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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: November 3, 1977

SUBJECT: Pramitol 5PS- Addition of Data to Files EPA Reg. No. 100-479
Caswell No. #96, 740, 753; Shaughnessy #020207, 073301, 011104

FROM: Toxicology Branch
Registration Division

TO: Robert Taylor
Product Manager #25

Thru: Dr. G. Whitmore
Acting Branch Chief, Toxicology E for GEW 1/9/78

Recommendation: The acute oral LD_{50}, dermal LD_{50}, inhalation LC_{50}, eye and skin irritation studies are adequate. The TOX Category I label, proposed by the registrant, requires changes in the First Aid statement. It should read:

First Aid: In case of contact with skin, wash immediately with plenty of soap and water. In contact with the eyes, flush with water for at least 15 minutes and get medical attention. If swallowed drink promptly a large quanity of milk, egg whites, gelation solution or if these are not available, drink large quanitities of water. Avoid alcohol. Call a physician immediately. In case of inhalation exposure, move from the contaminated area.

Note to Physician: Probable mucosal damage may contraindicate the use of gastric lavage. Measures against circulatory shock, respiratory depression and convulsion may be needed. The rest of the label (attached) is adequate.

*No RPAR criteria have been exceeded.

Review:

1. Acute Toxicity Studies with Pramitol 5PS - (Industrial Bio-Test, IBT #8530-09309, 9/8/76, Acc. #231844)

A. Acute Oral LD_{50}

24 Sprague-Dawley albino rats, weighing between 170-284g, were divide into 6 groups of 4 animals each (2 male, 2 female) and administered 177.8,600,2025,3038,4556 or 15380 mg/kg of the test material by gavag Initial and final body weights, mortalities, and reactions observed during the 14 day observation period were recorded. A necropsy examination was conducted on all animals.

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Results

LD_{50} = 2745 ± 278.7 mg/kg
Toxic Signs: hypoactivity, muscular weakness, salivation, labored breathing, diuresis.
Necropsy: Decedents - gastritis, red lungs, G.I. hemorrhages, pale kidneys
Survivors - unremarkable
Classification: Core-Minimum Data
(1) Although only 2 animals/sex/dose level were employed, 6 dos levels were used thus adding to the acceptability of the st
TOX Category: III

B. Acute Dermal LD_{50}

2000 mg/kg of the test material was dermally applied, as an aqueous slurry, the clipped skin of the backs of 2 male and 2 female New Zealand albino rab weighing between 2.68-2.74 Kg. Two animals were further prepared by abradi their skin. Test sites were occluded with an impervious plastic wrapping. the end of 24 hrs, the plastic sheeting and residual test material were rem Observations for mortality, local skin reactions and behavioral abnormaliti were continued 14 days post-application. Necropsies were performed.

Results

LD_{50} >2000 mg/kg (no deaths occurred)
Toxic Signs: pale red to red, well-defined erythema and moderate edema, desquam skin.
Necropsy: unremarkable
Classification: Core-Minimum Data
(1) The study has been raised from the Supplementary Category t Core based on the results, i.e. no deaths at 2g/kg

C. Primary Eye Irritation

100 mg of the undiluted test material was instilled into one eye of each 6 Zealand albino rabbits. In 3 rabbits the eye was washed with 300 ml water seconds after exposure. The cornea, iris and palperbral conjunctival were scored, according to Draize, at 1,2,3,7 and 14 days post-instillation.

Results

Unwashed Eyes: corneal opacity, iritis and conjunctivitis were present up to an including day 14.
Washed Eyes: corneal opacity present in 1/3 animals on day 14. Washing was beneficial.
Classification: Core-Minimum Data
(1) Although only 3 rabbits were tested without the eye wash, t results are definitive-the material is a severe irritant.

D. Primary Dermal Irritation

500 mg of the test material was applied to intact and abraded skin sites on New Zealand albino rabbits, under occlusive dressing. At the end of 24 hrs. plastic wrapping, patches, and residual test material were removed. The int and abraded test sites were examined and scored, according to Draize, at 24 72 hours.

Results

P. I. = 7.4/8.0; 2nd degree burns and desquamation occurred.
Classification: Core-Minimum Data
(1) Readings were not made on 2 intact and 2 abraded skin sites.
TOX Category: I

2. Acute Dust Inhalation Toxicity Study with Pramitol 5PS - (Industrial Bio-Test IBT #8562-09298, 8/13/76, Acc. #231844)

5 male and 5 female Charles River rats were exposed to Pramitol 5PS in the for of a dust at an analytical concentration of 3727.5 mg/M^3 for 4 hours in an 8C liter exposure chamber. Particle size was determined. The animals were observed for signs of toxicity and mortality for 14 days post-exposure. Necropsies were performed on all animals.

Results

LC_{50} > 3.7 mg/L (no deaths occurred)
Particle Size: 68.9% were in the respirable range, < 10
Toxic Signs: none observed
Necropsy: unremarkable
Classification: Core-Minimum Data
(1) Although only 1 dose level was tested, the level was sufficie high to determine the low toxicity of the test material by th inhalation route of exposure, especially when one considers t results, the exposure time and the necessity to pulverize th sample to facilitate dust generation.
TOX Category: III

William Greear

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RIN-0334-94 PROMETON REVIEWS (080804)

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