

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: January 23, 1980

SUBJECT: EPA Reg.#464-323; Picloram Teratology Study
CASWELL#39

FROM: William Dykstra
Toxicology Branch (TS-769) *WMD 1/23/80*

TO: Richard Mountfort
Product Manager#25

THRU: M. Adrian Gross, Chief *William M Butler for M. Adrian Gross*
Toxicology Branch (TS-769)

Recommendations:

- 1) The referenced study is only acceptable as supplementary data. Picloram was not teratogenic at the doses tested, but a NOEL for ossification retardation does not appear to be established for the study.

Review:

- 1) Teratology and postnatal studies on 4-amino-3,5,6-tri-chloropicolinic acid (picloram) in the rat; D.T. Thompson et al, Fd. Cosmet. Toxicol. Vol. 10, pp. 797-803 (1972)

Test Material

Four groups of 35 Sprague-Dawley - derived rats were given daily oral doses of 0 (corn oil), 500, 750 or 1000 mg picloram/kg/day on days 6-15 of gestation. Twenty-five dams from each group were killed on day 20 and the fetuses were removed by Cesarean section. At this time the following data were recorded: position of fetuses in utero; number of live fetuses; number of resorptions; number of corpora lutea; individual pup weights and sex. Following gross external examinations of all fetuses, fetuses comprising two-thirds of each litter were cleared in 1% KOH solution, stained with Alizarin Red S, and examined for skeletal abnormalities. The remaining fetuses were preserved in Bouin's fixative and examined for visceral abnormalities. The remaining ten dams in each group were used in a postnatal study and were allowed to deliver and wean their litters.

(2)

Results:

Dosage at 500 mg/kg/day produced no overt signs of toxicity, while rats given 750 or 1000 mg/kg/day developed hyperesthesia 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.

External examination of all fetuses immediately after maternal separation failed to reveal any abnormalities and, with the exception of two fetuses, only minor abnormalities were detected by skeletal and visceral examination.

Incomplete ossification of sternebrae and the presence of accessory ribs were the most frequently occurring irregularities in skeletal development in both control and treated animals. The incidence of unossified fifth sternebrae was significantly greater in treated groups than in controls and the occurrence of bilateral accessory ribs was significantly increased in fetuses of dams given 1000 mg/kg/day.

A minor visceral abnormality, characterized by moderate distension of the renal pelvis (hydronephrosis), occurred in a number of fetuses in the control and treated groups.

The condition was mild in virtually all affected fetuses, and occurred both unilaterally and bilaterally. At the highest dosage level, the incidence of unilateral hydronephrosis was increased significantly among the fetal population but not among litters. Unilateral hydroureter was increased significantly in fetuses of the 750 mg/kg/day group.

One fetus of the 78 examined from dams receiving 1000 mg/kg/day had a megaesophagus and persistent right fourth aortic arch.

Arising from the arch were a right ductus arteriosus, left innominate artery and right carotid and subclavian arteries.

A littermate has slightly distended lateral cerebral ventricles and flattened ovaries and fallopian tubes.

In the postnatal study, survival and development of pups was unaffected by treatment of the dams with picloram.

Conclusion: Picloram was not teratogenic in this study, but a NEL for ossification retardation does not appear to be established for the study.

Classification: Supplementary Data

(a) Individual litter data not submitted.