5-21-81

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

MAY 21 1981

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MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

DATE:

SUBJECT: EPA Reg. No. 279-EUP-IA. Multicrop Use of FMC 45806 2.5EC (AMMO®) Insecticide Containing Cypermethrin. Revised Submission.
TOX Chem. No. 271DD

FROM: John Doherty 5/10/81
Toxicology Branch/HED (TS-769)
RR Loche, for E. Budd 5/20/81

TO: F. D. R. Gee, PM #17
Registration Division (TS-767)

Action Requested:

The FMC Corporation is requesting an Experimental Use Permit to use cypermethrin (AMMO® 2.5 EC formulation) on 19 different crops in nearly all of the contiguous United States. Use of as much as 3635 lb./a.i. is requested and the duration of this permit is for 2 years. A total of 2022 acres of crops are involved in the request.

No food tolerances are requested and the label includes instructions that treated crops should be used for research purposes only or be destroyed by burning or burying.

NOTE: This EUP request was originally submitted to EPA by the FMC Corporation with a letter dated December 5, 1980. A revised request was submitted with a letter dated March 26, 1981. The revised EUP program requests some modifications in the types of crops to be treated and the total acreage involved. This memo addresses the conditions requested in the revised request.

Conclusions:

Toxicology Branch has no objection to granting this EUP program provided that:

1. The crop destruct clause is enforced and the treated crops are destroyed.

2. The product label should be changed to express more clearly that the DANGER signal word reflects the corrosive nature of the contents to the eyes.

For example the precautionary statement on the label should read:

CORROSIVE. Causes eye damage. Do not get in eyes, on skin or on clothing. Wear goggles or face shield when handling. May be fatal if swallowed (etc. as in original label).

Remarks:

Three reports related to incidences of human exposure were included in the data package, these were:

1. FMC report dated June 21, 1976 (M. A. Guiducci).

2. Chemical toxicity inventories FMC Corporation Princeton and Middleport, December 12, 1979 (F. L. Lyman, M.D.).

3. Article entitled: Exposure and Medical Monitoring Study of a New Synthetic Pyrethroid After one Season of Spraying on Cotton in Ivory Coast.

   G. H. Prinsen and N. J. Van Sittert
   Shell Corporation

Report No. 1 above provides evidence that some workers when exposed to cypermethrin may develop transient tingling sensations about the face and possibly other areas.

Summary of Toxicity studies with FMC 45806 2.5EC Cypermethrin formulation:

Study	Results	TOX Cat.	Core Classification
1. Acute Oral LD50, rats	220 (178-271) mg/kg both sexes	II	Guideline
2. Acute Oral LD50, rats	156 (139-176) mg/kg both sexes	II	Guideline
3. Acute Inhalation LC50, (4 hours)	2.26 mg/l	III	Minimum
4. Dermal Irritation, rabbits	Draize score 2.0	III	Guideline
5. Eye Irritation, rabbits	Corrosive	I	Guideline

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6. Acute Dermal LD50, rabbits	> 2.0 gm/kg	III	Minimum
7. Sensitization, guinea pig (Buehler)	Not a sensitizer	-	N/A

(These studies and the three reports listed above are in EPA Accession No. 243861.)

Review of Studies

A. Studies with FMC 45806 2.5EC:

1. Rat Acute Oral

Stillmeadow, Inc., October 16, 1980, (1846-80).

Groups of 5 male and 5 female rats (COBS, SD) were dosed with 112, 134, 161, 193, 232 mg/kg of test material and observed for 14 days. Two additional female groups were dosed with 278 and 334 mg/kg of the test material. Actual undiluted test material was administered so that the volume for each dose group was different.

The animals in test groups receiving 112 and 134 mg/kg (with one exception) were reported as not developing either clinical symptoms or internal lesions. The physical signs of intoxication noted in the other test groups included salivation, convulsions, piloerection, polyuria, lacrimation, and others. These symptoms were present on the first day only. Necropsy revealed the presence of mucoid material in the g.i. track in the animals which died as a result of the test chemical.

The following LD50's with 95% confidence limits were noted:

Males:	185 (153-223) mg/kg
Females:	242 (178-327) mg/kg
Combined:	220 (178-271) mg/kg

This test is Core Guideline, Toxicity Category II.

2. Acute Oral Toxicity in Rats:

Cosmopolitan Safety Evaluation, Inc., September 25, 1980. (Study No. 0397A)

Groups of 5 male and 5 female rats were treated by gavage with a dose of 0.1, 0.14, 0.16, 0.175, 0.19, 0.225, 0.25 or 0.30 gm of diluted test material (2.5 EC formulation of cypermethrin).

