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006939

DATA EVALUATION REPORT

Study: Teratology and Postnatal Studies on Picloram in the Rat

Laboratory: Dow Chemical Company; Midland, Michigan

Date: In Fd. Cosmet. Toxicology 10:6, 797-803 (1972)

Study No.: None provided

MRID No.: ~~None provided~~ (000 30 284)

Material Tested: Picloram, Lot No. 2RS17 (purity not stated)

Animals: Sprague-Dawley Rats

Methods:

Four groups of 35 female rats (10 for postnatal portion and 25 for teratology portion) were gavaged with picloram suspended in corn oil on days 6 to 15 of gestation. Dosages were 0, 500, 750, and 1000 mg/kg/day. The females were observed for signs of toxicity on a daily basis. Body weights were obtained on either day 20 or 21 postpartum for teratology. Normal teratology parameters, i.e., live and dead fetuses, resorptions, fetal weights, and skeletal and visceral evaluations were determined. The postnatal evaluations determined the following duration of gestation: litter weights at days 0, 5, and 21, and viability.

Results:

Maternal toxicity was noted at 750 and 1000 mg/kg as hyperactivity and mild diarrhea. Only evidence of unossified sternebrae was considered as the fetotoxicity end point (no NOEL). Bilateral accessory ribs were increased in numbers of fetuses, but not by litter, at 1000 mg/kg. There was a lack of evidence for postnatal effects from picloram.

Conclusions:

A fetotoxic NOEL was not determined at 500 mg/kg (LDT)

Toxicity Category: N/A

Core Rating: Supplementary for the lack of a NOEL

Repairability: None

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DATA EVALUATION RECORD

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CHEM 005101

BRANCH TOX DISC ____ Teratology

FORMULATION ___ - Technical Material

Thompson, D. J., Emerson J. L., Strebing, R. J., Gerbig, C. G., Robinson, V. B. Teratology and Postnatal Studies on 4-Amino-3,5,6-trichloropicolinic Acid (Picloram) in the Rat. Fd. Cosmet. Toxicol., 10(6), 797-803 (1972).

SUBST. CLASS = S

DIRECT RVW TIME = (MH)

REVIEWED BY: J. E. Betso
TITLE: Toxicologist
ORG: The Dow Chemical Company
LOC/TEL:

SIGNATURE: Jeanne Betso DATE: 18 Feb., 1983

APPROVED BY:
TITLE:
ORG:
LOC/TEL:

SIGNATURE: [signature] DATE: 10/11/83

CONCLUSIONS:

Teratology - rat

~~1. This is a scientifically valid study.~~

1. ~~2.~~ Picloram is not teratogenic to rats at maternal doses of 500 to 1000 mg/kg/day, even though 750 or 1000 mg/kg/day doses are toxic to the maternal animals.

2. ~~3.~~ Picloram is slightly toxic to the fetus (judging from the increased incidence of delayed ossification of 5th sternebrae which is usually associated with maternal toxicity) at doses of 500 to 1000 mg/kg/day. No NOEL for fetotoxicity was found.

3. ~~4.~~ Neonatal development/survival is not altered by maternally administered picloram at doses of 500 to 1000 mg/kg/day given on days 6-15 of gestation.

This study is classified as ~~core minimum for teratology and~~ supplementary for lack NOEL of fetotoxicity

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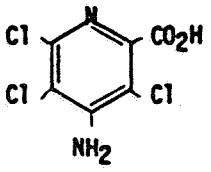
MATERIALS AND METHODS:



Picloram

Picloram (Lot No. 2RS17) was suspended in corn oil at a concentration of 200 mg/ml for administration to pregnant rats on days 6 to 15 of gestation. Four groups of 35 Sprague-Dawley rats (25 for teratology and 10 for the postnatal portion of the study) received 0, 500, 750 or 1000 mg picloram/kg/day by gavage. Rats were observed daily for signs of toxicity. Prebreeding and gestation day 20 body weights were obtained on teratology rats and prebreeding and postpartum day 21 body weights were obtained for postnatal females.

The following observations were made:

Fetal Examinations (Teratology Litters)	Postnatal Litters
in utero position	duration of gestation
# live fetuses	labor, delivery date (if possible)
# complete and partial resorptions	litter size, pup wt at birth and days 5, 21
# corpora lutea	sex at birth, day 21
fetal weights	age - eyes open
skeletal exam 2/3 each litter	% viability birth, days 5, 21
visceral exam 1/2 each litter (0, 750 and 1000 mg/kg groups only)	skeletal exam weanlings (2/sex/group)

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Maternal body weight gains, numbers of implantations, corpora lutea, resorptions, litter size and pup weights were evaluated at the 95% level by a one-way analysis of variance with Scheffe's Multiple Range Test. Fetal abnormalities among litters and fetal populations were analyzed at the 95% level using the 2 x 2 contingency table and chi-square test.

REPORTED RESULTS:

Dosage at 500 mg/kg/day produced no overt signs of toxicity, while rats given 750 or 1000 mg/kg/day developed hyperaesthesia and mild diarrhea after 1-4 days of treatment, and 14 maternal deaths occurred between days 8 and 17 of gestation in these dosage groups. In surviving dams, doses up to and including 1000 mg/kg/day affected neither maternal weight gains, litter size and resorption rate nor other reproductive parameters examined. Evidence of retarded fetal growth, as reflected by an increase in unossified fifth sternebrae was observed in all of the treated groups but not in an exactly dose-related manner. The occurrence of bilateral accessory ribs was increased significantly in fetuses of dams given 1000 mg/kg/day for 10 days during gestation, but in the usual evaluative mode (% litters) there was no significant effect.

DISCUSSION:

1. This study was conducted in a scientifically appropriate manner. Maternally toxic and non-effect doses were used.

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2. Complete review of this study is possible with the use of the "raw data" package in addition to the written publication.

3. Picloram appears to have no effect on the fetus that is unrelated to maternal toxicity -- and then the fetus appears to be fairly well protected from the insult upon the maternal animal.

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TB does not support the statement

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