Gaines (1960)

DATA EVALUATION RECORD

Releasable

(1) CHEMICAL: Trichlorfon

(2) TYPE OF FORMULATION: Technical

(3) CITATION: Gaines, T.B. 1960. The acute toxicity of pesticides to rats. Toxicol. Appl. Pharmacol. 2:88-99

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(6) TOPIC: This study has information pertinent to discipline toxicology, topic acute oral toxicity and acute dermal toxicity. It relates to the Proposed Guidelines data requirements 163.81-1 and -2.

(7) CONCLUSION: Both oral and dermal LD_{50} studies were conducted with Dipterex (trichlorfon) in Sherman rats. The oral LD_{50} was inadequate. The dermal LD_{50} for males and females (nonabraded skin) was calculated to be greater than 2,000 mg/kg indicating Toxicity Category III. However, this conclusion is tentative because of design and reporting inadequacies in this study.

CORE CLASSIFICATION:

Acute Oral Study: Invalid. The acute oral toxicity study was judged invalid because the doses administered and the mortality data were not provided.

Acute Dermal Study: Supplementary. The acute dermal toxicity study was judged supplementary because doses applied were unspecified, nonabraded skin was not tested, and the animals were not restrained to prevent ingestion.

(8) MATERIALS AND METHODS: The author compared the results of both oral and dermal LD_{50} studies with Dipterex (trichlorfon) and 43 other pesticides. In this evaluation, only the results with Dipterex will be reported.

Acute Oral Study:

Test Substance: A technical grade of Dipterex (purity and source unspecified) was administered in a 10% water solution. The solution was freshly made before being administered.

Test Organism: A total of 140 (70 male and 70 female) Sherman rats, obtained from the Technical Development Laboratories, Communicable Disease Center, Public Health Service, Bureau of State Service, U.S. DHEW, Savannah, Ga., were used in this study. The rats were at least 90 days old and weighed a minimum of 175 and 200 g for male and female, respectively. Animals were individually caged during the study and fed Purina Laboratory Chow (Ralston Purina Co., St. Louis, Mo.). The animals were not fasted the night before chemical administration.

Experimental Procedure: Dipterex was administered by stomach tube at a dosage rate of up to 0.01 ml/g of body weight (doses administered unspecified). The treated rats were observed at least once each hour during day 1, and twice a day thereafter for unspecified clinical signs of toxicity and time of death. The animals that survived were observed daily until recovery or a minimum of 14 days.

Statistical Method: The LD_{50} value with 95% confidence limits was determined by the method of Litchfield and Wilcoxon (1949. J. Pharmacol. Exp. Ther. 96:99-133).

Acute Dermal Study:

Test Substance: A technical grade of a 63% solution of Dipterex (purity and source unspecified) in 95% ethanol was used in this study. The Dipterex solution was freshly prepared before application.

Test Organism: A total of 30 (10 male and 20 female) Sherman rats were used in this study. Age, weight, housing, and diet were the same as in the acute oral toxicity study.

Experimental Procedure: The fur of the rats was clipped over the top of the shoulder and forward part of the back to provide a clean area of approximately 3.0x4.5 cm for the chemical application. The unbroken skin in the clipped area was washed with a 1:1 solution of acetone and 95% ethanol to remove dirt and excess oils. Dipterex was applied slowly with a 1-ml pipette at the rate of 0.0016 ml/kg of body weight (doses unspecified). The treated animals were not restrained after treatment, and no attempt was made to remove any of the chemical residue after application. The treated animals in this study were observed in the same manner as those in the acute oral study.

Statistical Methods: The dermal LD_{50} values were calculated in the same manner as in the acute oral study.

(9) REPORTED RESULTS: The authors stated that, "in general, female rats were more susceptible" than males to "poisoning" by organic phosphorus pesticides. Symptoms included muscle fasciculation, excessive salivation and lacrimation, tremor, diarrhea, and involuntary urination. They varied in intensity with the dose administered.

A. Acute Oral Study: The minimum survival time after the oral administration of Dipterex was 30 minutes for

an unspecified number of male and female animals, and the maximum survival time after oral administration was 2 days for an unspecified number of males and 9 days for an unspecified member of females. The oral LD_{50} value for males was calculated as 630 mg/kg with 95% confidence limits of 568-699 mg/kg. The oral LD_{50} value for females was calculated as 560 mg/kg with 95% confidence limits of 455-689 mg/kg.

B. Acute Dermal Toxicity: During the study, it was noted that some of the chemicals might be ingested when rats were dosed dermally with the test compound; however, "there was no indication that ingestion of the material was an important factor."

No deaths occurred in males or females in the dermal study. The dermal LD_{50} was said to be greater than 2,000 mg/kg in both sexes.

(10) DISCUSSION: The major defect with both the acute oral and acute dermal study was that the doses administered were not given, and no mortality data (i.e., number of deaths/dose group) were provided (oral study). In addition, the clinical signs of toxicity were not given for specific dose groups. There were essentially no raw data given to support the calculated LD_{50} values. Moreover, in the acute oral study, the animals were not fasted before the test chemical was administered. In the dermal study abraded

skin was not tested, the animals were not restrained, and no attempt was made to prevent ingestion of the test compound. Because of these inadequacies, the reported LD_{50} value for the oral study cannot be considered valid. Since no deaths occurred in the dermal study, the LD_{50} may be considered a general indicator of the dermal toxicity to nonabraded skin.

(11) TECHNICAL REVIEW TIME: 5.0 hours