July 19, 1984

To: Raymond H. Kowal

From: Leon L. Graham

Subject: Issue 85

June 1982

Henry Jacoby
Product Manager (21)

Applicant: Buckman Laboratories, Inc.
1256 D. McFadden Mill
Memphis, TN 38104

Active Ingredients:
Sodium N-methylthurocynamide: 33.0%

Inert Ingredients: 67.0%

Background of Laboratory Acute Oral, Acute Dermal, Percutaneous, Irritation, and Allergenicity Studies, conducted by Nejdan Laboratories, America, Inc. Studies in vivo according to Federal, Method 9221k6. Method of experimental indicated.

Recommendation:

ULHT 223 finds these studies acceptable to support conditional registration of this product.
Label:

1. The Rachman's Product Information "Use Promotions" or "Storage and Disposal" printed against under the heading "Directions for Use".

References:


Procedure: Four groups consisting of five male Sprague-Dawley rats each received one of the following doses: 1.03, 1.05, 1.20, 1.45, and 2.10 g/kg. Four groups consisting of five female Sprague-Dawley rats each received one of the following doses: 0.67, 0.93, 1.50, and 2.10 g/kg. Observations made at 1, 3, 5, and 7 hours after treatment, then daily for 14 days thereafter. Necropsy performed on all animals.

Results: 3. 0.93 g/kg, 15 F dead at 1.07 g/kg, 27.5% death at 1.45 g/kg, 93.0% death at 2.10 g/kg.
ata, brown, diffuse, haemorrhage, were
stained mucoid, caseous, red, yellow, pale,
translucent, red-stained areas of more and/or
yellow stained abdomen-predominantly loose concretes.
Gastrointestinal Tract: vagotomy resected stomach - no glandular mucosa. Declined lung - cyclic for all lobe. Current area ad
heaped to diaphragm. Red-brown peritoneal
discharge. Bilateral, red peritoneal discharge.
Peritoneum - yellow stains. Edges - bilateral.
Lungs - left not on cross-section, cut on re-
sected surface, several grey, together with cranial
pale, left bile - small, yellow, clear, firm, firm,
area present, 75% left lobe - brown - engorged leaves thickened). (Lungs matted, red and dashed -
Thyrocance, contains clear fluid). Osseous: cartilag-
yellow, cell-like material. Lump - firm, slightly
rounded, grey face on all lobe - red staining of
intermediate, cist and forelegs. Brown peritoneal
discharge. White opaque peritoneal discharge.
Lung - uncollapsed, matted with dark red areas.
2050 for males: 11.75 kg (0.97 to 1.89 kg, 75% confidence limits). 2050 for females: 11.75 kg (0.88 to 1.64 kg, 95% confidence limits).
between 938.9 and 9992 grams received.

The following doses: 1.0, 1.43, 1.73, 2.00 g/kg. Tested the other nine placed
under inclusive assay for 4 weeks preceeding
period. Observation made at 1, 2, 5 and 7
hours after treatment, then daily for 14 days
thereafter. Necropsy performed on all animals.

Results: At 1.43 g/kg, 1/5 M and 1/5 F died, at
1.73 g/kg, 1/5 M and 1/5 F died. Some symptoms reported included
lymphopenia, edema, cachexia, emaciation, nerosis
anemia, degeneration, coma, cyanosis, fever
hypoaesthesia, ataxia, bradypnea
Necropsy report revealed skin (test site) - dark
red to brown and tan, firm and hard, skin
adherent to muscle, necrotic, many
alterations along test site; penicillin stored
not fecal material, tissue - contains a white
necrotic material, white areas of necrotic
din (test site) - hemorrhage, atrophied yellow malign
thymus - necrotic red and tan. Necropsy - contains
dark red material; reddish gelatinous material
beneath test site, muscle - contains dark red
muscle, right kidney in one animal
muscle, right adrenal small. Tissues - left
dark red, C F 50 for males 1.47 g/kg (1.23 h 1.03 g/kg
95% confidence limits), 1.50 for females 1.53 g/kg
(1.35 to 1.74 g/kg) 95% confidence limits.

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Study Classification: AL, A, A A 1, 1986
Procedure: By New Zealand rabbit exposed to 0.5% of the test material at intact skin sites under occlusive dressing for 24 hour exposure period. Observations made at 6, 24, 48, and 96 hours and 7 days after treatment.

Results: at 24 hours 1/12 slight to severe erythema (scores of 1, 2, and 3) and 3/12 slight to moderate edema (scores of 1, 2, and 3). At 72 hours, 1/12 slight to severe erythema (scores 1, 2, and 3) and 4/12 slight edema (scores 1 and 2). Subcutaneous hemorrhage, blanching and possible necrosis areas noted.

Study Classification:ume Guideline Data

Severity Category:II - WARNING

(4) Eye Irritation Study, New Zealand rabbit.

Procedure: Six New Zealand rabbits exposed to the test material once per cheek. Observations made at 6, 24, 48, and 72 hours after treatment.

Results: At 24 hours, 4/6 severe conjunctivitis (scores 1, 2, and 3) and 5/6 chemosis (scores 1).

At 72 hours ocular irritation relieved.

At 4 hour post-treatment 3/6 inhibited blanching of the cornea and 1/6 pale cornea.
Experimenter: Two groups consisting of four male and four female rats were used. One group served as control group. The other group was exposed to 100% gas concentration of 1.94% (nominal concentration = 1.9%). Mass median aerodynamic diameter = 3.4 μm. with a geometric standard deviation = 2.19.

Temperature range from 70 to 80°F during exposure and study of animals. Relative humidity range from 31 to 55% during exposure and study of the animals. Observations made at 30 minutes post-exposure first daily for 14 days thereafter.

Results: No mortality. No signs reported included salivation, squinted eyes, depression and anemia appearing languid. Necropsy revealed kidney - pelvis dilated, contained white fluid.

Study Classification: Case, Highline Lab.

Identity Category: IV - CHITZON