

US EPA ARCHIVE DOCUMENT

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

000713

DATE: February 15, 1978

TO: Ontrack WE-1

EPA Registration #100-520

Caswell#96

FROM: Krystyna K. Locke
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TO: R. J. Taylor
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3/24/78

Action Type: Submission of 5 acute toxicity studies.

Summary

Ciba-Geigy Corporation submitted acute toxicity studies in order to update files and approval of signal word and precautionary statements on the herbicide formulation Ontrack WE-1. The EPA - registered label that is currently being used for this product carries the signal word WARNING. Acute toxicity studies submitted now support the signal word DANGER and associated precautionary statements. This formulation consists of 22.8% prometon (a symmetrical triazine compound), 8.6% pentachlorophenol, 1% other phenols and 67.6% inert ingredients. It should be noted that pentachlorophenol and other phenols are on the RPAR list (OSPR Chemical Status Report, 11/1/77). It should also be noted that prometon appears on the list of "Chemicals Potentially Containing Nitrosamines" (Memos from Dr. Rogoff and Mr. Camot, 10/20/76).

Ontrack WE-1 is clear brown liquid and was used as such in the studies summarized below. Specifically, the test product was identified as Ontrack WE-1 (FL-761495).

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Acute Oral	16 rats	600, 900, 1350, 2025 mg/kg	-	14	900 ± 106* mg/kg	III
Acute Dermal	24 rabbits	267, 400, 600, 900, 1350, 2000 mg/kg	24 hours.	14	900 ± 130* mg/kg	II
Eye Irritation	3 rabbits 3 rabbits	0.1 ml 0.1 ml	30 sec.	14	-	I
Skin Irritation	6 rabbits	0.5 ml	24 hours	3	-	I
Inhalation	10 rats	20.89 mg/liter	4 hours	14	> 20.89 mg/liter	IV

*Standard Deviation
 **All of these studies were conducted by the Industrial Bio-Test Laboratories, Inc. and, therefore, will require validation.

7.

The report on the inhalation study (IBT No. 8562 - 09301) from the Industrial Bio-Test Laboratories to Ciba-Geigy Corporation is dated 8/16/76. The report on the remaining four studies (IBT No. 8530 - 09312) is dated 10/14/76. All of these studies but one, the oral toxicity study, meet the core-minimum data requirements. The oral toxicity study can be accepted only as a supplementary study for the reasons listed below.

- 1) Too few rats (2 males and 2 females) per dose level were used and, therefore, the core-minimum data requirements are not met.
- 2) There are certain ambiguities in the Industrial Bio-Test's reporting of this study (see p. 4 of this evaluation).

Ontrack WE-1 is extremely irritating to skin and eyes (Toxicity Category I), and the label proposed by Ciba-Geigy (p.4 of this submission) contains the appropriate word DANGER and other pertinent precautionary statements. Detailed comments with regard to first aid and utmost importance of correct diagnosis (since poisoning by pentachlorophenol may be mistaken for poisoning by an organic phosphate compound) are also included. Both the signal word and the precautionary statements are acceptable as proposed by Ciba-Geigy.

Studies

1. Acute Oral Toxicity (16 rats).

Procedure

Four groups of Sprague-Dawley rats (weighing 162-252 g), 2 males and 2 females per group, received single doses of Ontrack WE-1 at the following levels (mg/kg of body weight): 600, 900, 1350 and 2025. The observation period was 14 days. All of the animals were necropsied shortly after death or at the end of the observation period. The LD₅₀ value was calculated by the methods of Weil, Thompson, and Thompson and Weil.

Results:

There was no mortality at the 600 mg dose level, 2 rats (50%) died at the 900 mg level and all of the animals died at the higher dosage levels used. All of the deaths, but one, occurred within 6-22 hours after dosing. The following symptoms were observed: hypoactivity, muscular weakness, salivation, labored breathing and diuresis (in female rats only).

Necropsy on the non-surviving animals revealed red lungs, pale kidneys and necrosis of the stomach lining (in some animals). The results of the necropsy on the surviving rats are not clear (see Comments below). The LD₅₀ value (mg/kg of body weight) was 900 ± 106 (standard deviation). 3

Comments

There are certain irregularities, or unclarities, in the Industrial Bio-Test's reporting of experimental data. These ambiguities are specified below.