The predominant signs were hypertoxicity, ataxia and convulsions. These were noted in most animals to varying degrees. The majority of the animals recovered within 24 hours. Body weight loss among survivors was considered within normal variation for the test groups except for some slight weight loss. Necropsy revealed fluid in the intestines of the animals which died as a result of the test chemical. Other discolorations of organs were also noted (red lungs, dark hearts, dark liver).

The following LD50's with 95% confidence limits were noted:

Males	180 (153-213) mg/kg
Females	137 (111-168) mg/kg
Combined	156 (139-176) mg/kg

Core Guideline, Toxicity Category II.

3. Four-Hour Acute Aerosol Inhalation Toxicity Study in Rats:

Toxigenics, Inc., September 22, 1980 (420-0275).

Five groups of 9 male and 9 female test rats were exposed to nominal concentrations of test material (FMC 2.5 EC cypermethrin formulation) for 4 hours and were then observed for 14 days before being sacrificed and necropsied.

The test material was generated into a 500 L test chamber and vented after the aerosol passed over the test animals.

Results:

LC50's were calculated:

Males	2.36 (2.13-2.62)	(95% confidence interval)
Females	2.18 (1.97-2.41)	
Combined	2.26 (2.08-2.47)	

Data are in time weighted average analytical concentration, it was stated that the particle size was less than 98% or more than 10 microns in diameter.

The test animals displayed oily fur, gasping, prostration, salivation, lacrimationn, ataxia, dyspnea, red stained fur, crusty eye and muzzle and other symptoms. Necropsy did not reveal unusual findings.

This test is Core-Minimum, Toxicity Category III.

NOTE: Atmospheric concentration was determined three independent ways:

i. nominal - test article used/total volume of air used,

ii. gravimetric - amount of material trapped on a glass filter/total volume of air

iii. analytical - samples of atmosphere.

Toxicology Branch has used the analytical method as most appropriate.

4. Primary Dermal Irritation Study in Rabbits:

Cosmopolitan Safety Evaluation, Inc., September 22, 1980 (0427E).

Six albino New Zealand rabbits were prepared and dosed with 0.5 ml of undiluted 2.5 EC formulation of cypermethrin on intact and abraded areas of their skin. The application was kept in place for 24 hours.

A primary irritation score of 2.0 was determined based on appearence of erythema. This erythema persisted for 16 days for some rabbits, by 21 days all signs of irritation had subsided. Only 1 rabbit developed edema, there was no eschar reported.

Core-Guideline, Toxicity Category III.

5. Primary Eye Irritation Study in Rabbits:

Cosmopolitan Safety Evaluaiton, September 16, 1980 (0427D).

Nine New Zealand type rabbits were dosed with 0.1 ml of test substance (2.5 EC formulation of cypermethrin) and observed for reactions for 21 days. The eyes of three rabbits were washed 20 seconds after instillation.

Corneal opacity developed and in three of the rabbits with unwashed eyes this was not reversed by day 7.

Core-Guideline, Toxicity Category I. A DANGER signal word is required on the label.

6. Acute Dermal Toxicity Study:

Cosmopolitan Safety Evaluation, August 1, 1980 (0397B).

A single dose of 2.0 gm/kg of test material (2.5 EC) formulation was applied to the prepared backs of five male and five female rabbits and the rabbits were observed for 14 days.

No rabbits died. Clinical signs of intoxication included ataxia, lethargy and diarrhea for 24-48 hours. Necropsy was reported as unremarkable.

Core-Minimum. Only a single dose was used. Toxicity Category III.

7. Guinea Pig Sensitization Study (Buehler)

Cosmopolitan Safety Evaluation, September 28, 1980 (0397E).

Induction:

Guinea pigs (10 males per group) were prepared and dosed with 0.5 ml of test material (2.5 EC formulation of cypermethrin). Applications were made on Mondays, Wednesdays and Fridays, for a total of 10 applications.

Challenge:

After a two week rest period, the test animals were challenged at both the treated site and at a virgin site. The challenge application was allowed to contact the skin for six hours.

Results:

No response indicative that the test material caused sensitization developed. The positive control, 2,4,-dinitrochlorobenzene, gave the predicted positive response.

OPP:HED:TOX: J.DOHERTY:sb 4/13/81 X73711 TS-769 Rm. 814 CM 2 #1

CYPERMETHRIN TOXICOLOGY REVIEWS

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