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

006209

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

APR 22 1986

MEMORANDUM

SUBJECT: EPA Registration Number 11603-3
Diuron Technical

FROM: Mary L. Waller
Technical Support Section
Fungicide-Herbicide Branch
Registration Division (TS-767C)

TO: Robert Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (TS-767C)

Applicant: Makhteshim-Agan (America) Inc.
c/o Solchem Division of Koa
2 Park Avenue
New York, NY 10016

ACTIVE INGREDIENT:
Diuron: 3-(3,4-dichlorophenyl)-1,1-dimethylurea . . 98%
INERT INGREDIENTS: 2%

BACKGROUND:

The registrant has submitted two acute oral toxicity studies and one acute dermal, primary eye, dermal sensitization, and primary skin irritation studies. The studies were conducted by Cosmopolitan Safety Evaluation Laboratories, Inc. The data Accession Number is 258114. The method of support was not indicated.

RECOMMENDATION:

FHB/TSS finds all the studies acceptable to support registration. The registrant did not submit an acute inhalation toxicity study and must satisfy this data requirement. The signal word is CAUTION; however, the signal word is subject to change based on acute inhalation data.

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LABELING:

1. Delete second and third paragraphs under the Precautionary Statements. Place second paragraph under Statements of Practical Treatment.

2. Add the following sentence to the first paragraph after the first sentence of the Precautionary Statements: Causes eye injury.

3. Add the following sentence to the Statement of Practical Treatment for skin exposure: Get medical treatment.

4. Add the following sentence to the Statement of Practical Treatment for eye exposure: Call a physician if irritation persists.

5. Add the following sentence to the Precautionary Statements: Wash thoroughly with soap and water after handling.

6. Additional labeling may be necessary upon submission of acute inhalation data.

REVIEW:

(1) Acute Oral Toxicity Study: Cosmopolitan Safety Evaluation Laboratories, Inc.; Study No. 1222A; April 18, 1985.

PROCEDURE:

Four groups of five male and five female Sprague-Dawley rats each received by gastric lavage one of the following doses of test material suspended in corn oil: 3155, 3972, 5000 or 6295 mg/kg. Animals were examined twice daily (once on weekends and holidays) for mortality and toxic symptoms. All animals were weighed on day of dosing and at 7 and 14 days. All animals were submitted for gross necropsy.

RESULTS:

At 3155 mg/kg, 1/5 males died. At 3972 mg/kg, 2/5 males died. At 5000 mg/kg, 3/5 males and 1/5 females died. At 6295 mg/kg, 3/5 males and 1/5 females died. The LD_{50} for females was reported to be > 5000 mg/kg. The LD_{50} for males was reported to be 4721 (2995-7441) mg/kg.

Toxic symptoms observed were ataxia, chromodacryorrhea, chromorhinorrhea, diarrhea, decreased locomotor activity, prostration, and perineal and abdominal staining. Gross necrospy of rats that died during study revealed gastric and/or intestinal congestion, mottling liver and pale kidneys.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category III - CAUTION.

(2) Acute Oral Toxicity Study: Cosmopolitan Safety Evaluation Laboratories, Inc.; Study No. 1279A; May 16, 1985.

PROCEDURE:

Four groups of five male and five female Sprague-Dawley rats each received by gastric lavage one of the following doses of test material suspended in corn oil: 2506, 5000, 6295 anmd 9977 mg/kg. Animals were examined twice daily (once on weekends and holidays) for mortality and toxic symptoms. All animals were weighed on day of dosing and at 7 and 14 days. All animals were submitted for gross necrospy.

RESULTS:

At 2506 mg/kg, no mortalities occurred. At 5000 mg/kg, 2/5 males died. At 6295 and 9977 mg/kg, 3/5 males and 2/5 females died. The LD_{50} for males was reported to be 5000 (1.8 - 13.8) mg/kg and the LD_{50} for females was reported to be > 10,000 mg/kg.

Toxic symptoms included decreased activity, ataxia, chromorhinorrhea, perineal/abdominal staining, and prostration. Gross necropsy of rats that died during the study revealed intestinal congestion and mottling of liver.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category III - CAUTION.

(3) Acute Dermal Toxicity Study: Cosmopolitan Safety Evaluation Laboratories, Inc.; Study No. 1222B; April 4, 1985.

PROCEDURE:

Five male and five female albino rabbits each received 2000 mg/kg of moistened test material applied to a previously shaven test site. The test site was kept under occlusive wrap for 24 hours. After removal of wrap, animals were observed for 14 days to note toxic symptoms and mortality. All animals were submitted to gross necropsy.

RESULTS:

No deaths occurred. The LD_{50} in males and females was reported to be > 2000 mg/kg. Animals exhibited no toxic symptoms and gross necropsy revealed no abnormalities. Animals exhibited very slight to well-defined erythema which cleared by day 7 and very slight to slight edema which cleared by day 3.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category III - CAUTION.

(4) Primary Eye Irritation Study: Cosmopolitan Safety Evaluation Laboratories, Inc.; Study No. 1222D; April 4, 1985.

PROCEDURE:

Six adult albino rabbits were examined prior to the study to detect fluorescein retention. All animals were found free of ocular injury and 24 hours later each animal received 0.1 g of test material instilled inside the lower eyelid. The eyelids were held shut for one second and the eyes were not washed after test material instillation. The other eye served as a control. Eye irritation was scored at 1, 24, 48 and 72 hours.

RESULTS:

Eye irritation was scored as follows: At 1 hour, conjunctivae redness (6/6 = 1) and chemosis (2/6 = 1); at 24 hours, conjunctivae redness (3/6 = 1) and no retention of fluorescein dye; at 48 hours, all irritation had cleared.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category III - CAUTION.

(5) Primary Dermal Irritation Study: Cosmopolitan Safety Evaluation Laboratories, Inc.; Study No. 1222E; April 4, 1985.

PROCEDURE:

Six albino rabbits were clipped on the dorsal surface and 24 hours later, each animal received 0.5 g of test material which was mixed with corn oil to form a paste. The paste was applied to the shaven test site on each animal and kept under occlusive wrap for 4 hours. After removal of wrap, all test sites were wiped clean. Observations and scoring of skin irritation were conducted at approximately 1, 4, 24, 48 and 72 hours.

RESULTS:

At 1 hour, 6/6 animals exhibited very slight erythema. At 24 hours, 3/6 animals exhibited very slight erythema and at 48 hours, 1/6 animals exhibited very slight erythema. All irritation had cleared by 72 hours.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category IV - CAUTION.

(6) Dermal Sensitization Study: Cosmopolitan Safety Evaluation Laboratories, Inc.; Study No. 1222F; April 4, 1985.

PROCEDURE:

Ten male albino guinea pigs were shaved on the right side. Twenty-four hours later, each animal received the first of three induction treatments which consisted of 500 mg of test material mixed with paraffin oil to form a paste which was applied to the shaven test site under occlusive wrap for 6 hours. Two more identical induction treatments were administered once a week for 2 weeks. Two weeks after the last induction treatment, the animals were challenged with the test material at the previously treated site and a new site. Skin irritation was scored at 24 and 48 hours after each induction treatment and challenge treatment.

RESULTS:

At 24 hours after the first induction treatment, 3/10 animals exhibited very slight erythema. All irritation had cleared by 48 hours. No irritation occurred after the second and third induction treatment. After challenge treatment,

3/10 animals exhibited very slight erythema at the induction site and 1/10 animals showed very slight erythema at the new site. No edema was observed.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Nonsensitizer.

DIURON SCIENTIFIC REVIEWS

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