PP-470
TXR-2436

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

204

DATE: April 16, 1980

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SUBJECT: EPA Registration Number: 524-89
Randox: Caswell #284

FROM: Deloris F. Graham DFG 5/27/80
FHB/TSS

TO:
Robert Taylor
Product Manager (25)

Applicant: Monsanto Agricultural Products Co.
800 N. Lindbergh Boulevard
St. Louis, MO 63166

Active Ingredient:

N,N-diallyl-2-chloroacetamide.....47.1%

Inert Ingredients.....52.9%

Background

Acute Oral, Acute Dermal, Eye and Skin Irritation Studies were submitted on this product in response to Mr. Johnson's letter of October 17, 1977 which requested validation of Younger Lab data. In lieu of validation, these new studies have been submitted. The data are in Accession Number 241302. A method of support was not indicated.

Recommendation:

1. The Acute Dermal, Eye, Irritation studies are acceptable and adequate to define the hazards by these exposure routes. For future submissions; please note:

   a. In the Acute Dermal Study [redacted] response data per sex/per dose level and individual necropsy reports, LD_{50} and 95% confidence limits must be reported separately for males and females.

   b. In the Eye Irritation Study you must use 9 animals, 6 animals with unwashed eyes and 3 animals with washed eyes.

   c. In the Skin Irritation Study you must use 2 abraded and 2 intact sites per animal.

2. The Acute Oral Study would be Core Minimum Data with a toxicity category of II-WARNING upon clarification of the following: on Table I at 0.5 g/kg, animal #6832 is listed as female and on Table III at 0.5 g/kg animal #6832 is listed as male.

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3. Acute Inhalation Study must be submitted. Please refer to Section 163.81-3 of the "Proposed Guidelines for Human Hazard Evaluation" concerning acceptable testing and reporting procedures.

4. Based on the Eye and Skin Irritation Studies, the appropriate signal word is DANGER.

5. FHB/TSS finds that the Acute Dermal, Eye and Skin Irritation Studies are acceptable in lieu of the previously submitted Younger Lab studies.

Labeling:

1. The appropriate signal word for this product is DANGER.

2. There must be the heading "PRECAUTIONARY STATEMENTS," with the subheading "HAZARDS TO HUMANS AND DOMESTIC ANIMALS, with the following or similar statement:

   DANGER. Corrosive. Causes eye and skin damage. Do not get in eyes, on skin, or on clothing. Wear goggles or face shield and rubber gloves when handling. May be fatal if swallowed, inhaled or absorbed through the skin. Avoid breathing vapors.

3. The following statements, which currently appear on the side paneling of the labeling, must be placed under the "Hazards to Humans and Domestic Animals" section.

   a. "Extreme care must be used when handling...goggles worn during application will minimize this hazard."

   b. "Vapors from Randox....preferably out-of-doors."

   c. "Wear heavy rubber gloves.....should become clogged."

   d. "Promptly change clothing.....clothing before reuse."

4. The "Environmental Hazards" section must follow the "Hazards to Humans" section. Beneath the "Environmental Hazards" subheading, there must appear the following (or similar) statements:

   "This product is toxic to fish and wildlife. Keep out of lakes, streams and ponds. Do not contaminate H_2O by cleaning of equipment or disposal of wastes."

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5. The heading "Physical or Chemical Hazards" must follow the Environmental Hazards section with the following (or similar) statements:

   "Combustible. Do not use or store near heat or open flame. In case of fire, use water spray, foam, dry chemical or CO_2. In case of spill or leak, flush area with water spray."

6. The following statements should appear under the heading "Directions For Use."

   "Do not allow the container to remain open when not in use. Before spraying, check all hose connections to see that they are firmly secured." and

   "Before making application, the spray equipment must be properly calibrated to avoid both over or under treatment."

7. The statment "It is a violation of Federal law to use this product in a manner inconsistent with its labeling." must appear beneath the "Directions for Use" heading.

8. An appropriate "Storage and Disposal" statement must appear under the "Directions for Use" heading. Enclosed you will find the required Storage and Disposal statements for the type of product and container you use.

9. The referral statement "See side panel for additional precautionary statements." must appear on the front paneling.

10. ~~Limitations~~ Further labeling revision may be necessary upon submission of the Acute Inhalation study.

Review:

1. Acute Oral Toxicity Study: Bio/dynamics, Inc., March 30, 1979; Project no., 4971-77.

Procedure: 5 groups, consisting of 5M and 5F Sprague-Dawley rats (200 to 300g) were dosed at one of the following dose levels: 0.13, 0.18, 0.25, 0.35 and 0.50g/kg by oral intubation. Observations were made at 0-2 hours and 4-6 hours following dosing and daily thereafter for 14 days. Body weights were recorded. A gross necropsy was performed on all which died during the study.

