



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

September 23, 1985

Honorable Lee M. Thomas
Administrator
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460

OFFICE OF
THE ADMINISTRATOR

Dear Mr. Thomas:

The Environmental Health Committee of EPA's Science Advisory Board has reviewed the Agency's draft Health Assessment Document for Beryllium. The document was prepared by the Office of Health and Environmental Assessment in the Office of Research and Development. On June 4, 1985 our Metals Subcommittee, chaired by Dr. Bernard Weiss of the University of Rochester, met publicly in New York City to hear comments by Agency personnel and members of the public, to discuss the document and to make recommendations to the Committee. The Subcommittee reported its findings on June 17, 1985. Based on this review, we advise that the draft document merits revision on several critical points. The remainder of this letter describes the rationale for a reanalysis of the risk estimate for beryllium.

The Committee agrees with the Agency's qualitative analysis of beryllium carcinogenicity for animals. Beryllium is a carcinogen for animal species and causes several kinds of tumors by different routes of administration. However, most of the experimental evidence in support of this conclusion is not suitable for quantitative risk assessment purposes, since many of the studies were exploratory in nature, often lacking controls.

The animal data that are appropriate for a quantitative assessment of inhalational risk lead to estimates which are inconsistent with the expectations from human epidemiological studies. Further, in extrapolating risk between species, the Agency has not differentiated between deposition in the respiratory tract and the absorption from the site of deposition of inhaled beryllium. Instead, the Agency has treated beryllium like a gas. However, beryllium is a particulate air contaminant, as administered in the most relevant animal studies and as humans mainly are exposed to it.

The Committee requests that Agency staff recalculate the risk to humans using models appropriate to particulate inhalation. Rats could serve as a sensitive species, and guinea pigs as a less sensitive species. The uncertainties and difficulties in extrapolation between species should be stressed. For example, the dose to the target tissue (bronchiolar or alveolar), particle size and absorption by target cells are factors in the risk to each of the species. Recalculation might lead to an animal estimate which is consistent with the epidemiological evidence.

The Agency's analysis of the epidemiology of exposure to beryllium shows a thorough understanding of the problems and questions embedded in these data. Although the International Agency for Research on Cancer (IARC) concluded that beryllium met its criteria for "limited" human evidence, given the more recent EPA evaluation, it is a difficult matter to specify whether this human evidence meets the criteria for "inadequate" or "limited" evidence. Many of the confounding factors that the draft document discusses have quantitative implications that have not been made explicit in the risk calculations. For this reason, we request that Agency staff calculate the quantitative implications of these confounding factors. Further, the risk estimates based on epidemiological and animal toxicological data need to be compared.

It will be difficult to provide meaningful advice about beryllium without the reanalysis by staff because it could alter the conclusions in at least three areas:

- The qualitative weight of the evidence for carcinogenicity.
- The difference between the human and animal estimates.
- The selection of appropriate data for quantitative estimation.

In summary, we ask that the Agency provide a reanalysis of the risk estimate, as briefly outlined above, and inform us if we will be requested to provide a further review of this document. Technical comments by Subcommittee members were sent directly to Agency staff.

Sincerely,

Richard A. Griesemer

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cc: A. James Barnes [A-101]
Assistant Administrators