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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: EPA Registration #4581-116. Acute Oral Toxicity and Delayed Contact Dermal Sensitization Studies with Kryocide. CAS No. 264 Accession No. 252071

TO: Marylin Mautz (16)
Registration Division (TS-767C)

THRU: Edwin Budd
Head, Review Section II
Toxicology Branch
Hazard Evaluation Division (TS-769C)

Budd 9/12/84

FROM: William Woodrow, Ph. D.
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WSW 8/15/84

Registrant: Pennwalt Corporation
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Action Requested:

The Pennwalt Corporation submitted the two toxicity studies mentioned above in response to cited data gaps listed in the Cryolite Registration Standard.

Recommendations:

The two toxicity studies reviewed in the present report are acceptable and have been classified Core Minimum Data:

1) Acute oral toxicity evaluation of Kryocide, rat.

LD_{50} > 5.0 g/kg
Toxicity Category IV

2) Dermal sensitization evaluation of Kryocide, guinea pigs. Kryocide was not a sensitizing agent.

Review of Data:

1) Acute Oral Toxicity Evaluation of Kryocide in the Rat. Sponsor: Pennwalt Corp. Tester: Hazleton Laboratories, Report No. 814515, ~~Oct. 12~~ Nov. 10, 1983.

Test Material. Kryocide formulation Na_3AlF_6 (Sodium fluoaluminate) approximately 96.0% pure.

Detailed Formulation (Confidential)

Active Ingredient

sodium fluoaluminate	96.0%

Inert ingredients

[redacted]

Following a 7 day laboratory acclimation period, 5 male and 5 female Sprague-Dawley rats weighing between 207 and 283 g were dosed by gavage with 5g/kg b. wt. each.

The test material was mixed with distilled water to a concentration of 0.5g/ml, and each animal was administered 10 ml of the Kryocide/water mixture.

Each animal was observed for clinical signs of toxicity and mortality at 1.0, 2.5 and 4.0 hours post-dosing and once daily for clinical signs and twice daily during a 14 day observation period. Body weights were recorded pre-treatment, at 7 days, and at termination.

All animals were subjected to gross necropsy at termination; all abnormalities were recorded.

Results

No mortality. Animals gained weight during the observation period. No lesions were visible at necropsy. Three males and one female rat appeared hypo-active on day 1 post exposure.

Acute oral LD_{50}, Kryocide in the rat:

$LD_{50} > 5g/Kg$

Toxicity Category IV
Classification: Core Minimum Data

2) Dermal Sensitization Evaluation of Kryocide in Guinea Pigs. Sponsor: Pennwalt Corp. Tester: Hazleton Laboratories. Report No. 814516, Dec. 13, 1983.

Test Material - Kryocide formulation.

Twenty four male Hartley strain guinea pigs were divided into: a) one group of 10 test animals, b) one group of 10 non-sensitized (but challenged animals), and c) one group of 4 positive control animals.

A dosing range study was conducted prior to the sensitization study to determine a threshold level for Kryocide; the test material for the actual study was administered at 50% W/V in 0.9% saline for both the sensitizing and challenge doses.

For the positive control with DNCB (dinitrochlorobenzene), a concentration of 0.3% DNCB W/V in 80% ETOH for the sensitizing doses, and 0.1% W/V in acetone for a challenge dose.

The delayed hypersensitivity test was actually a delayed contact hypersensitivity potential test. All of the challenge and sensitizing applications were 0.4 ml.

Hair was removed from the back of each animal prior to testing. 0.4 ml of appropriate test material was placed on an adhesive pad, and the pad placed on a skin test site and maintained in place with occlusive dressing for a period of 6 hours, after which the dressing and application pad was removed.

The test chemical and positive applications were similarly applied.

All animals (excepting untreated controls) received one application per week, for a total of three applications. Two weeks following the third sensitizing application a challenge dose of 90% W/V test material in 0.9% saline was administered to the flank opposite to the sensitizing doses of all test animals, and at the same time, all of the untreated control animals received the same challenge dose.

The positive control animals were similarly challenged with a 0.1% W/V suspension of DNBC in acetone.

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All application and challenge sites were examined for dermal irritation at 24 and 48 hours post treatment according to the Buehler method[1].

The Buehler sensitization scoring scale:

no reaction	0
very faint erythema, usually nonconfluent	0.5
faint erythema, usually confluent	1.0
moderate erythema	2.0
strong erythema, with or without erythema	3.0

Results

1) Test animals (Kryocide). One animal showed very faint erythema during sensitizing phase; 0.5 score. No reactions to challenge applications.

2) Positive controls (DNCB). All animals gave a score of 2.0 (moderate erythema), which was considered positive.

3) Untreated controls (challenged). No reactions.

NOTE: All animals on test appeared normal throughout the study. Body weights throughout the study were normal, except one of the untreated control animals, "which showed a 7 gram weight loss during the last 3 days of the study".

Conclusions: Kryocide was not found to be a sensitizing agent.

Classification: Core Minimum Data

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[1] Buehler, E.V., and Ritz, H.L. Planning, conduct, and interpretation of guinea pig sensitizing patch tests. Current concepts in cutaneous toxicity. p.28(1980).