



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

March 9, 1988

Hon. Lee M. Thomas
Administrator
U.S. Environmental Protection
Agency
401 M Street SW
Washington, D. C. 20460

SAB-EHC-88-018

OFFICE OF
THE ADMINISTRATOR

Dear Mr. Thomas:

On November 19-20, 1987 the Halogenated Organics Subcommittee of the Science Advisory Board's Environmental Health Committee met in Washington, D.C. to independently review the Office of Drinking Water's Draft Final Criteria Document for Dichloroethylenes. The Subcommittee concluded that, in general, the draft document has evaluated the relevant scientific studies and presented and interpreted their strengths and weakness in a balanced manner.

The major issue addressed by the Subcommittee in its review was whether chronic toxicity data for 1,1 Dichloroethylene (1,1 DCE) should be used to calculate lifetime drinking water health advisory values for both cis- and trans-1,2 Dichloroethylene. The Office of Drinking Water proposed to use this surrogate approach because specific data that would support a calculation do not exist for these other compounds. The general rationale for the proposals rests upon arguments and analogies relating to: 1) the similarity in structure of the three isomers; 2) the production of qualitatively similar effects upon certain liver plasma enzyme activities in rats following single exposures administered through gavage using corn oil; and 3) the comparatively greater potency of 1,1 DCE, relative to cis- and trans-1,2 DCE, in producing those specific acute effects.

In purely scientific terms, it is not possible to evaluate the validity of this proposal without comparable toxicity data for chronic exposure to all three isomers of Dichloroethylene. As a science policy choice, however, the proposal to use 1,1 DCE as a surrogate for cis- and trans-Dichloroethylene appears plausible. The proposal can be strengthened by providing a more detailed explanation of the assumptions and reasoning that supports it. In this regard, the recent review by Hanschler (1985) can be usefully applied.¹

Nevertheless, great uncertainty will remain in generalizing from similarities in acute response to those found in chronic responses, and from the specific pattern of toxicity induced by one isomeric form to that potentially induced by the others. Even if 1,1 DCE appears more potent than either 1,2 DCE isomer (via corn oil gavage), this provides no scientific assurance that the potencies for chronic exposure would also have the same rank order. Also, if the patterns of toxicity of the three isomers were identical following acute exposure, and the acute toxicity was caused by exactly the same mechanism

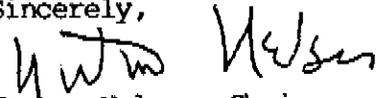
¹D. Henschler, "Halogenated Alkenes and Alkynes," in M.W. Anders, ed., Bioactivation of Foreign Compounds, (Orlando: Academic Press, 1985), pp. 317-347.

in each case, this would continue to provide no significant scientific assurance because the mechanisms of action under chronic conditions might be completely different. On the other hand, if extrapolation, of this type are made, it is not obvious why the recently demonstrated carcinogenicity of 1,1 DCE should not also be extrapolated by analogy to cis- and trans-1,2, DCE, especially if the mechanism of action is mediated by formation of an epoxide metabolite.

Such difficult issues can only be definitively resolved with adequate scientific data. Because no truly scientific basis for the Office of Drinking Water's proposal exists at the present time, it must make plausible scientific assumptions and science policy choices similar in nature to EPA's efforts to develop a toxic equivalency factor for various isomers of dioxin relative to 2,3,7,8-TCDD. The Subcommittee recommends, however, that EPA place more emphasis on acquiring more relevant data. Some of these data may be available from other sources in the near future.

The Subcommittee appreciates the opportunity to evaluate these scientific issues. We request that the Agency formally respond to the scientific advice presented in this letter.

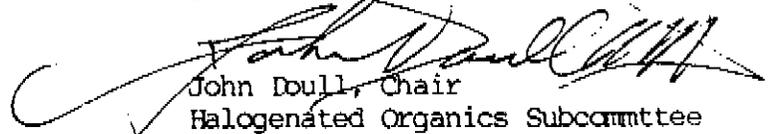
Sincerely,



Norton Nelson, Chairman
Executive Committee



Richard A. Griesemer, Chairman
Environmental Health Committee



John Doull, Chair
Halogenated Organics Subcommittee

U.S. Environmental Protection Agency
Science Advisory Board
Environmental Health Committee
Halogenated Organics Subcommittee
Roster for November 19-20, 1987 Review of the Draft Final
Drinking Water Criteria Document for Dichloroethylenes

Dr. John Doull, Chairman, Professor of Pharmacology and Toxicology, University of Kansas Medical Center, Kansas City, Kansas 66103

Dr. Seymour Abrahamson, Vice-Chairman, Professor of Zoology and Genetics, Department of Zoology, University of Wisconsin, Madison, Wisconsin 53706

Subcommittee Members and Consultants

Dr. George T. Bryan, Department of Human Oncology, K-4, Room 528, 608 Clinical Science Center, 600 Highland Ave., University of Wisconsin, Madison, Wisconsin 53792

Dr. Larry Hansen, College of Veterinary Medicine, University of Illinois, 2001 South Lincoln, Urbana, Illinois 61801

Dr. Ronald D. Hood, Professor and Coordinator, Cell and Developmental Biology Section, Department of Biology, University of Alabama, and Principal Associate, R. D. Hood and Associates, Consulting Toxicologists, P. O. Box 1927, University, Alabama 35486

Dr. Larry Kaminsky, Director, Wadsworth Center for Laboratories and Research, New York State Department of Health, Albany, New York 12201

Dr. Curtis Klaassen, Professor of Pharmacology and Toxicology, University of Kansas Medical Center, 39th and Rainbow Blvd., Kansas City, Kansas 66103

Dr. Don E. McMillan, Chairman, Department of Pharmacology, Mail #638, University of Arkansas, Medical Sciences, 4301 West Markham, St. Little Rock, Arkansas 72205

Dr. Martha Radtke, University of Cincinnati Medical Center, Department of Environmental Health 3223 Eden Avenue--M. L. #56, Cincinnati, Ohio 45267

Dr. Stephen Safe, Department of Veterinary Medicine, Physiology and Pharmacology, College of Veterinary Medicine, Texas A&M University, College Station, Texas 77843-4466

Dr. Thomas Starr, CIIT, P. O. Box 12137, Research Triangle Park, North Carolina 27709

Executive Secretary

Dr. C. Richard Cothorn, Executive Secretary, Environmental Health Committee, Science Advisory Board (A-101F), U.S. Environmental Protection Agency 401 M Street, SW, Washington, D.C. 20460