



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-88-016

OFFICE OF  
THE ADMINISTRATOR

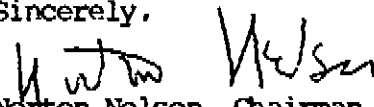
Dear Mr. Thomas:


The Halogenated Organics Subcommittee of the Science Advisory Board's Environmental Health Committee had completed its review of the Office of Drinking Water's Draft Final Criteria Document for Ortho-Meta-Para-Dichlorobenzene and is pleased to transmit its final report to you.


The major scientific/science policy issue discussed by the Subcommittee concerns the evidence for carcinogenicity and the classification of this compound using EPA's guidelines for cancer risk assessment. EPA staff has used a weight of evidence approach in recommending a classification of B<sub>2</sub> for drinking water based upon the staff's review of existing animal studies. The reasoning offered for this conclusion is scientifically defensible, but it is not the only defensible conclusion. In assessing the issue of carcinogenicity, a key question is the weight that should be assigned to the rat data for purposes of extrapolating risk to humans. The assessment of this and other issues led most Subcommittee members to conclude that this compound should more appropriately be classified as Category C of EPA's guidelines. The position adopted by the Subcommittee follows the reasoning stated in a companion letter of March 9, 1988 jointly developed with the Environmental Health Committee following a recent evaluation of the scientific evidence for perchloroethylene. The discussion of these and other issues is presented in the attached report.

The Subcommittee appreciates the opportunity to conduct this scientific review. We request that the Agency formally respond to our scientific advice.

Sincerely,

  
Norton Nelson, Chairman  
Executive Committee

  
Richard A. Griesemer, Chairman  
Environmental Health Committee

  
John Doull, Chairman  
Halogenated Organics Subcommittee

Review of the Office of Drinking Water's  
Draft Final Criteria Document for  
Ortho-Meta-Para-Dichlorobenzenes  
by the  
Halogenated Organics Subcommittee  
Environmental Health Committee  
Science Advisory Board

The Halogenated Organics Subcommittee conducted its review of the Office of Drinking Water's Draft Final Criteria Document for Ortho-Meta-Para-Dichlorobenzenes on April 20, 1987 in Kansas City, Kansas. In addition to the criteria document, the Subcommittee received the following documents:

- o National Primary Drinking Water Regulations: Para-Dichlorobenzene Proposed Rule (Draft, December 18, 1986).
- o Office of Pesticides and Toxic Substances (OPTS) Draft Summary Report of the OPTS Toxicology Peer Review Committee (April 8, 1987).
- o National Toxicology Program: Toxicology and Carcinogenesis Studies of 1,4 Dichlorobenzene in F344/N Rats and B6C3F1 Mice--Gavage Studies (Galley Draft, May 1986).

Two additional documents prepared by the Office of Drinking Water for this rulemaking were not reviewed by the Subcommittee. These included: Analytical Methods/Monitoring for VOCs in Drinking Water (June, 1985), and Technologies and Costs for the Removal of Volatile Organic Chemicals From Drinking Water (May, 1985). The Subcommittee also received comments on the criteria document from members of the public.

Since the Subcommittee's meeting EPA has finalized its rulemaking for Para-Dichlorobenzene. The Subcommittee recognized that many of the scientific issues that it addressed in its review of Para-Dichlorobenzene were common to halogenated compounds. Further, it and the Environmental Health Committee evaluated these issues in the context of responding to a set of questions posed by the EPA Administrator following their report of January 27, 1987 on EPA's assessment of Perchloroethylene. Rather than view these evaluations as unrelated events, the Subcommittee and the Committee have chosen to defer final submission of the Para-Dichlorobenzene report until a Committee-wide statement was prepared and transmitted.

#### Major Conclusions and Recommendations

The major scientific/science policy issue discussed by the Subcommittee concerns the evidence for carcinogenicity and the classification of this compound using EPA's guidelines for cancer risk assessment. The criteria document states two options: to classify Para-Dichlorobenzene in category B<sub>2</sub> (sufficient evidence of carcinogenicity in animals with limited or inadequate evidence in humans), or to place it in category C (limited evidence of carcinogenicity in animals in the absence of human data). The National Toxicology Program's (NTP) study concludes that "clear evidence of carcinogenicity" exists, the highest of the five categories in NTP's ranking system.

The Subcommittee's major conclusions and recommendations include the following:

1. The criteria document represents a well written, scientifically balanced interpretation of existing information for these compounds. The current document is scientifically and editorially better than many other EPA assessment or criteria documents previously reviewed by the Subcommittee. Individual Subcommittee members have made specific technical and editorial comments that have already been forwarded to the Office of Drinking Water.

2. The conclusions of the NTP study that the administration of the test compound resulted in the production of adenocarcinomas in the kidneys of male F344/N rats and adenomas and carcinomas in the livers of B6C3F1 mice of both sexes is supported by the data. There are also no questions regarding the adequacy of the identification of these tumors. The Subcommittee agrees with the reasoning in the NTP study that indicates that not all reported mouse liver tumors are of equal significance.

3. EPA staff has used a weight of evidence approach in recommending a classification of B<sub>2</sub> for drinking water based upon the staff's review of existing animal studies. The reasoning offered for this conclusion is scientifically defensible but, as noted below it is not the only defensible conclusion.

4. In assessing the issue of carcinogenicity, a key question is the weight that should be assigned to the animal studies, particularly the rat data, for purposes of extrapolating risk to humans. Most members of the Subcommittee (eight of nine) believe that this compound could justifiably be classified in category C. The reasons are as follows:

- o The absence of positive results in genotoxicity studies. Since the compound does not appear to be mutagenic and the tumors observed in the kidney of F344/N rats were identified histologically, it appears to act via an epigenetic mechanism in the male rat rather than through the formation of DNA-adducts. In the case of liver carcinomas in B6C3F1 mice, Para-Dichlorobenzene and other halogenated compounds may promote the expression of oncogenes.
- o The male rat kidney tumors may be the result of a mechanism that would not play a role in humans. The Subcommittee and the Environmental Health Committee recently transmitted to you our position on this issue in the context of Perchloroethylene. That position, forwarded to you on March 9, 1988 also applies to the Subcommittee's evaluation of Para-Dichlorobenzene.
- o There is no support for a higher classification from human epidemiology studies.

5. The selection of studies for the quantification of noncarcinogenic toxicological effects, as well as the derivation of health advisories and acceptable daily intakes, has been performed correctly.

6. The proposed drinking water standards, based upon the presented inhalation data, should also be designed to protect against developmental effects.

7. The statement on page VIII-7, that deaths in humans occur as a result of central nervous system toxicity, is unsubstantiated by the material presented in the document.

8. The Subcommittee generally concurs with the criteria document's conclusions on Ortho- and Meta-Dichlorobenzene.

U.S. Environmental Protection Agency  
Science Advisory Board  
Environmental Health Committee  
HALOGENATED ORGANICS SUBCOMMITTEE  
P-Dichlorobenzene Review  
April 20, 1987

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