



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Agency for Toxic Substances
and Disease Registry
Atlanta GA 30333

MAY 4 1995

Hasmukh C. Shah, Ph.D.
Manager, Vinyl Chloride Panel
Chemical Manufacturers Association
2501 M Street, NW
Washington, DC 20037

received
5/8/95

Dear Dr. Shah:

This is in response to your March 22 letter to Dr. William Cibulas regarding the intent of the Chemical Manufacturers Association (CMA) Vinyl Chloride Panel to address vinyl chloride data needs identified by the Agency for Toxic Substances and Disease Registry (ATSDR). In the letter, you enclosed a preliminary study protocol for a two-generation reproductive toxicity study of vinyl chloride by the inhalation route. You asked if ATSDR would consider including measures of developmental toxicity endpoints in the reproductive toxicity study protocol. You also submitted a review of the available data on the developmental toxicity of vinyl chloride.

After evaluating the available data on developmental toxicity studies for vinyl chloride, we determined that the CMA reproductive toxicity study protocol including examination of developmental toxicity endpoints provides an acceptable alternative to separately conducting a two-species developmental toxicity study. Generally, the Agency will consider proposals to simultaneously acquire reproductive and teratologic information in the absence of any reproductive or teratologic data. In view of the suggestive human data and limited animal data for developmental toxicity, as stated in the ATSDR Priority Data Needs Document for vinyl chloride, we believe it would be appropriate and efficient to simultaneously examine both toxicity endpoints in the same study.

In merging the study protocols for developmental toxicity and reproductive toxicity, we ask that you adopt the Environmental Protection Agency testing guidelines for inhalation developmental toxicity studies (Code of Federal Regulations, Part 798.4350, "Inhalation developmental toxicity study," July 1, 1992). For example, exposure duration shall be at least six hours daily and the exposure period shall cover the period of major organogenesis (days 6-15 for rats for this study protocol). At the time of sacrifice or death during the study, the dam shall be examined macroscopically for any pathological changes which may have influenced the pregnancy.

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