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

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 279-GREN Cynoff 2.5 EW Insecticide; 279-GRRI Prevail 4.0 Termiticide

FROM: Ian Blackwell
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

E 9/30/91

TO: George LaRocca PM13
Insecticide Rodenticide Branch
Registration Division (H7505C)

APPLICANT: FMC Corporation
Pest Control Specialities Operations
2000 Market Street
Philadelphia, PA 19103

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.	
	279-GRRI	279-GREN
Cypermethrin	43.2	27.9
Inert Ingredients:.....	56.8	72.1
	100.0	100.0

BACKGROUND: The applicant, FMC Corporation, has submitted acute oral, acute dermal, acute inhalation, primary eye irritation, primary dermal irritation and dermal sensitization studies to support the registration of the products Cynoff 2.5 EW Insecticide and Prevail 4.0 Termiticide. The studies were conducted at FMC Corporation Toxicology Laboratory using Prevail 4.0 Termiticide. The MRID numbers are 418176-01 and 417865-02 through 417865-06. In a letter dated January 24, 1991, the registrant states that the product Prevail 4.0 EW Termiticide is also known as FMC 30980 4EW and Ammo 4 EW.

RECOMMENDATIONS: RSB/PRS findings are as follows,

1. The studies conducted using Prevail are acceptable for the registration of Cynoff due to substantially similar formulations of the products. The only differences are a reduction from 43.2% active ingredient in Prevail to 27.9% in Cynoff and a compensatory increase in the volume of [redacted]

2. The acute oral toxicity, acute dermal toxicity, primary eye irritation, and primary dermal irritation studies are categorized as core guideline data and are acceptable for the registration of the product Prevail 4.0 Termiticide.

3. The dermal sensitization study is acceptable to support registration of the product Prevail 4.0 Termiticide. This study is graded as core-minimum because no positive control group was tested. It is recommended that a positive control test be conducted at least every six months.

4. The acute dermal toxicity, primary eye irritation, primary dermal irritation and dermal sensitization studies are acceptable for the support of the product Cynoff 2.5 EW Insecticide.

5. The acute oral toxicity study is not acceptable to support registration of the product Cynoff 2.5 EW. An acute oral toxicity study conducted on Cynoff 2.5 EW must be performed. Because this study received a toxicity category rating of II, the lower concentration of some components in Cynoff 2.5 EW may cause its signal word to vary.

6. The acute inhalation toxicity study is unacceptable to support registration of either product and must be reconducted. The concentration achieved in the study (0.222 mg/L) is too low for consideration as a limit test, and the study does not define whether the test material is in toxicity category II or III. The registrant should consider the following points when reconducting the study:

   a. Consider first testing Prevail 4.0 Termiticide. If acceptable acute inhalation data can be obtained demonstrating that Prevail 4.0 Termiticide is in toxicity category III or IV, then this data can be used to support Cynoff 2.5 EW. However, if inhalation data on Prevail 4.0 termiticide demonstrates that it is in category I or II, then an acute inhalation study study must be conducted using Cynoff 2.5 EW.

b. Perhaps the laboratory should consider using a nose-only exposure since the test material is rather toxic orally (Category II), and the laboratory took special efforts to minimize dermal exposure by using an elutriator which removed large particles and may have contributed to the extremely low test material concentration.

c. Regardless of the laboratory's decision to conduct a nose-only or another whole-body exposure, the study must provide an acceptable test material concentration and mass median aerodynamic diameter that will clearly indicate the toxicity category of the test material.

7. The signal word for both products is "WARNING" based on the acute oral toxicity study. The signal word may be changed upon submission of the outstanding acute inhalation toxicity data and acute oral data for Cynoff 2.5 Termiticide.

LABELING:

1. Precautionary statements for both products should be revised to:

"May be fatal if swallowed. Harmful if inhaled or absorbed through skin. Avoid contact with skin, eyes or clothing. Avoid breathing dust. Wash thoroughly with soap and water after handling and before eating or smoking. Remove contaminated clothing and wash before reuse."

2. Statements of Practical Treatment for dermal exposure to both products should be revised to:

"<u>If On Skin</u>: Wash with plenty of soap and water. Get medical attention."

