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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

004621

8/20/85

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA No. 35977-U. Fenoxycarb. Review of 21-Day Dermal Toxicity Study in Rats

Tox. Chem. No. 652C

FROM: Edwin R. Budd, Section Head
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769c)

TO: Tim Gardner, PM# 17
Registration Division (TS-767c)

CONCLUSIONS

The subject 21-day dermal toxicity study (reviewed below) is acceptable in fulfillment of the requirement for same.

Toxicology Branch has no objection to the full registration of Logic® 1% Fire Ant Bait for use on non-agricultural turf (including residential sites). All toxicology data requirements have been satisfied. The label precautionary statements are acceptable.

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21-DAY DERMAL TOXICITY STUDY OF FENOXYCARB (Ro 13-5223/000) IN RATS

Hazleton Laboratories Europe, Ltd; Report No. 4552-161/157; July 3, 1985

PROTOCOL: Groups of 5 male and 5 female Crl:CD(SD)BR rats (241-362 g) were dosed with 4 ml/kg/day of freshly prepared Ro 13-5223/000 (96.6% pure) in corn oil at dose levels of 0 (vehicle control), 20, 200, and 2000 mg/kg/day for 21 days. They were dosed on shaved nonabraded skin which represented at least 10% of the body surface area. Each dose was occluded for 6 hours (there was no mention of dose removal). Each rat was examined once daily for clinical signs and scored for skin irritation. Body weights and food consumption were measured at weekly intervals. Blood samples drawn from the orbital sinus of each fasted animal during the final study week were evaluated for the following parameters:

Hematology:

- Erythrocyte count
- Hemoglobin concentration
- Packed cell volume
- Mean cell volume
- Mean cell hemoglobin
- Mean cell hemoglobin concentration
- Leukocyte count
- Differential leukocyte count
- Platelet count

Clinical Chemistry:

- SGOT
- SGPT
- Alkaline phosphatase
- Bilirubin
- Total protein
- BUN
- Glucose
- Creatinine
- Albumin
- Albumin/globulin ratio
- Sodium
- Potassium
- Calcium
- Phosphorus (inorganic)

All rats were sacrificed on day 21 and examined grossly. Organ weights were measured for livers, kidneys, adrenals, ovaries, and testes. Sections of liver, kidney, treated skin, untreated skin, and any gross lesions were examined microscopically for the vehicle control and high-dose rats. Food and water were available ad libitum except prior to bleeding and necropsy. Dose concentration analysis was performed on days 1 and 15.

RESULTS: Dose concentration analysis demonstrated that samples were within 89.5-93.5% of nominal on day 1, and within 93.5-95.5% of nominal on day 15; this is clearly within an acceptable range. There were no compound-related effects on body weights, food consumption, or clinical pathology. Absolute and relative liver weights were moderately elevated (22% and 19%, respectively) in both sexes dosed at 2000 mg/kg/day, compared to the control group. Slight erythema was observed in 3 low-dose males and 1 mid-dose female during the first week of dosing; these lesions were probably not due to the test article. No other clinical signs were reported in any rats. Mild to severe abdominal alopecia in all rats, and occasional concurrent mild to marked sores were observed during gross necropsy and were attributed to the method of occlusion. Mild to severe hydronephrosis of the right kidney was also seen in a few of the dosed animals, but was probably not dose-related. Microscopic evaluations of skin did not reveal any dose-related effects. Two males and 3 females in the high-dose group 4 had slight liver hypertrophy.

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CONCLUSIONS: There were no deaths during this study, so the dermal LD_{50} is >2000 mg/kg/day. The NOEL is 200 mg/kg/day, and the LEL is 2000 mg/kg/day [slight liver hypertrophy]. Skin lesions including slight erythema and alopecia and sores on abdominal skin (dosing site?) were probably caused by the method of occlusion. The only dose-related toxicity was slight liver hypertrophy in the 2000 mg/kg/day dose group which resulted in elevated liver weights.

This study is CORE GUIDELINE. The report failed to describe the dosing sites used, the method of occlusion, and the means of removing the doses. The age of the rats was not supplied. During gross necropsy, all rats were reported as having mild to severe abdominal alopecia, and some had concurrent mild to marked sores. These lesions were certainly severe enough that they should have been recorded as clinical signs, yet they were not - thus making it impossible to determine the time of onset. This study was reviewed for Quality Assurance.

Reviewed by - John E. Whalan, Toxicologist
Section II, Toxicology Branch

Fenoxycarb toxicology review

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Pages 4 through 6 are not included in this copy.

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