UNITED STATES ENVIRONMENTAL PROTECTION AGENCY TOX.

DATE: September 24, 1979

CASWELL FILE

SUBJECT: EPA File Symbol: 748-EEE
EPTC 7E; Caswell #435

FROM: S. A. Sterling
FHB/TSS

TO: Mr. Robert Taylor
Product Manager 25

Applicant: PPG Industries, Inc.
P.O. Box 31
Barberton, OH 44203

Active Ingredient: S-Ethyl dipropylthiocarbamate 87.8%
Inert Ingredients: 12.2%

Recommendations:

1. The Acute Oral LD_{50}, Acute Dermal LD_{50}, Primary Skin Irritation and Eye Irritation Studies are adequate to partially meet the complete acute toxicological data requirements for the conditional registration of this product.

2. An acute inhalation study was not submitted with this application. However, under the "cite all" method of support, this study will not be required.

3. The signal word should be changed to "Warning" based on the results of the Eye Irritation study.

4. Labeling revisions should be made as noted below.

5. FHB/TSS would have no objection on the basis of adverse effects to man, domestic animals and the environment, to the conditional registration of this product with the label revisions indicated below.

Labeling:

1. Based on the Eye Irritation study, the appropriate signal word is "Warning".

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

white areas in lungs; 5F showed lung abnormalities (1/5 darkened and mottled, 4/5 darkened with white areas. At 2.034 g/kg, 8M died (5/8 no visible lesions, 2/8 blood at nose and mouth, 1/8 hemorrhage in stomach); 3F died (3/3 bloody nose and/or ocular discharge); 3F showed lung abnormalities (1/3 darkened and mottled, 2/3 raised white areas), 1F had no visible lesions. At 2.632 g/kg, 8M died (7/8 bloody nasal and/or ocular discharge, 2/8 brown material around mouth); 5F died (2/5 no lesions, 1/5 bloody ocular discharge, 2/5 bloody contents in stomach); 1F showed lung abnormalities (red foci and raised white areas); 2F had no visible lesions. At 3.229 g/kg, 8M died (4/8 no visible lesions, 3/8 bloody ocular discharge, 4/8 brown material at nose and mouth); 8F died (4/8 bloody nasal and/or ocular discharge, 4/8 no visible lesions). At 5.126 g/kg, 8M died (6/8 bloody nasal and/or ocular discharge, 1/8 brown material at nose and mouth, 2/8 no visible lesions); 8F died (6/8 bloody nasal and/or ocular discharge, 1/8 darkened lungs, 2/8 no visible lesions.

LD_{50} calculated for M is 0.916 g/kg with 95% confidence range from 0.686 to 1.247; LD_{50} for F is 2.322 g/kg with 95% confidence range from 1.962 to 2.658. Slope of the dose response curves are 2.318(M) and 2.076(F). Average body weights increased from day 0 to day 14.

Study Classification: Core Guideline Data.

Product Classification: Tox. Cat. III.

2. Acute Dermal Screen

Procedure: 5M, 5F New Zealand White rabbits (2329-2785 g) with abraded skin received an application of 2.0 g/kg of the test substance with 24 hours occluded exposure. Animals were observed for 14 days, sacrificed and subjected to gross necropsy.

Results: No mortalities, microscopic examination of skin showed 7/10 had slightly diffuse fibrosis of outer dermis, 2/10 had superficial infection of epidermis and 1/10 appeared normal. At gross necropsy 8/10 had no visible lesions, 2/10 showed white areas on liver. One animal showed external signs of diarrhea. Average body weights increased through day 14.

Study Classification: Core Guideline Data

Product Classification: Tox. Cat. III. The data sufficiently established that the acute dermal LD_{50} is greater than 2 g/kg.

3. Eye Irritation

Procedure: 0.1 ml of test material was applied into one eye of each of 9 New Zealand white rabbits. The treated eyes of 3 rabbits were flushed with lukewarm water for 1 minute starting no sooner than 30 seconds after exposure; remaining 6 rabbits were unwashed. Scoring done at 24, 48, 72 hours, 4, 7, 14 and 21 days.

