

DATE: October 30, 1979

SUBJECT: EPA File Symbol 352-GOR
Lorox 4L, Caswell #528

FROM: Sherell A. Sterling
FHB/TSS

TO: Robert Taylor
Product Manager (25)

Releasable

Applicant: E. I. du Pont de Nemours & Co., Inc.
Biochemical Dept.
Wilmington, DE

Active Ingredient

Linuron 41%

Inert Ingredients 59%

Background

DuPont has submitted Acute Oral, Acute Dermal, Eye and Skin Irritation studies in support of the conditional registration of this product. Each of the studies was conducted at the Haskell Laboratory for Toxicology and Industrial Medicine. In all of the studies the test material was Lorox 4L. The method of support is "Cite-All." The Accession Number is 237890.

Recommendations:

1. The signal word is "Caution" as proposed by the registrant.
2. The Acute Oral study is Core Supplementary Data until such time as the 95% confidence range for the Acute Oral LD₅₀ test can be explained. Also, the number of animals tested per dosage level (i.e., 20 at 1900 mg/kg; 30 at 2000 mg/kg should be included with these data. After the submission of this additional information, FHB/TSS can consider upgrading the study classification to Core Minimum Data.
3. The Acute Dermal, Eye and Skin Irritation studies are adequate and acceptable for the conditional registration of this product.
4. An Acute Inhalation study was not submitted. Under the "Cite-All" method of support, this study need not be submitted at this time.

5. FHB/TSE has no objection, based on adverse effects on humans and domestic animals, to the conditional registration of this product provided that the following labeling revisions are made and additional information on the Acute Oral study is submitted (see Recommendation #2).

Labeling

1. The statement "It is a violation of Federal law to use this product in a manner inconsistent with its labeling" must appear directly underneath the heading "Directions for Use."
2. The heading "Hazards to Humans" should be changed to "Hazards to Humans and Domestic Animals." This statement must be preceded by the signal word. Therefore, the order of Precautionary Statements should be (1) Child Hazard Warning, (2) Signal Word, (3) "Hazards to Humans and Domestic Animals" heading followed by the appropriate precautionary statements, (4) "Environmental Hazards" heading followed by the appropriate statements. Format labels have been enclosed for the convenience of the registrant.
3. Because of the Toxicity Category III rating on the Eye Irritation study, the following precautionary statements must be added to the labeling:

"In case of contact with eyes, immediately flush with plenty of water. Get medical attention if irritation persists."

Review:

1. Oral LD₅₀ Test; Report # 101-79; March 6, 1979.

Procedure: 11 groups of 10 M Chr-CD strain rats received oral dosages of 1000, 1500, 1850, 1900, 1900, 1950, 2000, 2000, 2000, 3000, and 4000 mg/kg of the test substance. Six groups of 10F Chr-CD strain rats received oral dosages of 1800, 2000, 2500, 2500, 3500, 4000 mg/kg of the test substance. Animals were observed 13-15 days, survivors sacrificed at termination of study and all animals subjected to gross pathological examination

Results: In the M groups no deaths at 1000 and 1500 mg/kg; at 1850 mg/kg 3/10 died; 1/20 deaths at 1900 mg/kg; no deaths at 1950 mg/kg; 10/30 died at 2000 mg/kg; 9/10 died at both 3000 and 4000 mg/kg. The LD₅₀ was 2437 mg/kg with a 95% confidence range of 2059-5661 mg/kg, slope was 8.7.

The P groups showed 2/10 deaths at 1800 mg/kg; 1/10 deaths at 2000 mg/kg; 3/20 deaths at 2500 mg/kg; 4/10 deaths at 3500 and 6/10 deaths at 4000 mg/kg. LD₅₀ was 3935 mg/kg with a 95% confidence range of 3120-13450 mg/kg, slope was 3.27.

Symptoms included ataxia, belly-to-cage posture, catarrhorrhea, lethargy, stained face/fur, exophthalmos, lacrimation, prostration, salivation, weakness, wet perineal area, alopecia, shallow and rapid breathing, cyanosis, diarrhea, corneal opacity, humped posture, limpness, pallor and piloerection. Pathological examination revealed: lungs - heavy, hyperinflated, discolored; liver - dark, lobular markings prominent; thymus - discolored, mottled; gastrointestinal tract - filled with paste-like material, sloughing of squamous mucosa and glandular section; heart - firm; spleen - discolored; abnormal size; brain - change in consistency; trachea - foamy exudate; kidneys - hydronephrosis; testis - small; adrenals - discolored.

Study Classification: Core Supplementary Data until such time as additional information is submitted. An explanation for the wide 95% confidence range in the Acute Oral LD₅₀ study should be submitted. Also, the reason for dosing so many animals at the 1800 and 2000 mg/kg level should be explained.

2. Skin Absorption LD₅₀ in Male and Female Rabbits;
Report # 746-73; December 15, 1973.

Procedure: SM and SF albino rabbits with abraded skin received an application of 2 g/kg of the test material. Exposure was for 24 hours under occlusive wrap. Animals were observed for 14 days. At termination of study 2M, 2F survivors were subjected to pathological examination.

Results: No mortalities. No significant gross pathological alterations were observed.

Study Classification: Core Minimum Data.

Toxicity Category: III-CAUTION.

3. Eye Irritation Test in Rabbits - Federal Hazardous Substances Act; Report #632-73; December 15, 1973.

Procedure: 0.1 ml of test material was applied into one eye of each of 6 albino rabbits. Scoring at 24, 48 and 72 hours.

Results: No effect observed on cornea or iris. 3/6 exhibited conjunctival redness, 4/6 exhibited conjunctival swelling on day 1; all scores were 0 by day 2.

Study Classification: Core Minimum Data.

Toxicity Category III - CAUTION

4. Federal Hazardous Substances Act - Skin Irritation Test on Rabbits; Report #673-78; December 1, 1978

Procedure: 0.5 ml of test material was applied to intact and abraded skin of 6M albino rabbits. The animals were exposed under occlusive wrap for 24 hours; observations at 24 and 72 hours.

Results: Primary Irritation Index was 1.1

Study Classification: Core Minimum Data. Individual scores were not submitted.

Toxicity Category: IV

RD/FHB:SSterling:rfr274:DCR#13558:RAVEN:479-2018:12/13/79