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-88-014

OFFICE OF
THE ADMINISTRATOR

Dear Mr. Thomas:

The Drinking Water Subcommittee of the Science Advisory Board's Environmental Health Committee has completed its independent scientific review of the Draft Drinking Water Criteria Document for Xylenes developed by the Environmental Criteria and Assessment Office (Office of Research and Development) for the Office of Drinking Water, dated June 1987, and is pleased to transmit its final report to you. The Subcommittee reviewed the draft criteria document at a public meeting in Washington, D.C. on October 8-9, 1987.

In general, the draft criteria document represents an improvement over a previous draft prepared by Agency staff. It includes an informative survey of the existing scientific literature for xylenes and appropriately discusses a range of scientific issues related to toxicity and exposure.

The primary issue in the review concerns the selection of studies used in determining the Drinking Water Equivalent Level (DWEL). The DWEL is based upon the experimental level below which a health effect is not observed and provides a non-carcinogenic basis for establishing a drinking water standard. The Subcommittee concludes that the Office of Drinking Water has selected the appropriate studies to calculate the DWEL, and that the calculation was developed in a scientifically supportable manner.

The Subcommittee recommends that taste and odor should be a scientific basis for a secondary Maximum Contaminant Level because most of the public will not drink water that smells. Discussion of this and other issues related to the draft criteria document are presented in the attached report.

We appreciate the opportunity to conduct this particular scientific review and request that the Agency formally respond to our scientific advice.

Sincerely,

Norton Nelson, Chairman
Executive Committee

Richard A. Griesemer, Chairman
Environmental Health Committee

Gary P. Carlson, Chairman
Drinking Water Subcommittee

Review of the Draft Drinking Water Criteria Document
for Xylenes
by the Drinking Water Subcommittee
Environmental Health Committee
Science Advisory Board

On October 8-9, 1987 the Drinking Water Subcommittee of the Environmental Health Committee of EPA's Science Advisory Board reviewed the Draft Drinking Water Criteria Document for Xylenes developed by the Environmental Criteria and Assessment Office (Office of Research and Development) for the Office of Drinking Water, dated June 1987. The Subcommittee's major conclusions and recommendations are presented below.

Major Conclusions and Recommendations

1. In general, the draft criteria document represents an improvement over the previous draft. It discusses the literature reasonably well. The sections on absorption, distribution, metabolism and excretion are thorough and convincing, while the discussion of human effects appropriately points out the difficulty associated with mixed exposures and the exposure estimation. The evaluation of developmental toxicity, comparing the effects seen at high doses in both the mother and the fetus with the absence of effects observed at lower doses, is balanced.

2. The primary issue in the review of this draft document concerns the selection of studies used in determining the Drinking Water Equivalent Level (DWEL). The DWEL is based upon the experimental level below which a health effect is not observed and provides the non-carcinogenic basis for establishing a drinking water standard. In the health advisory document, previously reviewed by the Environmental Health Committee in a report dated October 24, 1986, the DWEL was based on an inhalation study conducted by Jenkins, et. al., in rats, guinea pigs, monkeys and dogs. This new document uses data from the National Toxicology Program (NTP) studies in rats. Data from the subchronic study (No-ObservedEffect-Level [NOEL] = 500 mg/kg/day) are employed in deriving the long-term health advisory, and results from the chronic study (NOEL= 250 mg/kg/day) are utilized in the calculation of the DWEL.

3. Although it is somewhat surprising that the rats were not more susceptible to xylene exposure, the utilization of the NTP results is acceptable, particularly because the route of administration was oral. There is uncertainty because xylene was administered as a bolus dose in corn oil rather than in water, but the limited solubility of xylene in water prevented administration in this manner. The use of the data is also consistent with the recommendation made by the Environmental Health Committee when it previously reviewed the xylene health advisory.

