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Huntingdon Life Sciences

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| ATTENTION OF: | **Wendy Sherman** | FROM: | **R. E. Schroeder** |
| COMPANY: | **CMA (Chemical Manufacturing Association) Chemstar Department** | DATE: | **18 April 1997** |
| FAX NUMBER: | **703-741-6091** | CC: | |

MESSAGE: 96-4080: Vinyl Chloride Combined Inhalation Two-generation Reproduction and Developmental Toxicity Study in CD rats. Copies of Contract Required Progress Reports.

Dear Wendy,

Attached are copies of the contract requested progress reports for the reproduction and developmental phases of the vinyl chloride study. Please review and let me know if these are acceptable or if you need additional information (908) 873-2550 Ext 2910.

Best regards,

Raymond E. Schroeder, M.S., DABT
Study Director

Raymond E Schroeder

# Vinyl Chloride Combined Inhalation Two-Generation Reproduction and Developmental Toxicity Study in CD Rats

## Progress Report Developmental Phase

In this study, mated rats (24/group) were treated with vinyl chloride via whole-body exposure (6 hrs/day) over the Day 6-19 gestation period (day of mating evidence = Day 0 of gestation). Body weight, food consumption and clinical findings were recorded periodically throughout gestation. Animals were sacrificed on Day 20 of gestation and corpora lutea/uterine implantation data recorded. Fetuses were weighed, sexed and given a gross external examination. One-half of the fetuses in each litter were evaluated for visceral malformations/variations (microdissection procedure) and the remaining fetuses are being stained with Alizarin Red S for skeletal examination. Females were given a gross postmortem examination and liver, kidney and gravid uterine weights recorded. Gross lesions, kidneys and liver tissue were taken and preserved.

Exposures and the Day 20 gestation maternal sacrifices have been completed for the developmental phase. Dates for these events are as follows:

| | |
|---|---|
| Mating imitated: | March 12, 1997 |
| Treatment period (Days 6-19 of gestation, 6 hrs/day): | March 19 - April 10, 1997 |
| Maternal Day 20 gestation sacrifices: | April 2 - 11, 1997 |
| Submission of the audited draft final report: | Week of August 25, 1997 |

Study comments:

Animals in the developmental phase were exposed along with the animals in the reproduction phase of the study. The fetal evaluations are on-going.

Submitted by:_____ Date:_____
Raymond E. Schroeder, M.S., DABT
Title: Study Director
For: Huntingdon Life Science Inc.

# Vinyl Chloride Combined Inhalation Two-Generation Reproduction and Developmental Toxicity Study in CD Rats

## Progress Report Reproduction Phase

In this study, parental (P1,P2) generation animals (30/sex/group) are being treated via whole-body inhalation to vinyl chloride at exposure levels of 0, 10, 100 and 1100 ppm. The study is currently in the gestation/lactation periods of the P1 parental generation to produce the F1 litters. These animals have completed a 10 week premating treatment period (exposures were 6 hrs/day, 5 days/week - January 7 - March 18, 1997) and a 20 day mating period (exposure 6 hrs/day, 7 days/week - March 18 - April 6, 1997). Once mated, females were treated 6 hrs/day from Days 0-20 of gestation and females delivering litters will be treated from Days 4-25 of lactation). Following is a timetable for key events through the remainder of the study.

| Event | Proposed Date |
|---|---|
| P2 premating treatment period (6 hrs/day, 5 days/week): | |
| Initiate | May 20, 1997 |
| Complete | July 29, 1997 |
| Mating period P2 - F2 litters (6 hrs/day, 7 days/week): | |
| Initiate | July 29, 1997 |
| Complete | August 12, 1997 |
| Gestation/Lactation of F2 litters | |
| Initiate | July 30, 1997 |
| Complete | September 23, 1997 |
| Sacrifice Schedule: | |
| P1 Males | April 28 & 29, 1997 |
| P1 Females | May 19 & 20, 1997 |
| P2 Males | September 15 & 16, 1997 |
| P2 Females | September 24 & 25, 1997 |
| Submission of the audited draft report | Week of March 23, 1998 |

Study Comments:

The start of the study was delayed by approximately two months from the contract date (anticipated start October 28, 1996). Animals for the study (P1) arrived December 23, 1996. This delay was attributed to the following: additional time required to set up the chamber generation system (test material in a one ton cylinder arrived September 19, 1997) and monitor for leaks; GLP characterization of the lot of test material received; and calibration of the gas chromatograph for the periodic monitoring of the exposures concentrations for comparison with the infrared spectrophotometer (MIRAN) results. Mating period was extended by six days to achieve more matings.