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Date: May 13, 1981

PESTICIDES AND TOXIC SUBSTANCES

Subject: Butylate 7E
EPA File Symbol: 748-EGR

From: Sherell A. Sterling
FHB/TSS

To: Robert Taylor
Product Manager (23)

Applicant: PPG Industries, Inc.
Chemical Division
P.O. Box 31
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Active Ingredient:
S-Ethyl diisobutylthiocarbamate.....85.7%
Inert Ingredients.....14.3%

Background: Acute Oral, Acute Dermal, Acute Inhalation, Eye and Skin Irritation studies were submitted for this product. The studies were conducted by Raltech Scientific Services of Madison, Wisconsin and Cosmopolitan Safety Evaluation, Inc. of Somerville, New Jersey. The method of support is "cite-all."

Recommendations:

1. The Acute Oral, Acute Dermal, Acute Inhalation, Eye and Skin Irritation studies are considered adequate and acceptable for conditional registration purposes. For future studies, please note that the exposure level achieved in the Acute Inhalation study must be 5 mg/L actual concentration for 4 hours.

2. The appropriate signal word for this product is CAUTION. Please see the section below for necessary labeling revisions.

Labeling Recommendations:

1. Add the words"and Domestic Animals" to the "Hazards to Humans" heading.

2. The "Hazards to Humans and Domestic Animals" section must be revised as follows:

> Harmful if swallowed. Avoid contact with eyes, skin or clothing. Avoid breathing spray mist. Wash thoroughly with soap and water after handling.

3. A "Statement of Practical Treatment" must be added to the labeling under that heading, directly beneath the "Hazards to Humans and Domestic Animals" section. The following are the appropriate statements for this product based on data submitted:

   If swallowed: Call a physician or Poison Control Center. Drink 1 or 2 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 in eyes: Flush with plenty of water. Get medical attention if irritation persists.

   If on skin: Wash with plenty of soap and water. Get medical attention if irritation persists.

4. The "Environmental Hazards" section must be revised as follows:

   Do not apply directly to water. Do not contaminate water by cleaning of equipment or disposal of wastes.

   The statement "Do not contaminate irrigation water (used for crops other than corn) or water for domestic purposes" should be placed under the "Directions for Use."

5. The "Handling and Storage" section must be revised as indicated on the enclosed "Storage and Disposal"document. The preferred placement of this section is at the end of the "Directions for Use" statement.

6. Since this product is a carbamate, the registrant must determine if the active ingredient for this product is a cholinesterase inhibitor. If this product is a cholinesterase inhibitor, an appropriate statement of "Practical Treatment" and "Note to Physician" must appear on the labeling.

Review:

1. Acute Oral Toxicity; Raltech Lab #733422; September 12, 1979; Accession Number 244788.

   Procedure: Sprague-Sawley rats (200-286 g) were used in 4 range-finding tests and one dosage level test. One animal was used in each of the range-finding levels of 0.1, 0.5, 1.0, 5.0 g/kg; eight males and eight females were used in the 5.0 g/kg dosage level test. The test substance was butylate, PPG-814 7E in corn oil administered by oral gavage. Range-finding animals were observed for 6 days post-treatment. Dosage level test animals were observed for 14 days; these rats were subjected to necropsies at death.

Results: No mortalities observed in the range-finding group. All animals died at the 5.0 g/kg level. Observations included: salivation, ataxia, hypoactivity, decreased limb tone, decreased pain response, prostration, fasciculation, mydriasis, hypothermia, bradypnea, diarrhea. Necropsies revealed: stomach--hemorrhagic cardia; bloody ocular and nasal discharge; intestines--bloody contents; lungs--dark, pinpoint white areas, red foci. LD50 undetermined.

Study Classification: Core Guideline Data.

Toxicity Category: Undetermined. Refer to Raltech #744849 (see below).

2. Acute Oral Toxicity; Raltech #744849; September 28, 1979; Acc. No. 244788.

Procedure: Groups of 8 M, 8 F Sprague- Dawley rats (200-250 g) received either a 1.57, 2.31, 2,86, 3.40, 3.93 or 4.46 g/kg dosage of "Butylate PPG-814 7E." The test substance was mixed with corn oil and administered by oral gavage. Animals were observed for 14 days. All animals were subjected to necropsies.

Results: Mortalities were reported as follows: 1/8M at 1.57 g/kg; none at 2.31 g/kg; 1/8M and 4/8F at 2.86 g/kg; 5/8M and 6/8F at 3.40 g/kg; 7/8M and 8/8F at 3.93 g/kg; 8/8M and 8/8F at 4.46 g/kg. Observations included: hypoactivity, ataxia, bloody ocular and nasal discharge, hypothermia, decreased limb tone, lacrimation, placement reflex absent, urine stained abdomen, diarrhea, decreased grasping reflex, bradypnea, bradycardia, prostration, tremors, salivation. The LD50 for M was 3.34 g/kg with a 95% confidence range of 3.04-3.62 g/kg; the F LD50 was 3.00 g/kg with a 95% confidence range of 2.69-3.28 g/kg. Necropsies revealed: lungs--mild, diffuse raised white areas, multifocal; uterus--mild hydrometra; abdomen, thoracic cavity, intestines filled with bloody dluid; bladder--severe, diffuse hemorrhagic areas; scrotal sac filled with bloody fluid, testicles severely hemorrhagic; animals cannibalized.

