215B

(UNDATED)

007775

DATA EVALUATION REPORT RECORD

Reviewed By: John Chen, DVM
Section # I, TOX Branch (TS-769C)
Secondary Reviewer: R. Bruce Jaeger

STUDY TYPE: Mutagenicity MRID: 00147961

TEST MATERIAL: Pentachlorobenzonitrile

SYNONYMS: SDS-3297

STUDY #: 694-5TX-84-0095-002.

SPONSOR: SDS Biotech. Painesville, OH.

TESTING FACILITY: Microbiological Associates

TITLE OF REPORT: Salmonnella/Mammalian-Microsome Plate Incorporation Assay (Ames Test) with and without Renal Activiation with Pentachlorobenzonitrile.

AUTHOR(S):

REPORT ISSUED: 12/28/84

CORE CLASSIFICATION: Acceptable.

CONCLUSIONS:

Dr. Chen's review is generally acceptable and accurately reflects the experimental design and results of the study.

David L. Ritter, Toxicologist
Toxicology Branch, HED

1 of 6

* CHLOROTHALONIL 081901 PAGE 3, PAGE 5

007775

215 B

Document No. 694-5TX-84-0095-002
Salmonella Mammalian Microsome Plate Incorporation Assay (Ames Test) with and without Renal Activation with Pentachlorobenzonitrile Microbiological Associates Study No. T2581.501., December 28, 1984.

The test compound, Pentachlorobenzonitrile (SDS-3297) was tested for mutagenic activity in Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, and TA1538 according to the plate incorporation assay described by Ames et al (Mutation Res. 31:347-364, 1975). The following 5 concentrations were selected for the mutation assay with and without activation: 10, 50, 250, 500, and 1000 ug/plate. Under the test conditions reported, the test compound (SDS-3297) failed to induce any significant increase in the number of revertant colonies over the negative control in the five strains of Salmonella typhimurium with and without renal metabolic activation at the dose levels tested. Therefore, the test compound was not mutagenic in the Ames test either with or without metabolic activation by the Aroclor induced rat kidney microsomes.

147961

2

215B

007775

Primary Reviewer: D. Ritter, Toxicologist
Review Section # I

Caswell# :215B

Secondary Reviewer: R. Bruce Jaeger, Section Head
Review Section # I

82-2
Rabbit

DATA EVALUATION RECORD

Study Type: Subchronic Dermal Irritation, 21 Day, Rabbit

Guideline #:

MRID: 00158254

Accession #: 262395

Study No.: 5TX-85-0023

Laboratory: WIL Research Laboratories, Inc.

Study Director: James Laveglia, Ph.D.

Quality Assurance Compliance Statement:

Abstract:

PROCEDURES

Test Material: T-117-12 (Technical grade Chlorothalonil) in 0.125 % aqueous methylcellulose.

Animals Used: New Zealand White Rabbits, 6 males and 6 females per exposure group and one control group of 5 males and 7 females.

Administration of Test Material (TM):

An area of about 4 x 6 inches on the back of each animal was clipped free of hair and the TM was applied at doses of 0, 0.1 2.5 or 50.0 mg/kg bw/day once daily for six hours per day for 21 -22 days. The application sites were wrapped with occlusive dressings and the animals were placed in restraining stocks. Following each daily application the dressing were removed andthe sites cleansed and scored for dermal toxic effects according to Draize.

Feed and Water: Available ad libitum.

Husbandry: Standard GLP.

Observations: Daily for dermal effects.

Twice daily for overt toxicity.

3

Physical examination weekly and at termination.

Body weights initially and on days 7, 14 and at termination.

Food consumption was measured daily.

Clinical Studies: Initially and at termination; see Appendix I.

Pathology: See Apendix II.

Results: The only symptoms that appeared were a slight erythema.

Conclusions: CTN adminstered dermally daily for 21 days did not produced only mild irritation.

We tentatively classify this study as CORE Guideline.

The study satisfies the Guideline requirement for a 21 day dermal toxicity study.

215 B

007775

DATA EVALUATION REPORT

STUDY: Rabbit Teratology Study

LABORATORY: Institute of Environmental Toxicology (Japanese)

STUDY NUMBER & DATE: 000-5TX-75-2077-001 5-30-75

ACCESSION NUMBER: 071539 MRID 00127855

MRID:

MATERIAL TESTED: Chlorothalonil 99.3% pure

ANIMALS: Japanese White (Funabashi) rabbits: 8 control, 9 low dose, 9 high dose.

METHODS:

3 month old mated does (day of vaginal sperm or plug = day 0 of gestation) were gavaged once daily with 0, 5 or 50 mg/kg of test material in 5% gum arabic suspending medium on days 6 through 18 of gestation.

Test animals were offered basal Rabbit and Guinea Pig diet and tap water ad libitum.

ENVIRONMENTAL PARAMETERS: Not given.

HUSBANDRY: Not given.

OBSERVATIONS:

Body weight, and mortality were recorded initially, daily from days 6 through 18 and on days 24 and 29 of gestation.

Food consumption was recorded initially and on alternate days thereafter.

On day 29 of gestation the uteruses were emptied and the number of viable pups counted. The number of implantation sites and resorption sites were determined.

Pups were weighed and examined grossly for external and visceral anomalies.

Skeleton staining with alizarin was said to have been done; however, no methodology was described for this.

Pups were examined for the occurence of "lumbar ribs" and ossified caudal vertebrae.

No detailed reports for the individual pups were submitted.

5

RESULTS:

Body weight gain and food consumption did not appear to be affected by treatment with chlorothalonil although the overall rate-of-weight gain was less for the 50 mg/kg does than for the control does.

Four does in the 50 mg/kg group experienced spontaneous abortion in the final five days of the experiment. Examination for malformation or signs of fetal toxicity was not reported on the aborted embryos.

One 5 mg/kg pup had hydrocephalus and one 50 mg/kg pup had cleft palate.

There was no reported effect on the incidence of lumbar ribs or caudal vertebrae.

CONCLUSIONS:

No obvious teratogenic response was reported at oral levels up to 50 mg/kg/day on days 6 - 18 of gestation.

It is not possible to assess the overall fetotoxic effects in this study since detailed analytical data on the offspring was no provided. This should have included individual pup data, such as body weight and individual observations as to their condition, etc.

CORE Rating: Supplementary.

Repairability: Supply individual data on all pups; examination details of aborted embryos in the 50 mg/kg group.

Note: Data Supplied under MRID 00146937 -

Core Rating = Minimum Data
DCR