4. The calculations appear accurate and follow the usual methods for their application. The safety factor of 100 is appropriate in view of the criteria set for selection based upon the length of the study which, in this case, is a chronic study in animals. The DWEL of 63 mg/liter results in a substantial increase over the previously proposed value of 2.2 mg/liter based on Jenkin's inhalation studies. However, the obvious differences in experimental design, and the previously used formula, may have been conservative in estimating a respiratory

volume of 20 m^3 per day. Also, there is the simple matter of a ten-fold difference in the safety factor.

5. The fact that the taste and odor value may be in the range of 0.3 to 1.0 mg/liter is important. The Subcommittee recommends that taste and odor should also be a scientific basis for a regulatory decision by establishing a secondary Maximum Contaminant Level (MCL) because most of the public will not drink water that smells. Also, xylene can serve as a sentinel contaminant for other components found in the same compound such as ethylbenzene.

6. The draft document is inconsistent in stating that the longer-term health advisory for the 10 kilogram child is 36 mg/liter compared to the DWEL of 63 mg/liter. This needs to be explained carefully to avoid misunderstanding. The inconsistency may be related to the use of the lower weight for the child.

7. The Subcommittee agrees with the use of the longer-term health advisory number for the 1 and 10 day health advisories. The calculations previously used for the 1 day advisory had some advantage in that they were based on studies conducted in humans. However, these were inhalation studies that may not be as good a predictor for the effects of oral administration of this compound as previously thought. Furthermore, the use of the previous 1 day health advisory would lead to a discrepancy in that it would be lower than the longer-term advisory.

8. Some scientific problems with the draft document remain, however. These include:

- o The information likely to be in Chapter IV (not currently included in the document) for comparing the contributions from various sources is necessary for preparing an adequate analysis. The Subcommittee cannot endorse the document as written due to this deficiency. The information in this chapter on exposure is essential to making a judgment about the public health risk from xylenes.

- o The Drinking Water Equivalent Level that has been suggested for xylene is 60 mg/liter. At this level, an individual can have significant intake of xylene because of inhalation and dermal exposure. For example, if an individual took a 30 minute shower in an 18 m^3 room with a flow rate of 4 gallons of water per minute and half of the xylene volatilized, he/she would absorb about two times the amount (assuming 50% absorption through the lungs) ingested from 2 liters of water. The calculation of the Maximum Contaminant Level Goal should consider these exposures; however, they should be confused with the exposures that occur through background levels of xylene through other pathways such as air and food.

- o The Subcommittee has a question with regard to the statement that the deaths that did occur among the rats in the high dose group in the NTP study result from errors in gavage administration, although

"a behavioral effect may have caused the rats to resist dosing." Although this or a similar phrase is used several times in the draft criteria document, it is not at all clear what it means. Does it mean that there was some alteration in the behavior as a result of central nervous system perturbation suggesting that this level of exposure to xylene may have serious neurotoxic effects, or does it simply mean that rats learned to hate the stuff? The Subcommittee recommends that the Agency clarify this point with the laboratory that conducted the NTP study.

- The classification of xylene in Group D ("Not Classified as to Human Carcinogenicity") of EPA's risk assessment guidelines for carcinogenicity is inconsistent with the categories given on page VIII-4 of the draft document. In view of the fact that the NTP found xylene to be negative in both rats and mice, EPA should also consider classifying it in Group E ("Evidence of Non-Carcinogenicity in Humans") which uses the criteria of the lack of evidence in at least two adequate animal tests in different species. The Agency needs to clarify its scientific rationale for not accepting the NTP studies as evidence for this category.

- The Subcommittee recommends a greater discussion in the draft document of the possible role that the use of a mixture in the NTP study may play in the attribution of the toxicity to any particular isomer of ethylbenzene. This may also need to be considered in the ethylbenzene criteria document, depending on the results of studies with that compound.

- There is constant and unnecessary reptetition within the draft document. Also, many of the papers reviewed are essentially irrelevant to making risk assessment judgments.

U.S. Environmental Protection Agency
Science Advisory Board
Drinking Water Subcommittee

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*Not present at the meeting October 8-9, 1987