

US EPA ARCHIVE DOCUMENT

PP-515
TKR-879P
5-2-84



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

003798

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: EPA Reg. No. 279-GNET: Change in formulation: review
of acute toxicity studies to support labeling

TOX Chem. No. 271DD

TO: Timothy A. Gardner
Product Manager (17)
Registration Division (TS-767)

THRU: William Burnam, Branch Chief
Toxicology Branch,
Hazard Evaluation Division (TS-769)

ERIC 5/2/84

FROM: John D. Doherty *[Signature]* 5/2/84
Toxicology Branch
Hazard Evaluation Division (TS-769)

Background:

The FMC Corporation (Philadelphia, PA) has made changes in the formulation of their product Ammo 2.5 EC and has submitted acute toxicity studies and a dermal sensitization study to support the labeling of their new formulation.

The new formulation results in a change in the signal word from DANGER to CAUTION.

Comments:

1. The five studies submitted were reviewed and found to be CORE MINIMUM or higher.
2. The signal word CAUTION for the new formulation is appropriate based on review of the supporting studies.
3. The precautionary statements should contain the precaution "avoid contact with skin, may cause sensitization reaction in some individuals" or other precautionary statement for warning of possible sensitization reactions.
4. The inerts described [redacted] not listed in Toxicology Branch's files. These will have to be cleared for the proposed agricultural use.

INFORMATION WHICH MAY REVEAL INERT INGREDIENTS IS NOT INCLUDED

[Handwritten signature]

Studies Reviewed

Study	Results	Core Classification
Acute Oral LD50 -rats	1488(1230-1745)mg/kg-males 1182(916-1148) mg/kg-females 1403(1220-1586)mg/kg-combined sexes	Guidelines
Acute Dermal LD50 -rabbits	>2000 mg/kg (both sexes)	Minimum
Primary Dermal Irritation -rabbits	P.I.S. = 1.7	Minimum
Primary Eye Irritation -rabbits	Transient irritation	Guidelines
Dermal Sensiti- zation -guinea pigs	1/10 guinea pig showed a positive response	Minimum

Review of Studies (Refer to EPA Acc. No. 252014)Acute Oral Toxicity of FMC 45806 Ammo 2.5E in Rats.

FMC Toxicology Laboratory, Study No. A83-860, (signed June 10, 1983).

7 groups of 10 male Sprague-Dawley rats (~ 250 gm in body weight) were dosed with the test material (Ammo 2.5E) as a 10% solution in corn oil at dose levels of 100, 300, 500, 700, 1200, 1500 and 2000 mg/kg; 5 groups of 10 female rats were dosed with 700, 800, 1500, 2000 mg/kg. The rats were fasted overnight prior to dosing. The rats were observed for reactions for 14 days after dosing.

LD50's of

1488 (1230-1745) mg/kg for males
1182 (916 - 1148) mg/kg for females
1403 (1220-1586) mg/kg for combined sexes

were determined.

The clinical reactions to treatment included clonic convulsions, loss of muscle control, ataxia, decreased locomotion, abdominogenital staining, oral, ocular and nasal discharges. Most of the clinical signs persisted for only a day or so except for abdominal staining and in some cases decreased locomotion. Necropsy of the survivors was unremarkable; the survivors also gained weight.

Conclusion: The study is CORE GUIDELINES. The product may be classified as Tox Cat. III.

Acute Dermal Toxicity of FMC 45806 2.5E in Rabbits.

FMC Toxicology Laboratory, Study No. A83-861, dated May 31, 1983.

A single group of 10 New Zealand white rabbits (5 males and 5 females) were prepared by clipping (not abraded) and dosed with 2000 mg/kg of test material (Ammo 2.5E) and were observed for 14 days. [Note: The specific gravity of the test material is 0.97 gm/ml and the dose was adjusted accordingly.]

No rabbits died. The symptoms noted included loss of muscle control (persisting to 4 days) and occasional nasal discharge. Local irritation at the application site resulted that was described as "erythema, eschar and exfoliation" at termination. The rabbits lost weight following application but showed signs of recovery. Necropsy was unremarkable.

