3-20-91

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DATA EVALUATION REPORT

STUDY TYPE: Acute oral - Rats TOX. CHEM. NO.: 663-P

GUIDELINE NO.: 81-1

MRID NO.: 412906-22

TEST MATERIAL: DPX-43898-26 (brown solid granule)

SYNONYMS: FORTRESS 5G

STUDY NUMBER: HLR 794-88

SPONSOR: E.I.duPONT de NEMOURS, INC.
WILMINGTON, DELAWARE

TESTING FACILITY: HASKELL LABORATORY for TOXICOLOGY and INDUSTRIAL MEDICINE
NEWARK, DELAWARE

TITLE of REPORT: ACUTE ORAL TOXICITY STUDY with DPX-43898-26 in MALE and FEMALE RATS

AUTHOR: JOHN W. SARVER

STUDY DATES: 10/4/88 to 11/3/88

REPORT ISSUED: 12/16/88

CONCLUSION: Based on data presented from acute oral toxicity studies in male and female Crl:CDBR rats, the LD_{50} of DPX-43898-26 is 124mg/kg in male rats (with a 95% confidence interval of 93 to 166 mg/kg) and 44 mg/kg in female rats (with a 95% confidence interval of 38 to 55 mg/kg).

Toxicity Category: I (females) , II (males)

Classification: Core guideline

MATERIALS: Male and female Crl:CDBR rats, approximately 7 weeks of age served as the test animals. The test material was DPX-43898-26, containing 5.3% (by analysis) of the active ingredient, O,O-diethyl O-(1,2,2,2-tetrachloroethyl) phosphorothioate.The test material was administered orally in a suspension of Mazola corn oil.

METHODS: Single oral doses of the test material suspended in

Mazola corn oil were administered via intragastric intubation to groups of ten (10) male or 10 female rats. The groups of male rats received doses of 50, 100 or 200 mg/kg and the female rats received doses of 25, 35, 50 or 100 mg/kg. All animals were fasted for a 24 hour period prior to receiving the test material. At one hour following treatment, food was returned. Daily observations were conducted and body weights were taken during the 14-day observation period. Observations for mortality were also made on a daily basis.

When possible, a total of six rats from each group (3 found dead during the study and 3 which were sacrificed after the 14- day observation period) were selected for gross examination. LD_{50} values were calculated based on mortality data using the methods described by Finney (Finney, D.J., Probit Analysis, third edition, Cambridge University Press, 1971).

QUALITY ASSURANCE: A signed quality assurance statement dated December 15,1988 is included in this submission. A statement of compliance with Good Laboratory Practices, dated January 3,1989 has also been submitted.

RESULTS: The following information was provided on the dosage and mortality for both male and female rats:

DOSAGE (mg/kg)	BODY WTS. (grams)	MALES CONC. (mg/mL)	DOSE VOL. (mL)	MORTALITY RATIO
50	230	20	0.57	0/10
100	224	20	1.1	3/10
200	216	25	1.7	9/10

DOSAGE (mg/kg)	BODY WTS. (grams)	FEMALES CONC. (mg/mL)	DOSE VOL. (mL)	MORTALITY RATIO
25	188	20	0.24	0/10
35	194	20	0.34	2/10
50	196	20	0.49	7/10
100	199	20	0.99	10/10

The LD_{50} in male rats was calculated to be 124 mg/kg with a 95% confidence interval of 93 to 166 mg/kg. The LD_{50} for female rats was 44 mg/kg with a 95% confidence interval of 38 to 55 mg/kg.

No clinical signs of toxicity were observed in females at the 25 and 35 mg/kg levels (two deaths reported at the 35 mg/kg dose). At 50 mg/kg both male and female rats exhibited clinical signs of toxicity characterized by tremors, stained perineum, and red ocular, oral and nasal discharges. Incoordination was observed

in females that survived at least one day following the treatment. In the 50mg/kg group of females deaths occured for up to three days following treatment; however, all clinical signs of toxicity had resolved by day 4 post-treatment.

At 100 mg/kg, all but one female was found dead on the first day following treatment. The remaining rat exhibited lethargy,tremors, incoodination,salivation and a yellow stained perineum. This animal was found dead on the third day following treatment.

Male rats which received 100 mg/kg exhibited lethargic behavior, high carriage, hunched posture,hopping gait, labored breathing, tremors, incoordination and limp muscular effects. The red ocular, nasal and oral discharges observed in the rats treated with 50 mg/kg were also observed in animals from this group. Yellow stained or wet perineum were also observed. Signs of toxicity were observed for up to 7 days following treatment and deaths occurred for up to 2 days following the administration of the test material.

At 200 mg/kg, male rats died without exhibiting clinical signs of toxicity.

Weight losses characterized as slight to severe (up to 11% loss) in females and moderate to severe (6 to 20% loss) in males were reported. Gross pathological examinations of rats which were found dead after dosing or which were sacrificed after the 14-day observation period, did not identify significant lesions that could be associated with the toxicity of the compound.

CONCLUSIONS: The data presented demonstrate that the LD_{50} for DPX-43898-26 was 124 mg/kg in males and 44 mg/kg in females. Although the number of dose levels and the actual doses are not the same for both sexes, the minimum guideline requirement for three dose levels per sex has been met and both sexes received the compound at the 50 and 100 mg/kg levels.

Although gross pathology is not reflected in the calculation of LD_{50} values, it is noted that for animals found dead, varying degrees of post- mortem autolysis had occured which might impair the identification of a target organ if one existed.

The sponsor has not provided weight charts for female rats nor has he provided the actual calculation used by Finney to determine the LD_{50} and confidence intervals reported in the submission. Neither of these omissions is expected to alter the conclusions made from the information that was presented.

The study is classified as core guideline.