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012498

DATA EVALUATION RECORD

STUDY TYPE: Acute Oral Toxicity
OPPTS 870.1100 OPP 81-1

DP BARCODE: D227387 SUBMISSION CODE: S506628

PC CODE: 099901 TOX. CHEM. NO. 613 C

TEST MATERIAL (PURITY): Skane M-8 HQ Microbicide, (46.7%)

SYNONYMS: 2-Octyl-3(2H)-isothiazolone, Kathon, Octhilinone, Microbicide M-8, RH-893, CAS# 26330-20-1.

CITATION: Romanello, A.S., Krywicki, K.M. and G.A. Hazleton (1987) Skane M-8 Microbicide. Acute oral toxicity study in male and female rats. Rohm and Haas Company, Spring House, PA 19477 Laboratory Project ID 86R-178 A and B. March 18, 1987. MRID 41482502. Unpublished.

SPONSOR: Rohm and Haas Company

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 41482502), groups of fasted, young adult Charles River CD rats (10/sex) were given a single oral dose of Skane M-8 HQ Microbicide (46.7% a.i.) in propylene glycol at doses of 300, 500, 800, 1200 or 2000 mg/kg (representing 126, 210, 336, 504 or 839 mg/kg a.i.) and observed for 14 days.

Oral LD50 (Skane M-8 HQ) Males = 760 (603-937) mg/kg
(Skane M-8 HQ) Females = 767 (603-987) mg/kg
(a.i.) Males = 318 (251 - 396) mg/kg
(a.i.) Females = 324 (254-418) mg/kg

Toxicity Category: ~~II~~ III

Clinical signs included passiveness, ataxia, abdominal breathing and distension, moribundity, pale extremities, salivation, respiratory noise, cool to touch, lacrimation, scant droppings, diarrhea, tan or red stained muzzle and/or brown or yellow stained anogenital area occurring

within the first 4-5 days of dosing. One female showed signs of toxicity at days 8-14. Signs observed at necropsy in both sexes included reddened stomach mucosae or intestines, yellow or white fluid-filled stomach or intestines, red or tan stained muzzle and/or brown or yellow stained anogenital area. All other findings were considered incidental or post mortem changes and not treatment related. Necropsy of the survivors in both sexes revealed no treatment related changes. The changes in body weights by treatment might be significant based on the less body weight gain in the treated males vs. controls, however, no fair judgement could be made due to the poor copy of the report and missing raw data.

The acute oral toxicity study is classified as acceptable/guideline. This study does satisfy the guideline requirement for an acute oral toxicity study (81-1) in rats.

COMPLIANCE: Signed and dated Quality Assurance, GLP and Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Skane M-8 HQ Microbicide
   Description: yellow liquid
   Lot/Batch #: SW85-0311
   Purity: 46.7%
   CAS#: 26330-20-1

2. Vehicle and/or Positive Controls: propylene glycol 53.3%

   Test Animals: Species: Rat
   Strain: Charles River CD
   Age and/or weight at dosing: 211-225 for males (mean wts.)
   162-171 for females (mean wts.)
   Source: not reported
   Acclimation period: not reported
   Diet: not reported
   Water: not reported

B. STUDY DESIGN AND METHODS:

1. In life dates and start: August 4, 1986; end: August 18, 1986

2. Animal Assignment and treatment: Animals were assigned to the test groups noted in Table 1. Rats were fasted overnight and given a single dose of the test substance at a constant volume of 10 ml/kg by gavage and then observed daily for signs of toxicity and mortality. Body weights were taken initially and at termination. Survivors were sacrificed and a necropsy was performed.

Table 1. Doses, Mortality/Animals Treated

| Dose Skane M-8 HQ (mg/kg) | Dose a.i. (mg/kg)[1] | Males | Females | Combined |
|---|---|---|---|---|
| 0 | 0 | 0/10 | 0/10 | 0/20 |
| 300 | 126 | 0/10 | 1/10 | 1/20 |
| 500 | 210 | 1/10 | 1/10 | 2/20 |
| 800 | 336 | 7/10 | 4/10 | 11/20 |
| 1200 | 504 | 8/10 | 9/10 | 17/20 |
| 2000 | 839 | 10/10 | 10/10 | 20/20 |

1. Data provided in a memorandum of W. Greear dated August 26, 1993.

3. Statistics: not reported.

II. RESULTS AND DISCUSSION:

A. Mortality is given in Table 1. Deaths occurred within the first 3 days of dosing. One female died between days 8-14.

The oral LD50 for: Skane M-8 HQ in males is 760 (603-937) mg/kg.
Skane M-8 HQ in females is 767 (603-987) mg/kg.
a.i. in males in 318 (251-396) mg/kg
a.i. in females is 324 (254-418) mg/kg

B. Clinical Observations: Toxic signs included passiveness, ataxia, abdominal breathing, moribundity, salivation, distended abdomen, pale extremities, respiratory noise, cool to touch, lacrimation, scant droppings, diarrhea, tan or red stained muzzle and/or brown or yellow stained anogenital

areas. Recovery was generally with 4 days of dosing.

C. Body Weight: The changes in body weights by treatment might be significant based on the less body weight gain in the treated males vs. Controls, however, no fair judgement could be made due to poor copy of the report and missing raw data.

D. Necropsy: Signs included reddened stomach mucosae and intestines, yellow or white fluid filled stomach or intestines, red or tan stained muzzle and/or brown a yellow stained anogenital area. Necropsy of survivors revealed no treatment related changes.

E. Deficiencies: The most serious deficiency was that the TGAI was not tested. However, the study is still adequate. The onset of signs was not observed for each toxic sign, rather a general indication of onset of "toxic signs" was provided. Although parts of the report was illegible, the information provided was satisfactory. Lack of detail regarding source of animal, diet, etc., were minor deficiencies which did not seriously detract from the study.