CONCLUSION: This study is CORE MINIMUM. A single dose level was used. The product may be classified as Tox Cat. III.

Primary Dermal Irritation Study of FMC 45806 2.5E in Rabbits.

FMC Toxicology Laboratory, Study No. A83-862 May, ²⁰1983.

A single group of 6 New Zealand White rabbits (3 males and 3 females) were prepared by clipping their fur and abrading one test site. The rabbits were dosed with 0.5 ml of test material (Ammo 2.5E) at each side (one 0.5 ml application to an abraded and one 0.5 ml application to an intact site). The test material was kept in place for 4 hours.

A Primary Irritation Score of 1.7 (combined sexes) was determined.

CONCLUSION. This study is CORE MINIMUM. The product may be classified as toxicity category III.

Primary Eye Irritation Study with Ammo 2.5E in Rabbits

FMC Toxicology Laboratory, Study #A82-719, May 13, 1982.

9 New Zealand White rabbits were prepared and were dosed by instilling 0.1 ml of test material (Ammo 2.5E) into their right eye. The left eye served as a control. The eyes of three rabbits were washed with 100 ml of lukewarm water 20-30 seconds after instillation. The eyes were monitored for 4 days after instillation. They were examined by using sodium fluorescein dye.

Some signs of minimal corneal opacity developed in 2 rabbits, but this was transient (<24 hours). The eyes were reported as recovered from all signs of irritation by the fourth day.

This study is CORE GUIDELINES. The product may be classified as Tox Cat. **III**.

Guinea Pig Sensitization (FMC 45806 2.5E)

Stillmeadow, Inc. Project No. 2909-83 (FMC #A83-863), July 6, 1983.

Two groups of 10 male guinea pigs (Hartley-albino) were prepared and assessed for sensitization effects of the test material (Ammo 2.5E) or the positive control (0.05% w/v solution of 2,4-dinitrochlorobenzene). The induction phase of the study consisted of making 10 dermal applications (test material in gauze patches) of 0.5 ml of test material (as a 10% w/v solution in deionized water). The test materials were kept in contact for 6 hours. A challenge dose (same concentration) was made on "day 35" (14 days after the last induction dose).

The positive control produced the expected positive response.

The Ammo 2.5E produced a positive response in at least one guinea pig. The response was considered to be minimal.

CONCLUSION: This study in CORE MINIMUM. This study shows that Ammo 2.5E is potentially positive for a sensitization reaction. It should be noted that other studies with cypermethrin also showed potential positive responses in sensitization studies. In this regard, the label should contain the precautionary statement "Avoid contact with skin. May cause sensitization reactions in some individuals."

CYPERMETHRIN TOXICOLOGY REVIEWS

Page 5 is not included in this copy.

Pages _____ through _____ are not included in this copy.

The material not included contains the following type of information:

- Identity of product inert ingredients
 - Identity of product impurities
 - Description of the product manufacturing process
 - Description of product quality control procedures
 - Identity of the source of product ingredients
 - Sales or other commercial/financial information
 - A draft product label
 - The product confidential statement of formula
 - Information about a pending registration action
 - FIFRA registration data
 - The document is a duplicate of page(s) _____
 - The document is not responsive to the request
-

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

003798

HED:DCR-34226:J.Doherty:bje:Raven:557-2226:CBI.18:4/6/84
REVISED-34279:J.Doherty:pac:Raven:557-2226:CBI.18:4/13/84

CYPERMETHRIN TOXICOLOGY REVIEWS

Page _____ is not included in this copy.

Pages 7 through 12 are not included in this copy.

The material not included contains the following type of information:

- Identity of product inert ingredients
 - Identity of product impurities
 - Description of the product manufacturing process
 - Description of product quality control procedures
 - Identity of the source of product ingredients
 - Sales or other commercial/financial information
 - A draft product label
 - The product confidential statement of formula
 - Information about a pending registration action
 - FIFRA registration data
 - The document is a duplicate of page(s) _____
 - The document is not responsive to the request
-

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
