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

006064

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: July 9, 1985

SUBJECT: EPA File Symbol 38167-G
Setre Simazine-Bromacil 90 WP

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

TO: Richard Mountfort
Product Manager (23)

Applicant: Setre Chemical Company
5100 Poplar, Suite 3200
Memphis, TN 38137

Active Ingredients:
2-chloro-4,6-bis(ethylamino)-S-triazine 50%
5-bromo-3-sec-butyl-6-methyluracil 40%
Inert Ingredients 10%

Background:

The applicant has submitted an acute oral, acute inhalation, acute dermal, eye irritation, skin irritation, and dermal sensitization studies. The studies were conducted by Stillmeadow, Inc. The data accession numbers are 254882 and 256449. The method of support was not indicated.

Recommendation:

FHB/TSS finds the data submitted acceptable to support registration of EPA File Symbol 38167-G.

The appropriate signal word is "CAUTION."

Labeling:

1. Change the signal word on the front and side panel to "CAUTION."

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2. The first sentence in the precautionary statement should be modified to read as follows: "Harmful if swallowed, inhaled or absorbed through the skin."

3. The Statements of Practical Treatment for oral, inhalation and dermal exposure should be changed to read as follows:

> If Swallowed - Call a physician or Poison Control Center. Drink one or two glasses of water and induce vomiting by touching back of throat with finger. Do not induce vomiting or give anything by mouth to an unconscious person.
>
> If Inhaled - Remove victim to fresh air. If not breathing, give artificial respiration, preferably mouth-to-mouth. Get medical attention.
>
> If On Skin - Wash with plenty of soap and water. Get medical attention.

Review:

1. Acute Oral Toxicity Study: Stillmeadow, Inc., Project Number 3356-84, August 29, 1984.

Procedure:

Three groups each consisting of five fasted male rats received by gavage one of the following doses of test material: 3350 mg/kg, 4100 mg/kg and 5050 mg/kg. Six groups each consisting of five fasted female rats received by gavage one of the following doses of test material: 1800 mg/kg, 2210 mg/kg, 2730 mg/kg, 3350 mg/kg, 4100 mg/kg and 5050 mg/kg. Observations were made at least three times on the day of treatment and at least once daily thereafter for 14 days. Body weights were recorded prior to treatment and at 7 and 14 day intervals. Gross necropsy was performed on each animal at study termination or upon discovery of death.

Results:

At 5050 mg/kg, 4/5 males and 5/5 females died. At 4100 mg/kg, 3/5 males and 4/5 females died. At 3350 mg/kg 1/5 males and 4/5 females died. At 2730 mg/kg, 4/5 females died and at 2210 mg/kg, 3/5 females died. No deaths occurred at 1800 mg/kg. Toxic symptoms observed included decreased activity, bradypnea, chromodacryorrhea, constricted pupils, diarrhea, dilated pupils,

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emaciation, epistaxis, exophthalmos, gasping, hematuria, lacrimation, melanuria, muscle tremors, nasal discharge, nonuse of hindlimbs, piloerection, polyuria, ptosis, respiratory gurgles, salivation, sensitivity to touch, and swollen hindlimbs.

The LD_{50} for males was reported to be 4010 mg/kg with a 95 percent confidence limit of 3368 to 4773 mg/kg and the LD_{50} for females was reported to be 2421 mg/kg with a 95 percent confidence limit of 1936 to 3027 mg/kg.

Gross necropsy revealed the following toxic effects: green liquid in the bladder, orange mucoid material in the stomach, yellow-white slurry in the stomach, pronounced serosal blood vessels on the entire gastrointestinal tract.

Study Classification:

Core Guideline Data

Toxicity Category:

Category III - Caution

2. Acute Inhalation Toxicity Study: Stillmeadow, Inc., Project Number 3360-40, August 24, 1984.

Procedure:

Five male and five female Sprague-Dawley rats were exposed to an aerosol of test material with a gravimetric concentration equal to or greater than 4.98 mg/l for a 4-hour period. During exposure, animals were individually housed in stainless steel cages within a 200 liter stainless steel dynamic flow inhalation chamber. Due to chamber design only 2 males and 2 females could be observed during exposure. Observations after exposure were made on a daily basis for 14 days. Individual body weights were recorded prior to exposure and on days 7 and 14. Airflow, temperature and humidity were recorded at 30 minute intervals. The gravimetric concentration at the animals' breathing zone was determined once per hour.

Results:

No deaths occurred during the test. Observations noted during the experiment, which extended up to day 3 for one animal and day 11 for another animal, included piloerection, ptosis, nasal discharge, polyuria, dilated pupils, salivation and

lacrimation. Gross necropsy revealed light and dark red mottled liver in 2/10 animals. The LD_{50} was reported to be > 5.67 mg/l.

The mass median aerodynamic diameter of the aerosol particles was 4.785 micrometers at the 1 hour and was 3.444 micrometers at the 3 hour reading. The mean gravimetric concentration was 5.67 mg/l.