Study Classification: Core Guideline Data.

Toxicity Category: III-CAUTION

3. Acute Dermal Toxicity; Raltech #733422; September 12, 1979; Acc. No. 244788.

Procedure: 5 M, 5 F New Zealand white rabbits (2300-2537 g) each received 2 g/kg of "Butylate PPG-814 7E" on the skin; all sites were

abraded. Exposure was for 24 hours under occlusive wrap. Animals were observed for 14 days post-treatment. All animals were subject to necropsies.

Results: No mortalities; $LD_{50} > 2$ g/kg for males, females. Observations included very slight to severe erythema, edema; very slight to marked atonia; desquamation; very slight to moderate coriaceousness; fissuring; blanching. Pathology report of skin revealed: mild subchronic or chronic inflammation of outer dermis in 4/10; moderate inflammation in 6/10; superficial desquamation in 2/10; chronic panniculitis in 4/10. Necropsies included the following observations: white mass in renal fat with hemorrhagic area; blood clot in peritoneal cavity; lobulated, firm tan mass in sublumbar region; liver-white, discolored area.

Study Classification: Core guideline data.

Toxicity Category: III - CAUTION

4. Acute Inhalation Toxicity in Rats; Cosmopolitan #3456-0334; May 2, 1980; Accession No. 244788.

Procedure: 5 male, 5 female Sprague-Dawley rats (201-305 g) were placed in a chamber with an atmosphere containing "PPG-814 7E." The test chamber was a 57.7 L plexiglass chamber with an airflow of 10 L/min. Delivery of the test system was by the DeVilbiss Continuous-Flow Nebulizer; the nominal concentration was 5.04 mg/L, atmospheric concentration was 0.15 mg/L. Exposure was for 4 hours, whole body. The mass median diameter was found to be 3.8 microns. Animals were observed for 14 days post-treatment; all animals received necropsies.

Results: No mortalities, no abnormal behavior. Necropsy revealed no visible lesions.

Study Classification: Core minimum data. Concentration must be higher--greater than 5 g/kg actual concentration for 4 hours.

Toxicity Category: III-CAUTION. Since no adverse reactions are noted at 5.04 g/L nominal concentration for 4 hours, study will suffice for labeling purposes.

5. Primary Eye Irritation; Raltech #733422; September 12, 1979; Accession No. 244788.

Procedure: 9 New Zealand white rabbits each received 0.1 ml of "PPG-814 7E" in one eye. Three eyes were subsequently washed with lukewarm water for one minute no sooner than 30 seconds post-compound instillation. Eyes were scored at 24, 48, 72 hours; 4, 7, 14, 21 days.

Results: Unwashed eyes at 24 hours exhibited corneal opacity in 1/6=3.75, 1/6=5, 1/6=6.25; iris irritation in 2/6=5 and injected; redness in 4/6=1.5, 1/6=2.5, 1/6=3 with 1/6 blanching; chemosis in 4/6=1, 1/6=2, 1/6=2.5; discharge in 4/6=1, 2/6=2 with 3 purulent and 3 clear. By 7 days, corneal opacity in 1/6=2.5 with neovascularization; redness in 2/6=1; chemosis in 1/6=0.5. By day 21, corneal opacity in 1/6=2.5.

The washed eyes at 24 hours showed redness in 3/3=1, chemosis in 1/3=1 and clear discharge in 1/3=0.5. By 72 hours, all scores were zero.

Study Classification: Core guideline data.

Toxicity Category: III - CAUTION

6. Primary Dermal Irritation; Raltech #733422; September 12, 1979; Accession No. 244788.

Procedure: 6 New Zealand white rabbits received 0.5 ml of "PPG-814 7E" at each of 4 sites, 2 abraded and 2 intact. Exposure was for 24 hours under occlusive wrap. Scoring at 24, 72 hours.

Results: At 24 hours, intact sites exhibited very slight to well-defined erythema; very slight to slight edema. Abraded sites at 24 hours showed very slight to well-defined erythema and very slight to slight edema. By 72 hours, intact sites showed very slight to slight erythema and very slight edema. Abraded sites by 72 hours showed very slight to moderate erythema and very slight to slight edema. The Primary Irritation Index was 1.9.

Study Classification: Core guideline data.

Toxicity Category: III - CAUTION.

Butylate toxicology review

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Pages _____ through _____ are not included in this copy.

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 commercial/financial information

X A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

___ FIFRA registration data

___ The document is a duplicate of page(s) _____

___ The document is not responsive to the request

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.