

Huntingdon Life Sciences

18 April 1997

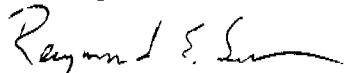
Ms. Wendy Sherman
Chemical Manufacturers Association
Chemstar Department
1300 Wilson Boulevard
Arlington, VA 22209

RE: Huntingdon Life Sciences Study No. 98-4080; Vinyl Chloride Combined Inhalation Two-Generation Reproduction and Developmental Toxicity Study in CD Rats: Progress Reports Reproduction and Developmental Phase.

Dear Ms. Sherman,

Enclosed are progress reports for the reproduction and developmental phases of the referenced study. As I indicated this afternoon, I will be out next week but if you need additional information on for these reports please call Mr. Gary Hoffman (908) 873-2550 Ext 2920 and he should be able to help you.

Best Regards



Raymond E. Schroeder, M.S., D.A.B.T.
Study Director

Enclosures

cc: Mr. Gary Hoffman (Huntingdon Life Sciences)

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 pre-mating 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 pre-mating 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.

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.

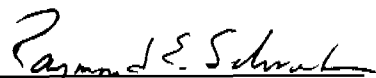
Exposures and the Day 20 gestation maternal sacrifices have been completed for the developmental phase. Dates for these events are as follows:

Mating initiated:	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: 18 Apr-1997

Raymond E. Schroeder, M.S., DABT

Title:

Study Director

For:

Huntingdon Life Science Inc.

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