3. The Note To Physician for both product should be revised to delete the phrase "Oral toxicity is low,..." as this claim is not supported by the data.

4. The Statements of Practical Treatment and Precautionary Statements for both products may be revised upon submission of the outstanding data.

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DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§81-1)

Product Manager: (13).
Reviewer: Ian D. Blackwell Report Date: 3/29/90
MRID No.: 418176-01. Study No: A39-3131.
Testing Facility: FMC Corporation Toxicology Laboratory.
Author(s): Christine Freeman.

Species: Sprague-Dawley rat.
Sex: 5 male + 5 female.
Age: young adult.
Weight: 205-274 grams.
Source: Taconic Farms, Germantown, New York.

Test Material: Ammo (Formulation EW).
Observation Days (Post Exposure): 14
Quality Assurance (40 CFR §160.12): Included.

Conclusion:

1. LD50 (mg/kg): Males (M) = Not determined *
   Females (F) = 193 (120-265)

* Because females were determined to be more sensitive at 250 mg/kg, males were not used for testing at 100 and 175 mg/kg. Therefore the ~~the~~ LD_{50} calculated for the females will used for both sexes.

2. Toxicity Category: II.
   Classification: core- guideline

Procedure (Deviations From §81-1):

Results:

Reported Mortality

Dosage (mg/kg)	Mortality Ratio (number killed/number tested)		
	Males (M)	Females (F)	Combined (C)
250	4/5	5/5	9/10
175	---	1/5	1/5
100	---	0/5	0/5

Observations: Toxic symptoms observed were clonic convulsions, tremors, rales, bloody oral discharge, ataxia, splayed hind limbs, mydriasis, abdominogenital staining, chromorhinorrhea, dyspnea, hypersensitivity to touch, loss of muscle control, lacrimation, decreased locomotion and recumbency.
No abnormalities were noted at gross necropsy.

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DATA REVIEW FOR
ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager (PM): 13 .
Reviewer: Ian D. Blackwell Study No.: A89-3132
MRID No.: 417865-02 . Report Date: March 19,1990.

Testing Laboratory: FMC Corporation Toxicology Labaratory .
Author(s): Christine Freeman .

Species : New Zealand White rabbit .
Sex : 5 males + 5 females . Wt.: 2.36 to 2.76 kg .
Source: Hazleton Research Animals, Inc. .

Test Material: Ammo (Formulation 4 EW) .
Dosage: 2000 mg/kg on 4x4 in. gauze pad .

Quality Assurance (40 CFR §160.12): Included

Summary:

LD50: >2000 mg/kg .
Toxicity Category: III .
Classification: core - guideline.

Procedure (Deviations From §81-2):

Results:

1. Reported Mortality

Dosage (mg/kg)	Mortality Ratio (number killed/number tested)		
	Males (M)	Females (F)	Combined (C)
2000	0/5	0/5	0/10

2. Observations: Animals exhibited abdominal distention, decreased or no feces, dehydration, diarrhea, mucoid anal discharge, poor food consumption, soft stool, weight loss, erythema and edema.
No abnormalities were noted at necropsy.

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DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3)

Product Manager (PM): 13 .
Reviewer: Ian D. Blackwell Study No.: A89-3133
MRID No.: 417865-03 . Report Date: June 29,1990 .

Testing Laboratory: FMC Corporation Toxicology Laboratory .
Author(s): Everett Mount .

Species: Sprague-Dawley rats .
Wt.: 222 to 270 grams .
Sex : 5 male + 5 female .
Source: Taconic Farms .

Test Material: Ammo (Formulation 4 EW) .
Conc.(mg/l): 0.222 gravimetric; 0.35 analytical.

Quality Assurance (40 CFR §160.12): Included .

Summary:
LC50:> 0.222 mg/l (gravimetric) .
Toxicity Category: .
Classification: core - supplementary.

Procedure (Deviations From §81-2):
Concentration was too low for the limit test.

Results:

1. Reported Mortality

Concentration (mg/l)	Mortality Ratio (number killed/number tested)		
	Males (M)	Females (F)	Combined (C)
0.222 (gravimetric)	0/5	0/5	0/10

MMAD =2.52 um
At second sampling, 43.6% of the particles were below 2.6 um.
(Airflow was above 10 air chamber changes per hour.)

