

Huntingdon

STUDY NO. 96-4080

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

Developmental Toxicity Study

Final Report

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ABSTRACT

This study conducted for Chemical Manufacturers Association, was designed to assess the potential maternal toxicity and/or developmental toxicity of vinyl chloride (CAS No. 75-01-4). The test material was administered via whole body inhalation (six hours/day) to 100 mated rats (25 per group) at concentration levels of 0, 10, 100 and 1100 ppm during the Day 6-19 gestation interval. The exposures for these animals were performed concurrent with those of an on-going two-generation reproduction study. Both studies are performed under the same study number; however, only the developmental toxicity study is included in this report.

Animals were observed twice daily for mortality/morbidity and for obvious pharmacologic and/or toxicologic effects and each animal was given a detailed physical examination on Days 0 and daily on Days 6-20 of gestation. During the treatment period, these latter examinations were conducted approximately one-half hour after exposures were completed. Body weights were recorded on Days 0, 6, 9, 12, 15 and 20 of gestation and food consumption was recorded over Days 0-6, 6-9, 9-12, 12-15 and 15-20. Animals were sacrificed on Day 20 of gestation and given a macroscopic postmortem evaluation which included weighing of the gravid uterus, kidneys and liver. The ovaries were evaluated for the presence and number of corpora lutea and uterine implantation data were recorded. Fetuses were removed from the uterus, weighed, sexed and evaluated for external abnormalities. Subsequently, one-half of the fetuses in each litter were processed for visceral examination (microdissection technique) and the remaining fetuses processed for staining of the skeletal structures with Alizarin Red S and examined for skeletal malformations and ossification variations.

Mean exposure concentrations over the course of the study as determined by infrared (IR) spectrophotometry, and confirmed by gas chromatography were close to the targeted concentration levels. The mean IR exposure concentration levels ($\pm$ standard deviation) for the 10, 100 and 1100 ppm groups were 10.8 ($\pm$ 1.1), 102 ($\pm$ 10) and 1110 ($\pm$ 43) ppm, respectively.

No maternal or developmental toxicity was seen at the 10 ppm exposure level. At the 100 ppm exposure level, the only maternal toxicity seen was an increase in the kidney weight relative to the Day 20 gestation weight. At the 1100 ppm exposure level, the only maternal toxicity was an increase in kidney and liver weights relative to the Day 20 gestation weights. No developmental toxicity was seen at either the 100 or 1100 ppm exposure levels. Thus, the no-observed-effect level (NOEL) for maternal toxicity with vinyl chloride in the pregnant rat was 10 ppm and the NOEL for developmental toxicity was 1100 ppm.