- 1). It is stated on p. 2 of this submission that "Necropsy of the survivors at 14 days revealed no gross lesions except necrosis of the stomach lining in a female dosed at 400 mg/kg." Yet, one sees in TABLE I, page 9, that the lowest dose level reported is 600 mg/kg of body weight.
- 2). It is stated on p. 8 of this submission that "Examination of the survivors revealed necrotic tissue in the stomach linings in animals No. 6-M, 7-F, 8-F and 11-F." Yet, one sees in TABLE I, page 9, that the animals No. 6-M, 8-F and 11-F were not survivors. They died within 6-22 hours after dosing.

Considering these unclarities and the fact that only 2 rats/sex/dose level were used, this study is acceptable as a supplementary study. Ontrack WE-1 falls into the Toxicity Category III, based on the reported LD₅₀ value.

2. Acute Dermal Toxicity (24 rabbits).

Procedure

Ontrack WE-1 was applied to the hairless backs of rabbits, using 2 males and 2 females per dose level. Six levels were used (mg/kg of body weight): 266.7, 400, 600, 900, 1350 and 2000. The rabbits (New Zealand strain) weighed 2.36-2.86 kg. The skin of one male and one female rabbit was abraded. After 24-hour exposure, the skin was left unwashed and the animals were observed for 14 days.

Results

None of the rabbits died at the two lowest dose levels, all of them died at the two highest levels, and one male rabbit died at each of the 600 mg and the 900 mg levels. All of the deaths occurred within 6-22 hours after dosing. In the case of the 2000 mg dose level, 3 rabbits (out of a total of 4) died 4 hours after dosing. The following toxic reactions were observed: hypoactivity, muscular weakness, salivation, labored breathing, weight loss, erythema, edema (moderate to severe), 2-nd and 3-rd degree chemical burns, and escharosis and necrosis at the site of application.

Necropsy on the non-surviving animals revealed pale, discolored livers and hemorrhagic lungs. Necropsy on the survivors revealed enlarged gall bladder and emaciation in 2 animals, gastroenteritis (1 animal) pale kidney (1 animal) and depletion of body fat.

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The LD₅₀ value was 900 ± 130 mg/kg of body weight.

Comments

Based on the LD₅₀ value, Ontrack WE-1 falls into the Toxicity Category II. This study meets the requirements of the core-minimum data category.

3. Eye Irritation (6 rabbits).

Procedure

Ontrack WE-1, 0.1 ml, was placed into the conjunctival sac of the right eye of 6 rabbits (New Zealand strain). The eyes of 3 rabbits were then left unwashed, whereas the eyes of 3 other rabbits were washed with water after 30 seconds of exposure. The eyes (cornea, iris, conjunctiva) of all animals were examined at 1 hour, and then at 1, 2, 3, 7 and 14 days, following exposure. The appearance of eyes was evaluated by the Draize procedure.

Results

Ontrack WE-1 was extremely irritating to the rabbit eyes, whether or not the eyes were washed after treatment with this formulation. The following symptoms were observed: corneal vascularization and opacity, and conjunctival redness, swelling and discharge. At 24 hours after exposure, the average irritation score was 37.7/110 for both washed and unwashed eyes. At 7 days after exposure, the average irritation score was 45.5/110 and 29.6/110 for washed and unwashed eyes, respectively. The irritation still persisted in both groups, 14 days after treatment.

Comments

Ontrack WE-1 falls into the Toxicity Category I. This study conforms to the core-minimum data requirements.

4. Primary Skin Irritation (6 rabbits).

Procedure

Ontrack WE-1, 0.5 ml was applied to the hairless backs of rabbits (New Zealand strain). One of the two test sites on each rabbit was abraded. The unwashed skin, both intact and abraded, was then examined for erythema and edema at 24 hours and 72 hours after exposure.

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Results

Ontrack WE-1 was extremely irritating to both intact and abraded skin. At 72 hours after exposure, 2-nd degree and 3-rd degree chemical burns were seen in all animals.

Comments

Ontrack WE-1 falls into the Toxicity Category I. This study can be accepted as the core-minimum data.