Study Classification:

Core Guideline Data

Toxicity Category:

Category III - Caution

3. Acute Dermal Toxicity Study: Stillmeadow, Inc., Project Number 3357-84, July 25, 1984.

Procedure:

Five male and five female albino rabbits with clipped dorsal trunk areas were treated with 2000 mg/kg of test material mixed with 4 ml of deionized water applied to the test site which was kept under occlusive wrap for 24 hours. After the wrap was removed, the test site was washed to remove any remaining test material. Observations were made at 1/2, 3 and 6 hours after treatment and at least once a day for 14 days. Individual body weights were recorded prior to exposure and at 7 and 14 day intervals or at the time of discovery of death. Gross necropsy was conducted on all animals.

Results:

One animal died during the study. The LD_{50} was reported to be > 2000 mg/kg. Observations included decreased defecation and diarrhea in 3/10 animals. Gross necropsy revealed signs of salivation, the entire gastrointestinal tract distended with gas, and a light brown liquid in the intestinal tract of the one mortality.

Study Classification:

Core Guideline Data

Toxicity Category: Category III - Caution

4. Eye Irritation Study: Stillmeadow, Inc., Project No. 3358-84; July 5, 1984.

Procedure:

Nine albino rabbits each received 100 mg of test material in the conjunctival sac of the right eye. Thirty seconds after treatment, the treated eyes of 3/9 animals were washed with deionized water for one minute. The untreated left eye served as the control.

Observations were made at 1, 24, 48, and 72 hours and at 4 and 7 days after treatment. The corneas of all treated eyes were reexamined immediately after the 24-hour observation with a 0.2% flourescein sodium ophthalmic solution. Corneas which exhibited positive fluorescein staining at the 24-hour observation were re-examined with the fluorescein sodium ophthalmic solution at each succesive reading until fluorescein staining of the cornea no longer occurred.

Results:

Animals with unwashed treated eyes exhibited the following effects: at one hour, redness (4/6 = 3, 2/6 = 2), chemosis (6/6 = 3), and discharge (4/6 = 3, 2/6 = 2); at 24 hours, fluorescein staining (2/6 positive, area of 1/6 was < 1/4 and 1/6 was > 1/4 but < 1/2), redness (3/6 = 3, 3/6 = 2), chemosis (1/6 = 3, 5/6 = 2) and discharge (1/6 = 3, 2/6 = 2, 3/6 = 1); at 48 hours, redness (5/6 = 2, 1/6 = 1); chemosis (3/6 = 2, 3/6 = 1) and discharge (3/6 = 1); at 72 hours, redness (6/6 = 1), chemosis (3/6 = 1) and discharge (1/6 = 1); at 4 days, redness (4/6 = 1) and chemosis (1/6 = 1). All irritation had cleared by the seventh day.

Animals with washed treated eyes exhibited the following effects: at one hour, redness (2/3 = 3, 1/3 = 2), chemosis (1/3 = 4, 2/3 = 3), and discharge (3/3 = 3), at 24 hours, redness (3/3 = 3), chemosis (1/3 = 3, 2/3 = 2), and discharge (2/3 = 2, 1/3 = 1), at 48 hours, redness (2/3 = 3, 1/3 = 2), chemosis (3/3 = 2) and discharge (2/3 = 1); at 72 hours, redness (2/3 = 2, 1/3 = 1); at 4 days, redness (3/3 = 1). All irritation had cleared by the 7th day.

Study Classification:

Core Guideline Data

Toxicity Category:

Category III - Caution

5. Skin Irritation Study: Stillmeadow, Inc., Project No. 3359-84, July 5, 1984.

Procedure:

Six albino rabbits with healthy skin each received 500 mg of test material moistened with 0.25 ml of deionized water to one test site per animal. The intact test sites were secured under occlusive wrap for 4 hours, after which time the occlusive wrap was removed and the test sites were washed with room temperature tap water to remove as much residual test material as possible. Observations were made at 1, 24, 48, and 72 hours after washing.

Results:

At one hour, 3/6 animals exhibited very slight erythema. All irritation was cleared by 24-hours.

Study Classification

Core Guideline Data

Toxicity Category:

Category IV - Caution

6. Dermal Sensitization Study: Stillmeadow, Inc., Project No. 3454-84, January 9, 1985.

Procedure:

Two groups each consisting of 10 albino guinea pigs with the hair clipped in the back trunk area each received on days 1, 3, 6, 8, 10, 13, 15, 17, 20, and 22 one of the following induction phase applications under occlusive wrap and restraints: 0.5 ml of 0.05% w/v solution of 2-4 dinitrochlorobenzane in ethanol administered to the positive control group and 500 mg of test material moistened with 0.4 ml of deionized water administered to the test group. Animals were clipped and/or dipilated as necessary approximately 24 hours prior to treatments. For the challenge treatment administered two weeks later on day 36, animals received one dose identical to the induction treatment except that the challenge dose was administered to a second site. Animals weighed were

at study initiation and termination. Observations for skin reactions were made approximately 24 hours after each treatment and 48 hours after initial and final induction treatments and challenge treatment.

Results:

The positive control group exhibited average skin reaction scores of 0.0 for the initial treatment (day 1) and 2.1 for the virgin challenge site (day 36) and 3.6 for the original test site (day 36). Animals treated with DNCB exhibited a sensitized reaction.

The test group exhibited a 0.0 average skin reaction score for the initial treatment site, the virgin challenge site (day 36) and the original test site (day 36). The test material did not produce a sensitized reaction.

Study Classification

Core Guideline Data

Toxicity Category:

Nonsensitizing

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