"VINYL CHLORIDE: COMBINED INHALATION TWO-GENERATION REPRODUCTION AND DEVELOPMENTAL TOXICITY STUDY IN CD RATS" (PROTOCOL)

PEER REVIEWER COMMENT FORM

August 1995

Name Ronald D. Hood, Ph.D.

1. Are the study objectives clearly stated and appropriate?

(Yes) No Unsure

Why?

This is a relatively routine type of study, and the protocol concisely states what is to be done.

2. Is the study design appropriate for the study objectives?

(Yes) No Unsure

Why?

The design is typical for studies assessing a chemical's potential for reproductive or developmental toxicity.

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3. Are the methods selected appropriate for the study objectives?

(Yes) No Unsure

Why?

The methods proposed are typical of the proposed types of tests.

4. Any overall comments on the protocol?

The protocol appears to be quite thorough and well planned. It should be quite adequate to carry out the proposed objectives. I did not find any technical flaws in the protocol, but there are a few typographical errors, which I have circled with pencil in the draft. I have only two additional questions/comments:

1. On page 6, first paragraph, the statement is made that the high inhalation dose of 1012 mg/kg/day "was selected based on the oral equivalent of the limit dose of 1 mg/kg body weight/day." Shouldn't that have been 1000 mg/kg body weight/day instead of 1?

2. The value in mg/kg/day that I obtain when I use the example on page 6 is 1009.8, which rounds to 1010, not 1012. The difference is trivial, but someone might want to check on the discrepancy.

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Select the appropriate category below (List recommended changes or reasons for not recommending:

A. Recommend ( ✓ )

B. Recommend with Required Changes ( )

C. Not Recommended ( )

Ronald D. Hood 8-3-95

Signature Date

CMA 115534

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Name Ronald D. Hood, Ph.D.

5. Any comments on ATSDR's peer review process?

The review process seems appealingly simple and straight forward.

6. Any other comments?

Call on me again if I can be of assistance.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Agency for Toxic Substances
and Disease Registry
Atlanta GA 30333

JUL 27 1995

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

received
7/31/95

Dear Dr. Shah:

This is in response to your June 9 letter in which you enclosed a study protocol, "Vinyl chloride: Combined inhalation two-generation reproduction and developmental toxicity study in CD rats." The study protocol was submitted by the Chemical Manufacturers Association (CMA) to the Agency for Toxic Substances and Disease Registry (ATSDR) for the purpose of conducting voluntary research to address ATSDR's priority data needs for vinyl chloride. In the letter, you asked if ATSDR could consult with the Environmental Protection Agency (EPA) regarding EPA's interest in the neurotoxicity of vinyl chloride and the feasibility of satisfying EPA's identified testing needs by expanding the enclosed protocol to address neurotoxicity endpoints. Also, you requested that ATSDR discuss with EPA an extension of time for the testing that will be satisfactory to both ATSDR and EPA.

As described in the *Federal Register* (57 FR 4758, February 7, 1992), ATSDR established the Tri-Agency Superfund Applied Research Committee (TASARC) to assure coordination of ATSDR's substance-specific research efforts. The CMA combined study protocol was shared with EPA and the National Institute of Environmental Health Sciences at the June 16 meeting of the TASARC. The EPA is currently reviewing the protocol to assess the suitability of including a neurotoxicity component in the protocol. We expect to hear from EPA soon and will notify you of their decision immediately thereafter.

Meanwhile, we have forwarded the CMA protocol for the combined reproductive and developmental study to ATSDR's Associate Administrator for Science who will identify and select peer reviewers. You will be requested to respond to the peer reviewers' comments. Upon satisfactory response, and upon agreement between our two organizations on the study plan (including the time schedule), ATSDR and CMA may then choose to enter into a memorandum of understanding.

It is clear that an MOU could not have been in place by May 31 as stated in your letter of June 9. However, we have notified EPA and NIEHS of the significant progress taken place and have agreed to continue to pursue voluntary research efforts with CMA beyond the deadline; hopefully leading to a successful voluntary research agreement between our two organizations. We will keep EPA informed of our progress on this effort. If you have any questions, please call me at 404-639-6300.

Sincerely yours,

Christopher T. DeRosa

Christopher T. DeRosa, Ph.D.
Director, Division of Toxicology