

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

PEER REVIEWER COMMENT FORM

September 1995

Name Barbara F. Hales, Ph.D.

1. Are the study objectives clearly stated and appropriate?

☒ **Yes** ☐ **No** ☐ **Unsure**

Why?

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

☒ **Yes** ☐ **No** ☐ **Unsure**

Why?

CMA 115527

PAGE 2 -- PEER REVIEWER COMMENT FORM

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

☒ Yes

☐ No

☐ Unsure

Why?

4. Any overall comments on the protocol?

The protocol has been carefully designed and is well planned.

It should provide a wealth of data on the effects of vinyl chloride on germ cells and on rodents in vivo.

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PAGE 3 -- PEER REVIEWER COMMENT FORM

Barbara F. Hales, Ph.D.

Name _____

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

A. Recommend (☒)

No chnages are required. The study should be carried out as it has been designed. I will be very interested in the results.

B. Recommend with Required Changes (☐)

C. Not Recommended (☐)

Signature Date

PAGE 4 -- PEER REVIEWER COMMENT FORM

Barbara F. Hales, Ph.D.

Name _____

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

This process appears to be very thorough. I expect that this has an impact on the quality of the proposals which are submitted.

6. Any other comments?

I enjoyed reading the proposal.

The overall chronology and study design for the developmental portion of this study is depicted in Tables 1 and 2, respectively. ✓

Developmental - Breeding Procedure

Sexually mature, adult virgin females, approximately 10 weeks of age and weighing approximately 200 - 250 grams, will be naturally mated with one male of the same strain at the Charles River Breeding Laboratory. Females will be checked for plugs the following morning and those found with a vaginal plug will be removed from the males' cage. The day on which a vaginal plug is detected will be considered Day 0 of gestation. Day 0 body weights will be provided by Charles River Breeding Laboratory, and maintained in the study record. Rats will be shipped on Day 0 or 1 of gestation and will arrive at our laboratory on Day 1 or 2 of gestation.

Developmental - Maternal Observations

All animals will be observed daily during the study for alterations in behavior or demeanor as previously described under the Reproduction Study "Physical Observation" section, with the exception that a thorough weekly clinical examination will not be conducted. Any animal which dies, appears moribund or shows indications of early termination of pregnancy will be submitted for a complete necropsy as described for the Reproduction Study. Body weights will be recorded on gestation days 0, 6, 14 and 21.

On Day 21 of gestation, all surviving animals assigned to the developmental study will be euthanized by carbon dioxide inhalation and given a limited necropsy. Any obvious structural or pathologic changes noted in the adult will be recorded and the weight of the liver, kidneys and gravid uteri will be recorded. Liver, kidneys and gross lesions will be preserved in neutral, phosphate-buffered 10% formalin, but microscopic examination of tissues will not be conducted unless deemed necessary to interpret other observations made during the study or requested by the sponsors.