5. Acute Inhalation Study (10 rats).

Procedure

Five male and 5 female rats (Charles River strain) were continuously exposed to an aerosol of Ontrack WE-1 (20890 mg/m³ of air), in an 80-liter chamber. Following the 4-hour exposure, the animals were observed for 14 days and then they were necropsied.

Results

All of the animals experienced hypoactivity, ptosis, enophthalmus and dyspnea, and had ruffed fur. These symptoms appeared within 4-10 min. after exposure and disappeared with 30-60 min. after the exposure was discontinued. One female rat died during exposure. The body weight gain during the 14-day observation period was 100 g for male rats and 39 g for female rats. Necropsy on all animals revealed no gross pathological alteration.

The LC₅₀ value is greater than 20.89 mg/liter of air, based on the nominally - determined concentration of Ontrack WE-1 in the exposure chamber.

Comments

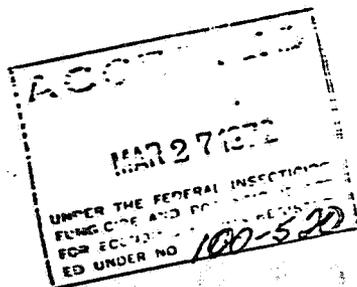
Ontrack WE-1 falls into the Toxicity Category IV. This study meets the core-minimum data requirements.

lp

Ontrack™ WE-1¹⁰⁰⁰⁷¹³

Herbicide

For weed control on rail-road rights-of-way and industrial sites



Active Ingredients:	32.4%
2,4-bis (isopropyl-amino)-6-methoxy-s-triazine	22.8%
Pentachloro-phenol	8.6%
Other Chloro-phenols and related compounds	1.0%
Inert Ingredients:	67.6%
Total:	100.0%

EPA Reg. No. 100-520

Warning:

Keep out of reach of children.

Harmful if swallowed. Avoid contact with eyes and skin. Harmful if absorbed through skin. In case of skin contact, wash with soap and water. Avoid inhalation of spray mist. Avoid contamination of food and feed. Do not get on clothing. Wash thoroughly after handling.

Do not use or store near heat or open flame.

Store at temperatures above 32°F.

Precautionary Statement:

Do not contaminate water used for irrigation or domestic purposes. Do not store near fertilizers, seeds, insecticides or fungicides. Thoroughly clean equipment with a suitable cleaner before using for other purposes.

Fish and Wildlife Caution:

This product is toxic to fish and wildlife. Birds and other wildlife in treated areas may be killed. Keep out of lakes, streams or ponds. Do not contaminate water by cleaning of equipment or disposal of wastes.

DIRECTIONS FOR USE AND CONDITIONS OF SALE AND WARRANTY

IMPORTANT: Read the entire Directions For Use and the Conditions Of Sale And Warranty before using this product.

Conditions Of Sale And Warranty

The Directions For Use of this product reflect the opinion of experts based on field use and tests. The directions are believed to be reliable and should be followed carefully. However, it is impossible to eliminate all risks inherently associated with use of this product. Crop injury, ineffectiveness or other unintended consequences may result because of such factors as weather conditions, presence of other materials, or the manner of use or application all of which are beyond the control of Geigy or the Seller. All such risks shall be assumed by the Buyer.

Geigy warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes referred to in the Directions For Use, subject to the inherent risks referred to above. Geigy makes no other express or implied warranty of Fitness or Merchantability or any other express or implied warranty. In no case shall Geigy or the Seller be liable for consequential, special or indirect damages resulting from the use or handling of this product. Geigy and the Seller offer this product, and the Buyer and user accept it, subject to the foregoing Conditions Of Sale And Warranty which may be varied only by agreement in writing signed by a duly authorized representative of Geigy.

Directions For Use

Apply 5-30 gallons of Ontrack WE-1 in a minimum of 50 gallons of water per acre as a pre-emergence or post-emergence treatment. Use the lower rate to control annual and susceptible perennial weeds (such as downy brome grass, oat grass, goosegrass, quackgrass, puncturevine, wild radish and plantain). Use the higher rate to control hard-to-kill perennial weeds and grasses (such as Johnson grass, bindweed and wild carrot).

Do not apply to areas underlain by roots of desirable trees and shrubs. Avoid spray drift to desirable plants.

Ontrack™ trademark of CIBA-GEIGY U.S. Patent No. 2,909,420

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Geigy