Glyphosate / Tox

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

Releasable (743)

Supplier information has been deleted from pages 2 and 3

JAN 11 1982

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

661A

DATE: December 29, 1981

SUBJECT: ROUNDUP Glyphosate Formulation. Letter from Connecticut Department of Environmental Protection re Possible Testicular Effects 5F1536

FROM: Roland A. Gessert, D.V.M.
Toxicology Branch/HED (TS-769)

Roland A. Gessert 12/29/81

TO: Robert Taylor (25)
Registration Division (TS-769)

THRU: Orville E. Paynter, Chief
Toxicology Branch/HED (TS-769)

The State of Connecticut, Department of Environmental Protection, had contacted Mr. Robert Taylor, PM 25, Registration Division, concerning data of apparent effects of surfactants used in a ROUNDUP glyphosate formulation. According to the Connecticut correspondence, the damage was observed down to the 5x use level. Purportedly testicular atrophy appeared in rabbits treated for 21 days dermally with the ROUNDUP formulation. The initial study showing testicular atrophy was the 21-day subacute dermal study conducted by Industrial Bio-Test, IBT No. A1549, dated July 18, 1972. A later test, including the surfactant alone, was conducted by Industrial Bio-Test, IBT No. A2144, dated January 11, 1973.

It should be pointed out that the above-mentioned studies and other studies with glyphosate and ROUNDUP were conducted by Industrial Bio-Test (IBT), and therefore are subject to validation by EPA; this validation process is currently being conducted. Of these studies, IBT No. 1549 (the initial study showing testicular atrophy) was found to be invalid by Canada.

In a third test (IBT No. A2468, dated January 11, 1973 and found to be invalid) the formulation was applied at 2x and 3x the use level and no significant differences in mean testes weights occurred between test and control animals.

In the invalid IBT study A1549, decreased weight gains or weight loss were observed on a dose-related basis with both intact and abraded skin. There was also significant dermal irritation, associated with vocalization, and significant increases in total leucocyte counts and in the percent of neutrophils, and decreases in the percent of lymphocytes.

Atrophic changes in the testes were observed in one rabbit, at 37.0 mg/kg (abraded skin).

In regard to testes weights, testes/body weight ratio, and testes/brain weight ratio, there were no statistically significant differences detected at the 95% confidence level between the untreated controls and any of the treatment groups.

IBT No. A2144 is yet to be evaluated by Canada, and has been replaced by Bio/dynamics study 75-1245, which showed no testicular histomorphological changes. But the mean testes/brain weight ratio was increased statistically in the high dose (113.7 mg/kg) intact-skin group (p less than 0.05), and the mean testes/body weight ratio was increased statistically (p less than 0.05) in the high dose abraded skin group. While statistically significant these differences are not considered to be of toxicological significance since histopathologically, the testes from all rabbits following 3 weeks of treatment and 4 weeks after termination of treatment were determined to be within the limits of normal histology. (William R. Rapp, D.V.M.; Pathologist.) Histopathologic examination of the skin of these rabbits following treatment revealed dermal inflammation in all treated groups of rabbits, the inflammation characterized by an infiltration of mononuclear and polymorphonuclear leucocytes in the subepithelial dermis. This response was without notable change of the epidermis.

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A 14-week oral study in beagle dogs conducted by [redacted] No. MRD165, January 3, 1973) using the surfactant at 10, 20, and 30 mg/kg showed no effect on the testes.

In a 13-week feeding study in rats by Litton Bionetics for [redacted] (LBI Project 2290; December, 1972), the surfactant in ROUNDUP formulation was fed at dietary concentrations of 0, 1250, 2500, and 5000 ppm, corresponding to 0, 1.6, 3.8, and 6.5 mg/kg/day. No toxic signs were observed except for slow acclimation to the highest dosage in the first 3 weeks. Microscopic examination of organs collected at necropsy revealed only histiocytic infiltrations of the lamina propria of the small intestine and sinusoids of mesenteric lymph nodes at all doasge levels.

Since the studies which purportedly show testicular atrophy were conducted by IBT, and since these studies appear to be invalid (as per Canadian review), we have no valid data on which to base Connecticut's concern of testicular atrophy. IBT studies A2468 A&B also have been judged invalid.

Director Stephen Hitchcock of the Connecticut Department of Environmental Protection questions the suggestion that stress might cause testicular atrophy. It is unclear to what extent stress per se might cause testicular atrophy. But the rabbits showed significant reduction in weight gains or significant weight loss, and it is well known that impaired nutrition and weight loss in species much less sensitive than the rabbit may have a pronounced effect on reproduction.

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In conclusion, it is good that findings such as these are noted and re-evaluated. But since the data which purportedly demonstrated testicular atrophy were conducted by IBT and appear to be invalid, and since subsequent studies (some of which were conducted by Bio/dynamics [redacted] Litton Bionetics and are considered to be valid) do not demonstrate testicular atrophy, it is evident that the Agency's initial actions were proper in handling this registration and that no significant reproduction risk is present from dermal exposure in the manufacture or use of ROUNDUP formulation when used in accordance with labeling.

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