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3/6/88

## DATA EVALUATION REPORT

Study Type: 21-Day Dermal (Rabbit)

TOX Chem No.: 893C

EPA ID No.: 476-FFFL

Accession No.: 408937-02

Test Material: Sulfosate

Synonym(s): N-phosphonomethyl glycine trimethyl sulfonium salt:  
SC-0224

Study Number(s): HLA 6142-107

Sponsor: ICI Americas, Inc.  
(T-13038)

Testing Facility: Hazelton Laboratories America, Inc.  
Madison, WI

Title of Report: 21-Day Dermal Toxicity Study With SC-0224  
Concentrate in Rabbits.

Author(s): Susan M. Henwood

Report Issued: March 1, 1988

Classification: Core-Guideline

Conclusions:

This study, which was well conducted, did not reveal any remarkable adverse effects of dosing upon the Guidelines-prescribed parameters, including hematology, clinical chemistry, organ weight data, and gross or microscopic pathology. There were no clinical signs of toxicity. The only noteworthy finding was that of slight dermal irritation noted for both males and females in all dose groups. This phenomenon was slightly worse for males, but Toxicology Branch (TB) does not consider the finding of slight dermal irritation to compromise the conclusion that for this study, NOEL  $\geq$  1000 mg/kg/day for systemic toxicity (HDT).

A. Materials:1. Test Compound: SC-0224 Tech (57.3%)

Description: Yellowish liquid  
Identifying Number: WRC 10387-47-01  
Sample Number: HLA 70902074  
Purity, contaminants: Not provided except as above,  
"On file with sponsor" (page 12)

2. Test Animals

Species: Rabbit  
Strain: Hra:(N2W) SPF  
Age: Young adult  
Weight: 2 1/2 kg  
Source: Hazelton Research Products, Inc.  
Denver, PA

B. Study Design:

(The following is quoted or paraphrased from pages 14 to 17 of the study.)

Rabbits were acclimated for 20 days before being placed on test. Five animals of each sex were allocated to each of four test groups which were to receive doses of test material of 0 (control) 10, 100, or 1000 mg/kg/day. Animals were fed and watered ad libitum during the acclimation and dosing periods.

Dosing solutions were prepared weekly in distilled water (vehicle). Solutions of sulfosate were prepared of such concentration that the intended dosage levels would be achieved via application of 2 mL/kg body weight to the skin of the rabbit. Fur was clipped from the dorsal surface of each animal, yielding a surface test area of approximately 10 percent of the total body surface area. The applied volume (2 mL/kg) of test material was spread over the clipped area of skin once daily and held in place by a bandage for a period of 6 hours, whereupon the wrapping was removed and the test site washed. The dosing procedure was repeated daily, 5 days/week, for 3 weeks. Animals wore flexible plastic collars during the daily 6-hour exposure period.

Animals were examined twice daily for moribundity or mortality, and at least once daily for clinical signs.

Individual body weights were recorded at the initiation of the study, weekly thereafter, and at termination of the study.

Dermal irritation was scored before each application of test or control material and at necropsy.

After at least 3 weeks on test, rabbits were weighed, anesthetized, exsanguinated and necropsied. Hematology and clinical chemistry parameters were assayed on all animals. At the termination of the study, all animals were subjected to a macroscopic (gross) pathologic examination. Brain, kidneys, liver, and testes with epididymides were weighed at necropsy. The following tissues from control and high-dose group animals received a microscopic pathologic examination: treated and untreated skin, liver, kidneys, and target organ lesions.

Statistical treatment of the data was pursued as described on pages 17 and 18 of the study report.

#### Results:

The study author indicates that in general, animals appeared healthy throughout the study and there were no dosing related effects on body weight, food consumption, hematology, clinical chemistry, organ weight data or evidence of pathologic (macro- or microscopic) effects. Mild dermal irritation was noted in those animals treated with the test material (page 11). TB has examined the findings and concurs with this overall assessment of the data.

Hence, excepting the dermal irritation findings, considered as local effects of dosing, the NOEL = 1000 mg/kg/day for dermal exposure.

From an inspection of dermal parameters as reported in Tables 6 (males) and 7 (females) (pages 32 to 39), it is apparent that only erythema was observed. This phenomenon occurred only in dosed groups, males and females, and to a slightly greater extent in males. However, the magnitude of the effect, at worst, would be considered as slight and thus not a finding of particular concern in this study.

The following additional observations are made with respect to those various assessments rendered in the study in conformity with Guidelines requirements:

1. Hematology - No remarkable effects were noted at any dose on the various hematology parameters (Tables 8 and 9, pages 40 to 43).
2. Clinical Chemistry - Of the various parameters examined, there were no remarkable effects of dosing with the exception of an increase in calcium levels

in males of the low-dose group (for control, low-, mid-, and high-dose groups, the respective calcium levels [mg/dl] were: 15.6, 17.9, 17.1, and 16.7). The low-dose value, 17.9 mg/dl, was statistically significantly elevated over that of the controls. In the absence of a dose response, TB does not consider this 15 percent increase at the low dose to be of particular concern (Tables 10 and 11, pages 44 to 47).

3. Organ Weight Data - Organ weight data, whether expressed in absolute terms of organ-to-body weight or organ-to-brain weight, were unremarkable for both sexes, at all doses (Tables 12-14, pp. 48-53).
4. Pathology - Macroscopic/Microscopic Data - Neither macroscopic examination of all animals of all dosed groups (Table 15, page 54) nor microscopic examination of selected tissues (kidney, liver, and skin) from animals in the control and high-dose groups (Table 16, page 55) yielded any remarkable findings.