Observations: Clinical signs noted during the exposure were difficulty breathing, nasal discharge, oral discharge lacrimation and squinting eyes. Clinical signs noted post exposure were abdominogenital staining, ataxia, decreased locomotion, swollen cheeks, chromodacryorrhea, chromorhinorrhea, lacrimation, nasal and oral discharge, rales, walking on toes and tremors.
No gross lesions were found at necropsy.

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DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager (PM): 13 .
Reviewer: Ian D. Blackwell Study No.: A89-3134
MRID No.: 417865-04 . Report Date: 3/21/90 .

Testing Laboratory: FMC Corporation Toxicology Laboratory .

Author(s): Christine Freeman .

Species: New Zealand White rabbit (six) .
Source: Hazleton Research Animals, Inc. .
Age: Young adult .
Weight: 3.13 to 3.71 kg .

Test Material : Ammo 4 EW .
Dosage: 0.10 ml into right eye .

Quality Assurance (40 CFR §160.12): Included

Summary:

Toxicity Category: IV .
Classification: core - guideline .

Procedure (Deviation From §81-4): An anesthetic, 0.5% Tetracaine hydrochloride, was used two times in each eye prior to the administration of the test material.

Results:

	Observations (number "positive"/number tested.							
	Hour 1	Days 1	2	3	4	7	14	21
Cornea	0/6	0/6	0/6	0/6	0/6	---	---	---
Iris	1/6	0/6	0/6	0/6	0/6	---	---	---
Conjunctivae								
Redness	0/6	0/6	0/6	0/6	0/6	---	---	---
Chemosis	0/6	0/6	0/6	0/6	0/6	---	---	---
Discharge	3/6	0/6	0/6	0/6	0/6	---	---	---

Comments: No observations given for period after Day 4.

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DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5)

Product Manager (PM): 13 .
Reviewer: Ian D. Blackwell Study No.: A89-3135
MRID No.: 417865-05 . Report Date: 3/20/90 .

Testing Laboratory: FMC Corporation, Toxicology Lab.

Author(s): Christine Freeman .

Species: New Zealand White rabbits (young adult) .

Sex : 3 males + 3 females .
Weight: 3.21 to 3.59 kg .
Source : Hazleton Research Animals, Inc.

Test Material : Ammo (Formulation 4 EW) .
Dosage : 0.5 ml on a 2x2 inch gauze pad .

Quality Assurance (40 CFR §160.12): Included .

Summary: The Primary Irritation Index = 0/8.0 .

Toxicity Category: IV .

Classification: core - guideline .

Procedure (Deviations From §81-5): None

Results:

No dermal irritation was noted at 30 minutes, or 24, 48 or 72 hours.

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DATA REVIEW FOR
SKIN SENSITIZATION TESTING (§81-6)

Product Manager (PM): 13 .
Reviewer: Ian D. Blackwell Study No.: A89-3136
MRID No.: 417865-06 . Report Date: 4/18/91

Testing Laboratory: FMC Corporation Toxicology Lab .

Author(s): Christine Freeman .

Species: Hartley guinea pigs .
Source: Hazleton Research Animals, Inc. .
Sex : 15 males + 15 females .
Weight: 348 to 431 grams (initial) .

Test Material : Ammo 4 EW (tan liquid) .
Dosage: 0.30 ml .
Positive Control: Not specified .

Quality Assurance (40 CFR §160.12): Included .

Method: Modified Buehler Method .

Summary:

This product is not a dermal sensitizer.

Classification: core - minimum .

Procedure (Deviation From §81-6): No positive control test was performed.

Results: After 1st induction treatment, 3/20 test animals exhibited very slight to well-defined erythema and 3/20 exhibited very slight to slight edema. After the 2nd induction treatment, 2/20 test animals exhibited very slight erythema. After the 3rd induciton treatment, 2/20 test animals exhibited very slight erythema, 1/20 exhibited very slight edema and 1/20 exhibited scabbing at the test site.

At challenge, 7/20 test animals displayed very slight to well defined erythema and 1/20 exhibited slight edema. In the naive challenge control group, 8/10 exhibited very slight erythema and 2/10 exhibited very slight edema.