OF 410
TXR-002434

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE:

SUBJECT: EPA Registration No. 524-104
Randox granular: Caswell #284

002434

FROM: Deloris Graham 5/28/80
FHB/TSS

TO: Robert Taylor
Product Manager (25)

Applicant: Monsanto Agriculture Products Co.
800 N Lindbergh
St. Louis, Missouri 63166

Active Ingredient: 2-chloro-N,N-diallyacetamide 20%

Inert Ingredient: 80%

Background:

In response to Mr. Jonnson's letter of October 17, 1979 an Acute Oral, Acute Dermal, Eye and Skin Irritation studies were submitted in lieu of validation of the Younger data. These new studies were conducted by Bio/dynamics, Inc. of East Millstone, N.J. The data are under Accession Number 241302.

Recommendation:

1. Acute Dermal, Eye and Skin Irritation Studies are acceptable to support conditional registration of this product. For future submissions; please note,

   a. In the Acute Dermal Study must submit individual necropsy reports for all animals and LD50 and 95% confidence levels for males and females separately.

   b. In the Eye Irritation Study dosage must be 100 mg.

2. The Acute Oral Study would be Core Minimum Data, with a toxicity Category of III-CAUTION upon clarification of the following; on Table I at 2.8g/Kg rat #8584F is listed as dead, but on Table III at 2.8g/Kg rat #8589F is listed. Also for future submissions ~~you must submit~~ individual necropsy reports for all animals and LD50 and 95% confidence levels for males and females separately.

3. The Acute Inhalation Study must be validated or submitted.

4. The Acute Dermal, Eye and Skin Irritation studies are acceptable in lieu of the Younger Labs data.

5. As determined by the Eye Irritation Study the appropriate signal word is DANGER.

EPA FORM 1320-6 (REV. 3-76)

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Label

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

2. Precautionary statement under the heading "Hazards to Humans and Domestic Animals" must be revised similar to the following:

   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 harmful if swallowed. Wash thoroughly contaminated clothing before reuse. Do not contaminate feed or foodstuffs.

3. The heading "Hazards to Humans and Domestic Animals" must precede the following statement:

   "Extreme care must be used when handling Randox Granular to prevent irritation of the skin and eyes. During hot weather, granules or dust may adhere to moist skin causing irritation. If the particles are brushed from the skin, little or no irritation should occur. When pouring the granules from the container into the application hopper, wear goggles to prevent dust from getting into the eyes. Avoid breathing dust."

4. The Statement of Practical Treatment must be revised similar to following:

   In case of contact with eyes, immediately flush eyes with plenty of water for at least 15 minutes. Call a physician. In case of contact with skin wash with soap and water. Call a physician. If swallowed, call a physician.

5. There should be a referral statement "Please See Side Panel For Additional Precautionary Statements" on the front panel.

6. The heading "ATTENTION" which appears on the side panel should be replaced with the heading "Precautionary Statements".

7. The statement "Calibrate application equipment carefully to avoid applying too little or too much material." should appear under the heading "Calibrating Granular Equipment".

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8. The statement "This product is toxic to fish. Keep out of lakes, ponds and streams. Do not apply to any area not specified on the label. Do not contaminate water by cleaning of equipment or disposal of wastes". must appear under the subheading, "ENVIRONMENTAL HAZARDS".

9. The heading "WARNING NOTICE" should be replaced by a more appropriate heading "WARRANTY NOTICE".

10. The statement "It is a violation of Federal law to use this product in a manner inconsistent with its labeling" must appear on the labeling. The proper placement for such a statement is beneath a "Directions For Use" section heading.

11. A "Storage and Disposal" statement must appear on the labeling, placed under the set of Use directions. Please see the enclosed Storage and Disposal sheet for the appropriate statement.

12. Please see enclosed labeling procedure and format.

13. Further labeling revisions may be necessary upon submission of an Acute Inhalation study.

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Review:

1. Acute Oral Toxicity Study: Bio/dynamics, Inc., March 30, 1979; Project No. 4975-77.

Procedure: Five groups, each group consisting of 5M and 5F Sprague-Dawley rats (200 to 315g) were dosed at one of the following dose levels: 1.0, 1.4, 2.0, 2.8, and 4.0g/Kg. The test material (Randox granular) was administered by oral incubation as a 25% w/v solution in distilled water. Observations were made at 0-2 and 4-6 hours after dosing and daily thereafter for 14 days. Body weights were recorded. Necropsy was performed on all which died during the study

Results: At 1.0g/Kg dose level no mortalities; at 1.4, 3/5F died; at 2.0, 4/5M and 5/5F died; at 2.8, 2/5M and 5/5F died; at 4.0, 10/10 died. All surviving animals gained weight. Symptoms observed included red and clear nasal discharge, red and clear oral discharge, urinary staining, soft stool, piloerection, motor activity decrease and increase, ataxia, fine tremors, respiratory rate decrease, labored breathing, prostration, irritable, hypothermia, opacity, coarse tremors, clear ocular discharge, blanching, abdominal griping, fecal staining.

