

7.1 Jan 7, 1984

Subject: E.H. Registration Number: 100-55
Burax 1020

005279

From: Richard J. Graham
JHG/SSS E 6/5/84

To: Henry Jacoby
Product Manager (21)

Applicant: Buckman Laboratories, Inc.
1356 W.D. McLean Blvd.
Memphis, TN 38103

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Active Ingredient:
Sodium N-methyl-dithiocarbamate 33%
Inert Ingredients 67%

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

Recommendation:

(1) JHG/SSS finds these data acceptable to support
conditional registration of this product

(2) the appropriate animal number is 100-55

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(5) A Chemical Investigation Study was not submitted

005279

Label:

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

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Received:

(1) Acute Oral Toxicity Study: Hazelton Laboratories,
13 Lab. No. 806868; October 25, 1983

Procedure: Four 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: 0.52, 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.

Results: At 0.93 g/kg 1/5 F died at 1.05 g/kg, 3/5 M died at 1.40 g/kg, 1/5 M and 4/5 F died at 1.75 g/kg, 2/5 M and 5/5 F died at 2.10 g/kg.

ataxia, mucus, dyspnea, lacrimation, urine
stained uro-genital area, red stain around 005279,
piloerection, red stained around nose and mouth,
yellow stained abdomen, prostrate, clonal contractions
effort salivation. Necropsy report revealed
stomach - no glandular mucosa thickened;
lungs - cysts $\frac{1}{2}$ on all lobes; cranial nerves
adhered to diaphragm; red brown perinasal
discharge; bilateral, red perocular discharge;
perineum - yellow stains; kidneys - bilateral
cysts, left seen on cross-section, right seen on
caudal surface, several groups together at cranial
pole; left testis - small, white area beneath
tunica covering $\frac{2}{3}$ 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
nursed, grey foci on all lobes; red staining of
interior 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.

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Procedure: Six groups consisting of five male
and five female New Zealand rabbits weighing

between 2389 and 2992 grams received 005379
of the following doses: 1.02, 1.43, 1.72
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
hereafter. Necropsy performed on all animals.

Results: 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,
ulceration, desquamation, ~~corrosion~~ coriaceousness,
fissuring, ~~hyper~~ hypoaesthesia, ataxia, bradypnea,
emaciated, dyspnea, prostrate, cyanotic.
Necropsy report revealed skin (test site) - dark
red to brown and tan, firm and thickened,
subcutaneous hemorrhage, fascia as fibrous
~~adherent~~ adhered to muscle, necrotic, crusting,
ulcerations along test site; perineum stained
with fecal material; cecum - contains a white
brackish material, white areas in mucosa;
skin (test site) - thickened, stained yellow and green;
thymus - mottled red and tan; trachea - contains
dark red material; reddish gelatinous material
~~test~~ 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 1.72 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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Study Classification: Can. Schedule Data

Toxicity Category: II - WHF N1106

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(3) Primary Skin Irritation Study: Hazelton Laboratories, R3 Lab No. 806868, October 5, 1983 005279

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 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 4/6 slight edema (scores of 1 and 2). Subcutaneous hemorrhage, blanching, and possible necrotic areas noted.

Study Classification: Core Guideline Data

Toxicity Category: II - WARNING

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(4) Exp. Irritation Study: Hazelton Laboratories, R3 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, 4/6 conjunctive redness (5/6 = 1, 1/6 = 2) and 5/6 chemosis (5/6 = 1). At 72 hours irritation had cleared. At one hour posttreatment 3/6 exhibited blanching of the conjunctive and 1/6 pale hemorrhage.

Study Classification: Core Guideline Data

Study Category: III - CAUTION 005279

(5) Acute Inhalation Toxicity Study: Hayleton 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~~ to mean geometric concentration of 7.94 (nominal concentration = 16.96) ^{ppm}. Mass median aerodynamic diameter = 2.34 μ with a geometric standard deviation of 2.19.

Temperature range from 76 to 80°F during exposure and study of the animal. Relative humidity range 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 reported included salivation, squinted eyes, dyspnea and animals appearing languid. Necropsy revealed kidney - pelvis dilated, contained white fluid.

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Study Classification: Core Guideline Data

Study Category: IV - CAUTION