Date: June 7, 1984

Subject: EPA Registration Number: 1448-55
Busan 1020

005279

From: Delores F. Graham
TAB/RSS
E 6/5/84

To: Henry Jacoby
Product Manager (21)

Applicant: Buckman Laboratories, Inc.
1256 N. McLean Blvd.
Memphis, TN 38108

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Active Ingredient:
Sodium N-methyldithiocarbamate . . . 33%
Inert Ingredients 67%

Background: Submitted Acute Oral, Acute Dermal, acute inhalation, Dermal Irritation and Eye Irritation Studies. Studies conducted by Hazleton Laboratories America, Inc. Studies under accession number 252116. Method of support not indicated.

Recommendation:
(1) TAB/RSS finds these data acceptable to support conditional registration of this product.

(2) The appropriate signal word is ...

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(3) A Dermal Irritation Study was not submitted

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Label:

(1) The subheadings "Product Information", "Use Precautions" and "Storage and Disposal", must appear under the heading "Directions For Use".

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Review:

(1) Acute Oral Toxicity Study; Hazleton Laboratories; RT Lab. No. 806868; October 25, 1983.

Procedure: Five groups consisting of five male Sprague-Dawley rats each received one of the following doses: 0.93, 1.05, 1.40, 1.75 or 2.10 g/Kg. Four groups consisting of five female Sprague-Dawley rats each received one of the following doses: 0.62, 0.93, 1.40 or 2.10 g/Kg. Observations made at 1, 2.5 and 4 hours after treatment, then daily for 14 days thereafter. Necropsy performed on all animals.

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Results: At 0.93 g/Kg 1/5 F died; at 1.05 g/Kg, 3/5 M died; at 1.40 g/Kg 3/5 M and 4/5 F died; at [illegible]

[illegible] ataxia, ptosis, dyspnea, lacrimation, urine stained uro-genital area, red stain around 005279 piloerection, red stained around nose and mouth, yellow stained abdomen, prostrate, clonic convulsions, excess salivation. Necropsy report revealed stomach - nonglandular mucosa thickened; lungs - spots on all lobes; cranial serosa adhered to diaphragm; red-brown perinasal discharge; bilateral, red periocular discharge; perineum - yellow stains; kidneys - bilateral spots, left seen on cross-section, right seen on cortical surface, several group together at cranial pole; left testis - small, [illegible] area beneath tunica involving 2/3 of left testis; liver - enlarged lobes thickened; lungs - mottled red and dark red; thoracic cavity contains clear fluid; stomach - contains yellow, oil-like material; lungs - firm, slightly raised, gray foci on all lobes; red staining of entire head, chest and forelegs; brown perioral discharge; white opaque perioral discharge; lungs - uncollapsed, mottled with dark red areas. LD50 for males 1.26 g/kg (0.97 to 1.57 g/kg, 95% confidence limits). LD50 for females 1.17 g/kg (0.88 to 1.64 g/kg, 95% confidence limits).

Study Classification: Core Guideline Data

Toxicity Category: III - CAUTION

(2) Acute Dermal Toxicity Study: Hazleton Laboratories; RJ Lab. No. 806868; October 23, 1983.

Procedure: Four groups consisting of four male and four female New Zealand rabbits weighing

between 2389 and 2992 grams received of the following doses: 1.02, 1.43, 1.72 or 2.00 g/kg. Treated skin sites were placed under occlusive wrap for 24 hour exposure period. Observations made at 1, 2.5 and 4 hours after treatment, then daily for 14 days thereafter. Necropsy performed on all animals.

<u>Results:</u> At 1.43 g/Kg, 2/5 M and 1/5 F died; at 1.72 g/Kg, 5/5 M and 5/5 F; at 2.00 g/Kg, 5/5 M and 4/5 F died. Toxic symptoms reported included erythema, edema, eschar, exfoliation, necrosis, atonia, desquamation, ~~coro~~ coriaceousness, fissuring, ~~hypoa~~ hypoactive, ataxic, bradypnea, emaciated, dyspnea, prostrate, cyanotic. Necropsy report revealed skin (test site) - dark red to brown and tan, firm and thickened, subcutaneous hemorrhage, fascia is fibrous, ~~[illegible]~~ adhered to muscle, necrotic, crusty, ulcerations along test site; perineum stained with fecal material; cecum - contains a white, tenacious material, white areas in mucosa; skin (test site) - thickened, oozing yellow and green; thymus - mottled red and tan; trachea - contains dark red material; reddish gelatinous material ~~[illegible]~~ beneath test site; trachea - contains dark red material; right kidney in one animal missing, right adrenal small, lungs - diffusely dark red. LD50 for males 1.47 g/Kg (1.23 to 1.77 g/Kg 95% confidence limits). LD50 for females 1.53 g/Kg (1.35 to 1.74 g/Kg, 95% confidence limits).

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<u>Study Classification</u>: Core Guideline Data

Toxicity Category: II - WARNING

(3) Primary Skin Irritation Study; Hazleton Laboratories, RI Lot No. 806868, October 5, 1983
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Procedure: Six New Zealand rabbits received 0.5ml of the test material at intact skin sites under occlusive wrap for 4 hour exposure period. Observations made at 24, 48, and 72 and 96 hours and at 7 days after treatment.

Results: At 24 hours, 5/6 had slight to severe erythema (scores of 1, 2, and 3) and 3/6 slight to moderate edema (scores of 1, 2, and 3). At 72 hours, 3/6 slight to severe erythema (scores of 1, 2 and 4) and 2/6 slight edema (scores of 1 and 2) Subcutaneous hemorrhage, blanching and possible necrotic areas noted.

Study Classification: Core Guideline Data

Toxicity Category: II - WARNING

(4) Eye Irritation Study; Hazleton Laboratories, RI Lab. No. 806868; September 30, 1983.

Procedure: Six New Zealand rabbits received 0.1ml of the test material in one eye each. Observations made at 1, 24, 48 and 72 hours after treatment

Results: At 24 hours, 6/6 conjunctival redness (5/6=1, 1/6=2) and 5/6 chemosis (5/6=1). At 72 hours, all irritation had cleared. At one hour posttreatment 3/6 exhibited blanching of the conjunctiva and 1/6 petechial hemorrhage.

Study Classification: Cat. Guideline Ref.:

Toxicity Category: III - CAUTION 005279

(5) Acute Inhalation Toxicity Study in Rats (Bio-Research Laboratories); Project No. 2200-104; Dec. 21, 1983.

Procedure: Two groups consisting of five male and five female rats were used. One group served as control group. The other group was exposed for four hours to mean gravimetric concentration of 7.94 (Nominal concentration = 16.96) mg/l. Mass median aerodynamic diameter = 2.34 µ with a geometric standard deviation = 2.19. Temperatures range from 70 to 80°F during exposure and study of the animals. Relative humidity ranged from 31 to 58% during exposure and study of the animals. Observations made at 30 minutes post-exposure, then twice daily for 14 days thereafter. Necropsy performed on all animals.

Results: No mortalities. Toxic signs noted included salivation, squinted eyes, dyspnea and animals appearing languid. Necropsy revealed kidney - pelves dilated, contained white fluid.

Study Classification: Cat. Guideline Ref.:

Toxicity Category: IV - CAUTION