Necropsy of mortalities revealed clear oral discharge; lungs: pale with dark edges; pale with dark red patches; bright red; liver: pale red; dark, mottled, red , dark red and tan; light patches on left lobe; dark red with clear edges; stomach: distended with gas and compound, distended with clear fluid and granular solid; vascularized, walls red, contains yellow fluid; contents tan, mucosa red; spleen: pale, dark edges; small intestine: contents yellow-red; yellow fluid and gas; contents clear yellow, red fluid, red, contains thick yellow fluid; adrenals: red, kidney: pale, dark, dark red; caecum: contains red fluid; red oral discharge; red nasal discharge; clear nasal discharge; fecal staining of the abdomen; urinary staining of the abdomen. The LD50 is 1.9g/Kg with 95% confidence limits of 1.51 to 2.29g/Kg.

Study Classification: Invalid

2. Acute Dermal Toxicity Study: Bio/dynamics, Inc., May 17, 1979; Project No. 4976-77.

Procedure: Four groups, each group consisting of 2M and 2F New Zealand white rabbits (2.3-3.0Kg) were administered one of the following doses (2.0, 2.8, 4.0 and 5.6g/Kg) under occlusive wrap for 24 hours. The skin of half the animals (1M and 1F) was abraded.

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Observations were made 0-2 and 4-6 hours following dosing and daily thereafter for 14 days. Body weights were recorded. Necropsy was performed on all animals which died during the study.

Results: At dose level of 2.0g/Kg, 1M animal died; at 2.8g/Kg, 0/4; at 4.0g/Kg, 1M died; and at 5.6g/Kg, 2M, 1F died. Majority of the animals lost weight. Severe erythema and edema in all animals recorded at 24 hours. Two animals that died spontaneously were not recorded.

Necropsy revealed heart: right ventricle dark brown; right atrium enlarged, heavy vascularization of ventricles; stomach: 25% black, mucosal ulcerations; lining white; kidneys: mottled, 25% hemorrhaged; spleen: pale, small, light colored with tan patches; thymus: red; lungs: mottled, mottled with red patches; liver: mottled, mottled with tan patches. LD50 is 4.75g/Kg with 95% confidence limits of 2.91 to 6.59g/Kg.

Study Classifications: Core Minimum Data. Must submit individual necropsy reports of all animals and LD50 and 95% confidence limits separately for males and females.

Toxicity Category: III-CAUTION

3. Eye Irritation Study: Bio/dynamics, Inc., August 6, 1979; Project No. 4977-77.

Procedure: Six New Zealand white rabbits received 0.1cc of the test material into one eye. Observations were made on days 1, 2, 3, 4, 7, 10 and 14 following instillation.

Results: At day 1, 2/6 animals had corneal opacity (1/6 = 15, 1/6 = 20); 4/6 iris irritation (2/6 = 5, 2/6 = 10); 6/6 conjunctival redness (6/6 = 3); chemosis (1/6 = 1, 2/6 = 2, 2/6 = 3, 1/6 = 4); discharge (1/6 = 1, 4/6 = 2, 1/6 = 3). Other symptoms observed included purulent discharge and necrosis. AT day 7, 3/6 animals had corneal opacity (1/6 = 5, 1/6 = 10, 1/6 = 40); 2/6 iris irritation (1/6 = 5, 1/6 = 10); 6/6 conjunctival redness (4/6 = 1, 1/6 = 1, 1/6 = 3); 5/6 conjunctival chemosis (3/6 = 1, 1/6 = 2, 1/6 = 3); 1/6 conjunctival discharge (1/6 = 2). Other symptoms observed included pannus, alopecia, white area on cornea, necrosis. AT day 14, the corneal opacity in 1/6 animals was of such severity that this parameter could not be evaluated. Corneal opacity, iris and conjunctival irritation had reversed itself in 5/6 animals.

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Study Classifications: Core Minimum Data. Dosage must be 100 mg.

Toxicity Category: I-DANGER

4. Skin Irritation Study: Bio/dynamics, Inc., August 6, 1979; Project No. 4978-77.

Procedure: Six New Zealand white rabbits (2.65 to 3/0Kg) were administered a 0.5 ml dose of the test material at 1 abraded and 1 intact site per rabbit under occlusive wrap for 24 hours. Observations were made at 24 and 72 hours after application.

Results: At 24 hours, 6/6 intact sites and 5/6 abraded sites had severe erythema (6/6 = 4, 5/6 = 4) and 1/6 abraded sites had moderate to severe erythema; all animals had slight to moderate edema at both intact and abraded sites. At 72 hours at all intact and abraded had very slight edema. Primary Irritation Index = 6.1.

Study Classification: Core Guideline Data

Toxicity Category: II-WARNING

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MINIATURE FACSIMILE
Smallest Type size on package 12 point

Monsanto

Granular

RANDOX

For weed control at planting time in corn, sorghum, beans, onions, cabbage, sweet potatoes, tomatoes, sugar cane, celery, potatoes and castor beans. Do not use on other crops.

50 LBS.

KEEP OUT OF REACH OF CHILDREN.

WARNING!
MAY CAUSE SKIN IRRITATION
OR EYE INJURY.

MONSANTO COMPANY • AGRICULTURAL DIVISION • ST. LOUIS, MISSOURI • U.S.A.

Granular

RANDOX

Net 50 lbs.

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