Results: At 24 hours corneal opacity observed in 6/6 unwashed eyes (scores = 1.0-1.5), 3/3 showed no signs of corneal opacity in washed eyes; 6/6 unwashed eyes showed slight iris abnormality (scores = 1.0), 3/3 washed eyes showed no adverse iris reaction. Conjunctivae in 9/9 showed redness (scores = 1.5-3.0); 9/9 chemosis exhibited swelling (scores = 1.0-2.5); 5/6 unwashed eyes showed purulent discharge (scores = 1.5-2.0), 1/6 unwashed eyes had no discharge. Corneal epithelial peeling (10%) seen 1/9 (in unwashed eye group). At 7 days, 7/9 exhibited no adverse effects; 1/9 showed very slight redness in conjunctivae (score = 0.5) and 1/9 exhibited pannus (score = 0.5) in less than one quarter of the cornea (score = 0.5) with redness in conjunctivae (score = 1.5). Negative results 8/9 in sodium fluorescein exam, 1/9 read positive (less than 5%). At day 21 all sodium fluorescein exams were negative.

Study Classification: Core Guideline Data.

Product Classification: Tox. Cat. II,5/6 eyes with corneal opacity recovered by day 7.

4. Primary Skin Irritation

Procedure: 0.5 ml test material was applied to each of 2 sites (1 abraded, 1 intact) on each of 6 New Zealand white rabbits. All animals were exposed for 24 hours under occlusive wrap. Draize scoring at 24, 72 and 96 hours.

2. The subheading "Hazards to Humans" should be changed to read something like "Hazards to Humans and Domestic Animals".

3. Under the human hazards section, the statement "Avoid contact ... or clothing" must be deleted. Instead a statement such as the following must appear:
"Causes eye irritation. Do not get in eyes, on skin or on clothing."

4. A "Statement of Practical Treatment" section should be added to the precautionary statements and should read something like:
"In case of contact with eyes, flush eyes with pleaty of water for at least 15 minutes. Call a physician."

5. A precautionary statement should be added which reads something like the following:
"Avoid contamination of food and feed."

Review:

The following studies were conducted on the product for registration, EPTC 7E, at Raltech Scientific Services, Inc., in Madison, WI. Studies were done under purchase order number D-477390-R, reported August 9, 1979.

1. Oral Defined LD_{50}

Procedure: Groups of 8M,8F Sprague-Dawley rats (200-299g) received oral dosages at levels of 0.508, 0.807, 1.281, 2.034, 2.632, 3.229 and 5.126 g/kg. Observations made at 1, 2.5, 4 hours and daily thereafter for 14 days. Mortalities noted; survivors sacrificed at 14 days. All animals received gross pathological examination.

Results: At 0.508 g/kg 1M died (bloody nose and mouth, severe hemorrhage in thymus); 5M showed lung abnormalities (4/5 darkened, 3/5 showed white areas); 2M had no visible lesions; 5F showed lung abnormalities (2/5 darkened, 5/5 white foci); 2F had no visible lesions. At 0.807 g/kg, 4M died (1/4 stomach hemorrhage, 1/4 darkened lungs, 2/4 no visible lesions); 1M showed lung abnormalities (white areas); 3M had no visible lesions; 6F showed lung abnormalities (5/6 darkened/mottled, 3/6 white areas); 1F exhibited hemorrhagic areas in thymus; 2F had no visible lesions. At 1.281 g/kg, 6M died (4/6 blood at nose and mouth, 1/6 cannibalized and mucous in small intestine, 1/6 no visible lesion); 2M had

Results: At 24 hours, 24/24 sites showed erythema (scores = 0.5-2.0), 9/12 intact sites exhibited edema (scores = 0.5-2.0) and 10/12 abraded sites showed edema (scores = 1.0 -2.0). At 72 hours 4/12 abraded sites exhibited erythema (scores = 0.5-2.5) and 11/12 abraded sites showed erythema (scores =0.5-2.5); 4/12 intact sites showed edema (scores = 1.0-2.0) and 6/12 abraded sites exhibited edema (scores =0.5-1.5). However, in 8/12 M erythema scores increased and 3/12 M edema scores increased from 24 to 72 hours. No F scores increased.

Study Classification: Core Minimum Data

Product Classification: Tox. Cat. III.

TS-767:SSterling:jjd3:DCR#47434:Raven:479-2018:9/27/79