvin Alm
Mr. Joseph Cannon
Dr. Bernard Goldstein
Dr. Lester Grant
Dr. Terry Yosie

Additional Environmental Health Committee Key Findings, Recommendations and Conclusions on the Draft Health Assessment Document for Inorganic Arsenic (June 1983)

1. At least several alternative models predicting cancer incidence with dose can be calculated. The epidemiological data appear to fit linear models better than non-linear (quadratic) models. While EPA has limited its consideration to linear models with zero intercept, public testimony presented to the Committee suggested that linear dose-response models with a positive intercept on the Y axis may provide an even better fit to the available data. In view of this situation, Agency staff should discuss alternative models more fully in the document, present the scientific merits of each model, and then discuss why the linear nonthreshold dose-response curve was chosen as the preferred method for establishing a rough but plausible estimate of the upper limit of risk. This should not be too difficult a task for the document has already presented brief discussion of the basis and the relevance of the linear nonthreshold model. The Committee's recommendation follows the tradition of scientists to present negative as well as positive evidence surrounding an hypothesis. In addition, the Committee desires to further strengthen the Agency's use of scientific data and mathematical models as a basis for determining the appropriate management of the risk resulting from arsenic emissions into the environment.

2. The Committee concurred with the Agency's statement that arsenic is to be judged as an environmental mutagen. The discussion on the mutagenic characteristics of arsenic, however, should be expanded and updated. It should be noted, for example, that microbial mutagen tests or Ames type tests are not as useful for assessing heavy metals as they are for organic substances. More discussion of the teratogenic qualities of arsenic is also needed. Specific references for expanding both the mutagenic and teratogenic discussions are included in the Committee transcripts.

3. In regard to the epidemiological studies of arsenic, there seems to be growing evidence from the study by Brown and Chu, and also from Enterline and Marsh, that arsenic may act as a cancer promoter rather than an initiator; that lung cancers may develop in less than ten years after initial exposure to arsenic compounds; and that the effects of arsenic compounds, as reported by Enterline and Marsh, may tend to disappear over time. These unusual aspects of the epidemiology of lung cancer from arsenic should be more carefully reviewed in the document.

4. The Executive Summary should make better use of the comments on pages 5-141-142 of the "apparent" differences between the Taiwanese dose-response model and the U.S. dose-response e.g., that there are major differences in

sample size as well as other contaminants in the Taiwanese water supplies not present in U.S. water supplies. A minor point is that the reference on page 5-143 by Andelman (1983) does not appear in the reference list. Perhaps Andelman presents a sufficiently detailed analysis to further strengthen this point.

5. A generic issue should also be noted: the Agency expressed a willingness to use toxicokinetic and more biologically formulated models of predicting risk, but the components of such models, e.g., dosimetry, toxicokinetics, injury function and scaling factors from animals to man, are currently not available to the Agency or, for that matter, available in the scientific literature. The Committee, therefore, recommends that the Agency place a high priority on supporting intra- and extramural studies directed toward dosimetry and mechanistically-based modeling.

6. Both public and Agency testimony noted that a substantial amount of potentially relevant research addressing human health impacts of arsenic is now being conducted. This information is expected to be evaluated and published during the course of the coming year. Should it lead to a different understanding than that in the current document, the Committee believes the Agency should evaluate the desirability or the need to publish an addendum at that time. Agency staff concurred with this observation.