UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

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DATE: September 26, 1979

SUBJECT: EPA Reg. No. 524-308, N-Nitrosoglyphosate, Sodium Salt

Caswell #661A + 604AAB

FROM: M. L. Alexander mla 9/27/79 Back 10/2/79 10.4.79
Toxicology Branch/HED (TS-769)

TO: Product Manager, #25, RD (TS-767)

Action Type: Ninety-day subchronic studies in rats and mice.

Summary

1. Organ-to-body weight ratios were significantly increased for kidney in male rats and liver in females at 2000 mg/kg/day. Mean brain weight for females at 200 mg/kg/day was less than controls. Clinical chemistry, hematology, urinalysis, and gross and microscopic pathology were unremarkable. A NOEL for the study was at least 2000 mg/kg/day.

2. Compound-related histopathological findings included increased incidence of inflammatory cell infiltrate in liver, lungs, kidneys, salivary glands, and uteri of high-dose mice. The same group also exhibited increased incidence of peribronchéal lymphocytic accumulation and of uterine endometrial fibroplasia. No gross pathological lesions or other evidence of toxicity were observed. NOEL is 50 mg/kg/day for this study.

Review of Data

(1) Ninety-one day rat intubation study (Pharmacopathics Research Laboratories, Inc.; Laurel, Md.; Lab. Report No. 7778; February 20, 1979; Test material--N-nitrosoglyphosate, sodium salt [CP76100]).

Four groups (25M, 25F each) of Sprague-Dawley rats were intubated with aqueous solutions of test material at 200, 600, or 2000 mg/kg/day for 91 days. One group served as vehicle control. Animals were individually housed and food intake and body weights measured weekly. All animals received gross necropsy examination.

Results: Immediately after intubation 3 control, 3 middle dose, and 2 high dose animals died of probable suffocation. Otherwise, no signs of toxicity were noted. Ten male, ten female rats per group were sacrificed at 45 days.

a) Clinical chemistry-alkaline phosphatase, fasting blood sugar, BUN, SGPT and GGTP were within normal ranges.

b) Hematology-RBC, hemoglobin, hematocrit, WBC, WBC differential count, blood cell morphology, and platelet estimate were normal.

c) Urinalyses-color, appearance, pH, specific gravity, protein, sugar, WBC/hpf, and RBC/hpf were unremarkable.

d) Organ weights and organ-to-body weight ratios--significant increases in kidney-to-body weight ratios in high dose males and in liver-to-body weight ratios in high dose females as compared to controls. Mean brain weight for low dose females was less than controls. No histopathological basis for differences was noted.

e) Pathology-no compound-related gross or microscopic findings.

Conclusion: (NOEL for the study is at least 2000 mg/kg/day).

Classification: Core-minimum data.

(2) Ninety-day mouse intubation study (IRDC; IRD-77-222; January 18, 1979; Test material -CP76100)

Three groups (15 males, 15 females each) of Charles River CD-1 mice were individually housed and dosed daily by intubation with test material solutions at 50, 150, or 500 mg/kg for a 90-day period. Control animals were given sodium ion solution equivalent to the sodium concentration of the high-dose test material. Animals were observed at least twice daily; body weights were recorded weekly.

Results: Five deaths occurred over the test period--1M, 1F at the low dose; 1M at the middle dose; and 2F at high dose. All were attributed to incidental causes.

No compound-related, gross pathological lesions of lungs, trachea, urinary bladder, liver, heart, kidney, spleen, brain, or gonads were noted in any test or control animal.

Histopathological findings included increased incidence of inflammatory cell infiltrate in livers, kidneys, lungs, salivary glands, and uteri of high-dose animals. Increased incidence of peribronchial lymphocytic accumulaton and of uterine endometrial fibroplasia noted in high-dose group.

Conclusion: NOEL is 50 mg/kg/day.

Classification: Core-minimum data

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