conditional registration of the product.

Warning:

1. The appropriate signal word is "WARNING".

Label:

1. The precautionary statement must be revised to include "Causing injury".

2. The statement of practical treatment must be revised to include: "If swallowed, drink 1 and 2 glasses of water and induce vomiting by placing fennel seeds back of throat and call a physician, hospital or local poison control center. If inhaled, remove victim to fresh air. If not breathing, give artificial respiration. Preferably, mouth-to-mouth or medical attention.

3. An enclosed copy for appropriate storage and disposal statements.

Review:

1. Acute Oral Toxicity Study: Stillwater, Inc.
   Project #: 2834-82: January 27, 1983.

Procedure: 5 groups consisting of five male rats each received one of the following doses: 1000, 2240, 3500 and 5000 mg/kg. 5 groups consisting of five female rats each received one of the following doses: 1000, 1200, 1400, 1790 and 2500 mg/kg.

Observations made at least three times on the day of treatment, then daily thereafter for 14 days."
Accupay performed on all animals.

Results: all 1210 mg/kg 75% died; at 1900 mg/kg 75% died; at 1700 mg/kg 50% died; at 2000 mg/kg 3/5 died; at 3500 mg/kg 75% died; at 5000 mg/kg 75% died. Toxic signs observed included activity decrease, ataxia, contractile pupils, convulsions, cervicofacial edema, dilated pupils, lacrimation, hiccups, nasal discharge, pale mucous membranes, piloerection, piloerection, rapid breathing, and salivation. Necropsy: incidental findings included increased salivation, polyuria, lacrimation, epistaxis, hiccups, decapitation of the brain, and increased salivation. The contents of the stomach and the intestines were empty, and dissection of the brain revealed no focal lesions. The stomach was filled with a small amount of food. Males were 5000 mg/kg with 95% confidence limits of 2830 to 3491 mg/kg. LD50 for females was 1289 mg/kg with 95% confidence limits of 1095 to 1575 mg/kg. LD50 for males and females combined was 1822 mg/kg with 95% confidence limits of 112 to 3011 mg/kg.

Study Classification: Core Study Data

Toxicity Category: III - CAUTION

A) Acute Dermal Toxicity Study: Stillwater, Inc.; Project # 2835-82; January 4, 1983.

Procedure: 5M and 5F New Zealand rabbits received 20% mg/kg of the test material, at a shaved skin site, under occlusive wrap for 24 hour exposure. Observations made at 12, 24, and 48 hours after treatment and at least once daily thereafter for 14 days. Necropsy performed on all animals.

Results: no mortalities. Toxic signs observed included contractile pupils, activity decrease.
Phasic salivary, decreased defecation, unable to coordinate use of right and left hind limbs. Slight to well-defined exopthalmos, and mild deviation to sides. Edema, atrophy and brown discoloration of exposure area. Hair and shallow lateral fissuring also noted. LD50 greater than 2010 mg/kg.

Study Classification: Ocular Draize Data

Toxicity Category: III - CAUTION


Procedure: Twelve New Zealand rabbits received 0.1 ml of the test material in one eye each. The treated eyes of three of the rabbits were washed 30 seconds post-treatment. Observations made at 1, 24, 48 and 72 hours and at 4, 7, 14, 16, 19, and 21 days after treatment.

Results: At 24 hours, 8 animals of the uncapped group and 5 animals of the washed group had cornal opacity (4/5, 4/10, 4/5 = 20). 3/5 irritation (4/7 = 5) (3/5, 4/7, 5/7 redness (4/7 = 1), 3/5, 4/7 = 2) (4/7 = 2) (4/7 = 2). 2/5 corneal edema (4/7 = 1, 4/7 = 2, 4/7 = 3, 4/7 = 4, 4/7 = 2). 1/5 corneal edema (4/7 = 1, 4/7 = 2, 4/7 = 3). C/8 = 1, 4/7 = 2.

At day 7, 10/12 unicapped group had cornal opacity (10/12 = 10). 12/12 redness (12/12 = 1). 12/12 corneal edema (12/12 = 1). 2/12 discharge (12/12 = 1). At day 7, observation one animal was sacrificed due to corneal scarring.

At day 14, 5/12 had cornal opacity (5/12 = 5). 5/12 had corneal edema (5/12 = 5), and discharge (5/12 = 5).
At day 24, central opacity present in 73.03% of animals (Y3 = 10, 0.3% had mild). A study classification: Care Guideline Data.

Severity Category: II - WARNING


Procedure: Six New Zealand rabbits received 0.5 ml of test material at two abdominal and two intact skin sites, procedural, and occurred at 24 hours exposure period. Observations made at 24 and 72 hours after treatment and daily thereafter through 19 days.

Results: At 24 hours, 70% had well-defined to moderate erythema (scores of 2.0 to 3.0) and slight to moderate edema (scores of 1.0 to 3.0). At 72 hours, 2 % had well-defined to moderate erythema (scores of 0.0 to 3.0) and slight to moderate edema (scores of 1.0 to 3). Foam score was 3.9. Erythema through day 10, decreasing in severity. Edema persisted on one animal through day 18.

Study Classification: Care Guideline Data

Severity Category: III - CAUTION


Procedure: 5M and 5F rats were exposed for four hours to a 0.13 mg/l aerosol concentration.
Concentration: The mass median diameter and geometric standard deviation were 2.01 micrometers and 1.82, respectively. The temperature was 70-72°F and humidity was 32-62%. Observations were made daily for 14 days. Necropsy performed on all animals.

Results: 10% of animals died during the study. Some signs observed included irregular breathing, crusty nose, squinting, crusty eye, damp fur, red skin, fur, ataxia, matted eye, proliferation of the skin, crusty nose, crusty muzzle, poor coat, quality, vision, hyperactivity, respiratory, possible rashes, and crusty substance around ear tag. At necropsy 40% of animals showed normal appearance, and 60% lung and skin abnormalities were noted. All animals greater than 4.53 mg/l.

Study Classification: Acute Guideline Data

Toxicity Category: III - CAUTION

(6) Dermal Irritation Study: Stillwater, Inc.
Project No. 283-82; February 4, 1983.

Procedure: Two groups consisting of 10 male guinea pigs each. Received one of the following treatments. Group A animals were treated with a 0.05% dilution of 2,4-dinitrochlorobenzene in ethanol as a positive control group. Group B animals were treated with a 0.1% dilution of the test material in deionized water as a test group. The animals were treated on days 0, 5, 7, 9, 12, 14, 16, 18, 21, 35, and 43. The animals were treated on each of the first 10 treatment days by introducing 0.5 ml of the appropriate test material with gauze patch secured by a piece of adhesive tape wrapped in clear polyethylene film to secure
patches in place. Each animal was then placed in a container for approximately six hours. At end of exposure period, animals were removed from the containers, the wrappings removed, and the animals were returned to their cages. Observations made at 24 hours after each treatment.

Results: The average skin reaction scores for Group I (Active Control Group) were 0.0 for initial treatment (day 1) for the first and second sites and for the original test site after the eleventh treatment (day 72). The skin reaction scores were significantly greater than the initial treatment. Therefore, a sensitizing reaction was produced.

The average skin reaction scores for Group II (Test group) were 0.0 for the initial treatment, 0.4 for the first, second, and third sites and for the original test site after the eleventh treatment, and 0.4 for the second, third, and fourth sites and 0.2 for the original test site after the final treatment. The skin reaction scores were significantly greater than the initial treatment. Therefore, a sensitizing reaction was produced.

Study Classification: CORE Threshold Value

Sensitivity Category: Sensitizing