Results: At dose levels 0.13 and 0.18g/kg, no mortalities; at 0.25g/kg, 4/5M and 5/5F animals died; at 0.35 and 0.50 all animals died. Surviving animals gained weight. Symptoms included red and clear nasal discharge, clear oral discharge, respiratory rate increase and decrease, clear ocular discharge, piloerection, motor activity decrease, ataxia, urinary staining, motor activity-decrease, convulsions, fecal staining, soft stool, prostration, squinting eyes, coarse tremors and arched back. LD_{50} = 0.21gm/kg, 95% confidence limits of 0.17-0.25 gm/kg.

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Necropsy of mortalities revealed: lungs-red; liver-discolored, dark to white; stomach - contained gas, fluids; spleen-discolored; fecal staining of abdomen; red nasal discharge.

Study Classificatior. Core Minimum Data

Toxicity Category: II-WARNING

2. Acute Dermal Toxicity Study: Bio/dynamics, Inc., December 21, 1978; Project no. 4972-77.

Procedure: Four groups, each consisting of 2M and 2F New Zealand white rabbits (2.3 to 3.0 kg) were administered one of the following dose levels: 0.25, 0.35, 0.50 and 0.7g/kg at abraded and nonabraded sites under occlusive wrap for 24 hours. Observations were made at 0-2 and 4-6 hours following dosing and daily thereafter for 14 days. A necropsy was performed on animals which died during the ... Body weights were recorded.

Results: At a dose of 0.25g/kg, no mortalities; at 0.35 and 0.50g/Kg, 1/4 died; at 0.71, 3/4 died. At 24 hours, moderate to severe erythema and edema at both abraded and intact sites in all animals at all dose levels. Other symptoms included, lethargy, clear nasal discharge, soft stool, fecal staining of the abdomen, ataxia, tremors, and piloerection. The majority of animals lost weight.

Necropsy revealed abdomen distended; clear nasal discharge; fecal staining of the abdomen; lungs: pale edges, red spots, fluted perimeter, red patches; liver: purple; small intestines: red spots and patches, contained red fluid; large intestines: red patches, contained gas and fluid; peritoneum: filled with red fluid; edema in abdominal and thoracic walls; pericardium: 80% dark red patches; cardiac-pale. LD_{50} was 0.59g/kg with 95% confidence limits of 0.33 to 0.85g/kg.

Study Classification: Core Minimum Data. Must submit response data per sex/per dose level and individual necropsy reports on all animals. LD_{50} and 95% confidence limits must be calculated separately for males and females.

Toxicity Category: II-WARNING

3. Eye Irritation Study: Bio/dynamics, Inc., August 6, 1979; Project no. 4973-77.

Procedure: 6 New Zealand white rabbits received 0.1 ml of test material in one eye. Eyes were examined daily for first 4 days and every 3 days thereafter until day 14.

Results: Corneal opacity in all 6 animals at 1 day (1/6=10, 1/6=15, 2/6=20, 2/6=30); iris irritation in 4/6 (2/6=5, 2/6=10), 1/6, due to severity of the reaction, could not be evaluated; 6/6 conjunctival redness (6/6=3), chemosis (1/6=2, 4/6=3, 1/6=4), and discharge (2/6=3, 4/6=4). Corneal opacity began reversing itself after day 4. Iris irritation and conjunctival irritation persisted through day 7. Corneal opacity present in 3/6 animals (1/6=5, 1/6=20, 1/6=30) through day 7. Other symptoms included alopeci, pannus, ulceration, necrosis and stippling.

Study Classification: Core Minimum Data. Must use 9 rabbits, 6 rabbits with unwashed eyes, and 3 rabbits with washed eyes.

Toxicity Category: I-DANGER

4. Skin Irritation Study: Bio/dynamics, Inc., November 10, 1978; Project no. 4974-77.

Procedure: 6 New Zealand white rabbits (2.4 to 3.0kg) received 0.5 ml of the test material at one abraded and one intact site under occlusive wrap for 24 hours. Observations were made at 24 and 72 hours after application.

Results: 4 animals died before the 24-hour observation. Severe erythema and edema were present at both intact and abraded sites at 24 and 72-hour observations. Dermal irritation index = 7.9 (two animals).

Study Classification: Core Minimum Data. Must use 2 abraded and 2 intact sites per animal.

Toxicity Category: I-DANGER

Toxicology Reviews of Randox

Page 6 is not included in this copy of the registration file for the product.

Pages _____ through _____ are not included in this copy of the registration file for the product.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commerical/financial information

✓ A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

___ FIFRA registration data (*)

___ Supplier information

The information not included generally is considered confidential by product registrants. If you wish to obtain the information deleted, please contact the individual who prepared this response to your request.

(*) FIFRA registration data can be released to individuals who submit an Affirmation of Non-Multinational Status.