CASE - PM

CHEM Chlorsulfuron

BRANCH TB DISC TOPIC Skin Irritation - Rabbit

002635

FORMULATION Formulated, 75% active

FICHE/MASTER ID CONTENT CAT

Skin Irritation Test On Rabbits For EPA Pesticide Registration, Haskell Laboratory Report No. 355-80, Silber, L. S.

SUBST. CLASS =

OTHER SUBJECT DESCRIPTORS

DIRECT RVW TIME = 1 1/4 hours START-DATE END DATE

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002635

Conclusion:

A. Core Guideline
B. Category IV
C. The chlorsulfuron formulation is not a skin irritant on intact and abraded skin of rabbits.
D. This study conforms to EPA Proposed Guidelines in Section 163.81-5 Primary Dermal Irritation Study (43 Federal Register 37360, 8/22/78).

Methods:

Six male albino rabbits were clipped free of hair on the trunk and lateral areas and placed in FDA-type stocks. Doses of 0.5 gm of test material, slightly moistened with saline, were applied to two intact and two abraded skin areas of each rabbit under gauze squares. The animals trunks were then wrapped. After 24 hours, the rabbits were removed from the stocks, the patches taken off and the site was wiped to remove any remaining test material. Observations were made upon removal of patches at 72 hours, six and seven days after treatment. Scoring was according to Draize.

Results:

The chlorsulfuron formulation produced no to mild skin irritation when tested on intact and abraded skin of six rabbits. The range of Primary Irritation Scores is 0.125-1.75 according to the technique of Draize and therefore is not a primary skin irritant. No irritation was present at day seven. There was no mortality.

Discussion:

The methods, scientific principles, validity of conclusions, and adequacy of data for conclusions were adequate for the study.

Conclusion:

3-Generation Reproduction - Rat

002635

A. Core Guideline
B. A NOEL of 500 ppm based on decreased fertility indices were established when technical chlorsulfuron was fed to rats in a 3-generation 6-litter reproduction study at dietary levels of 0, 100, 500, and 2500 ppm.
C. This study generally conforms to EPA Proposed Guidelines in Section 163.83-4 Reproduction Study (43 Federal Register 37384, 8/22/78) with some modifications.

Methods:

3-Generation Reproduction - Rat

Charles River CD® male and female rats were fed diets that contained 0, 100, 500, or 2500 ppm chlorsulfuron in a long term feeding study. After 103 days of feeding, 20 rats/sec/level were selected for the three-generation six-litter reproduction study and temporarily removed from the long-term study.

Male and female F_0 rats within each dietary group were mated for a 15-day period to reproduce F_{1a} litters. During the mating and reproduction phases, F_0 rats continued to receive their respective test group's diets. Approximately seven days after weaning the F_{1a} litters, the F_0 rats were mated a second time for a 15-day period to different rats to produce F_{1b} l tters. At weaning, the F_0 rats were returned to their respective groups in the long-term feeding study. The number of pups in each F_{1b} leter was reduced to ten and twenty-one days after delivery, surviving pups in the F_{1b} litters were weighed and sexed. 20 pups/sex/level were then representatively selected to initiate the second feeding/reproduction period to produce F_{2a} and F_{2b} litters. Similarly F_{3a} and F_{3b} litters were produced. Twenty-one days after delivery of the F_{3b} litters, ten male and ten female weanlings were sacrificed and subjected to gross and histopathological examinations. During the study diet, consumption and body weight data were taken, and values for food efficiency and daily intake were calculated. Rats were examined at least once daily for abnormal behavior, mortalities, and clinical signs of toxicity. The following tissues from the F_{3b} rats/sex/level were examined histopathologically: brain, adrenals, spinal cord (cervical, thoracic, lumbar, sacral), pancreas, lungs, trachea, thyroid, and parathyroid glands, heart, skeletal muscle, sciatic nerve, spleen, thymus, liver, kidneys, testes (with epididymides), ovaries, uterus, stomach, duodenum, jejunum, ileum, colon, and bone marrow.

Results:

Rats in the 2500 ppm group had slightly decreased fertility indices when compared to controls. Mean number of pups/litter, gestation, lactation, and viability indices, litter survival, mean weanling body weights, and weight gains,diet consumption, and food efficiency were not adversely influenced. Slight differences in mean weanling body weights in the 2500 ppm group were not consistently related to dietary concentrations.

and were not considered biologically significant. Clinical observations were not considered to be compound-related. Mean organ body weights and organ weight ratios of weanling rats from the test groups were comparable to those of the controls. No gross or histopathological abnormalities that could be related to dietary administration were observed in the F_{3b} weanlings. The no observable effect level was considered to be 500 ppm based on decreased fertility indices.

Treatment Group (ppm)	Fertility Index (7.)			
Litter	0	100	500	2500
F_{1a}	95	90	95	95
F_{1b}	100	95	95	89
F_{2a}	95	90	85	84
F_{2b}	100	95	89	100
F_{3a}	95	100	90	79
F_{3b}	95	100	100	79

Discussion:

3-Generation Reproduction -Rat

The methods and materials, scientific principles, validity of conclusions and adequacy of data for conclusions were adequate for the study. Modifications in the guideline such as reproduction through three generations rather than the guideline's two, breeding twice within each generation to produce F_a and F_b litters, and doing histopathology on F_{3b} weanlings rather than on weanlings of each generation are variations which do not affect the validity of the study. This study was reviewed in connection with teratology study HLR 583-78.