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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 279-GNIR
CYNOFF 2 EC Insecticide

FROM: William S. Woodrow WSW 5-17-89
Precautionary Review Section E 5/17/89
Registration Support Branch
Registration Division (H75-05C)

TO: George LaRocca (PM 15)
Insecticide-Rodenticide Branch
Registration Division (TS-767C)

APPLICANT: FMC Corp.
Agricultural Chemical Group
2000 Market St.
Philadelphia, PA 19103

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
α (±)-cyano-(3-phenoxyphenyl) methyl(±)-cis, trans-3-(2,2-dichloroethenyl)-2,2-dimethyl-cyclopropane carboxylate	24.8
Inert Ingredient(s):	75.2
Total	100.0%

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BACKGROUND:

The FMC Corp. submitted Acute oral, dermal, Primary eye and dermal irritation, and Dermal sensitization studies, to support Registration of CYNOFF 2EC Insecticide. MRID NOS. used were: 406809-02 through 406809-06.

RECOMMENDATION:

1) The 5 acute studies submitted by FMC are acceptable to RSB/PRS. The Dermal sensitization study was designated Core minimum data, due to the lack of a positive control experiment.
2) An Acute inhalation toxicity evaluation of CYNOFF 2 EC Insecticide, will be necessary.

~~LABELING:~~

NOTE: Upon submission of an acceptable acute inhalation study, Precautionary labeling may require revision.

LABELING:

1) The CAUTION Signal word is appropriate.
2) The Precautionary Statements are acceptable.
3) The Statements of Practical Treatment are acceptable.

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

Product Manager: (15)
MRID No.: 406809-02
Testing Facility: FMC Tox. Lab.
Author(s): C. Freeman
Species: Rat, Sprague Dawley
Age: young adult
Weight: M 211-248, F 201-237g
Source: Taconic Farms, N.Y.
Test Material: Cypermethrin (Cymbush) 2E
Quality Assurance (40 CFR §160.12): satisfactory

Reviewer: ~~M. Waller~~ Woodrow
Report Date: 5-16-89
Report No. 487-2546

Observation Days (Post Exposure): (14); other ( )

Conclusion:

1. LD_{50} (mg/kg): Males = 1085 (645-1524); Females = 1246 (1048-1443); Combined = 1105 (841-1369)
2. The estimated LD_{50} is 1105 (841-1369)
3. Tox. Category: III. Classification: Guidelines

Procedure (~~Deviations From §81-1~~): 25% (W/V) sol. in tapwater. by gavage to groups of 5M+5F rats. Animals observed for mortality & toxicity, to 14 day or longer if exhibiting clinical signs. Bodywts. Necropsies on dying/dead, and surviving animals.

Results:

Reported Mortality

M DOSAGE (mg/kg) F		(NUMBER KILLED/NUMBER TESTED)		
		Males	Females	Combined
2000	2000	4/5	5/5	9/10
1000	1500	4/5	4/5	9/10
950	1300	2/5	5/5	7/10
900	1225	1/5	3/5	4/10
800	1200	0/5	1/5	1/10
500	1000	1/5	0/5	1/10

Symptomology & Gross Necropsy Findings:

Clinical signs included tremors, hypersensitivity to touch, ataxia, clonic convulsions, abdominogenital staining & oral discharge. All survivors gained weight by termination. The only gross internal necropsy finding was blood in the intestines observed in the 1200 mg/kg group.

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

Product Manager: (15)
MRID No.: 406809-03
Testing Laboratory: Emc Tox. Lab.
Author(s): C. Freeman
Species: Rabbits, NZ White
Sex: 5M & 5F
Test Material: cypermethrin (Cymbush) 2 EC
Quality Assurance (40 CPR §160.12): Satisfactory

Reviewer: Woodrow ~~H. Weller~~
Report Date: 5-17-89
Report No. A87-254B

Wt.: M 2.32-2.70, F 2.46-2.81 kg.

Summary:

1. LD_{50} (mg/kg): Males = —; Females = —; Combined = —;
2. The estimated LD_{50} is > 2.00 mg/kg.
3. Tox. Category: III. Classification: Guidelines

Procedure (~~Deviations from §81-2~~): 2000 mg/kg to clipped backs of 5M+5F rabbits; 4x4" gauze pad/tape. Occluded w tape. 24 hr contact. Sites washed, animals observed for mortality & visible toxic signs at 0.5, 1, 2, 3, 4, 6 hrs day of dosing, 2x daily for 14 days & necropsy

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
2.000 mg/kg	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:

During 1st 3 days: loss of muscle control, decreased locomotion, recumbency, hypersensitivity to touch, thrashing in cage, lethargicity, and dyspnea. One sacrificed female (mechanical injury) showed brown material in stomach. Remaining animals normal.

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

Product Manager: (15)
MRID No.: 406909-04
Testing Laboratory: Env. Tox. Lab.
Author(s): C. Freeman
Species: Rabbit, NZ White
Sex: Female
Source: [illegible]
Dosage: 0.1 ml
Test Material: cypermethrin (cynoff) 2 EC 27% A.I.
Quality Assurance (40 CFR §160.12): Satisfactory

Reviewer: Andrew ~~M. Kohler~~
Report Date: 5-17-89
Report No. A87-2549
Weight: 2.36 – 3.51 kg.

Summary:

Tox. Category: III   Classification: Guidelines

Procedure ~~(Deviation from §81-4)~~: 0.1 ml instilled into 1 eye of 9 rabbits. 6 treated eyes unwashed, 3 eyes washed c̄ 100 ml tap water, approx. 20-30 sec. after treatment. Eyes were examined and scored according to Draize at 1, 24, 48 & 72 hrs.

Results:

	Observations (number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	0/9	0/9	0/9	0/9				
Iris	0/9	0/9	0/9	0/9				
Conjunctivae Redness	6/9	7/9	3/9	0/9				
Chemosis	0/9	1/9	0/9	0/9				
Discharge	7/9	2/9	1/9	0/9				

Comments: No iris or corneal involvement. All irritation absent by day 3.

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

Product Manager: (15)
MRID No.: 406909-05
Testing Laboratory: FMC Tox. Lab.
Author(s): C. Freeman
Species: Rabbit, NZ white
Age: Young adult
Sex: 3m & 3f
Weight: 2.32 – 2.82 kg
Dosage:
Test Material: Cypermethrin (Cynoff) 2 EC 27% AI
Quality Assurance (40 CFR §160.12): Satisfactory

Reviewer: Woodrow ~~Cutter~~
Report Date: 5-17-89
Report No. A87-2545

Summary:

The Primary Irritation index = P.I. Index = 0.40

Toxicity Category: IV

Classification: Guideline

Procedure (~~Deviations from §81-5~~): 0.5 ml to clipped backs of each of 6 rabbits, under 2" sq. gauze - Entire trunk wrapped c̄ semi-occlusive cheesecloth bandage - 4 hr exposure - Dressing removed, sites wiped. Scoring of sites beginning 30 min after unwrapping, and at 24, 48, 72 hrs, and on days 4 & 5, according to Draize.

Results:

Scoring interval	irritation score
4.5 hrs	0.2
24.0 hrs	0.3
48.0 hrs	0.5
72.0 hrs	0.4
day 4	0.3
day 5	0.0

P.I. Index = 0.4; practically not an "irritant"

Special Comments:

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

Product Manager: (15)
Reviewer: Woodrow ~~M. Walker~~
MRID No.: 406960-06
Report Date: 5-17-89
Testing Laboratory: FMC Tox. Lab.
Report No.: A87-2550
Author(s): C. Freeman
Species: guinea pigs, Hartley
Sex: not stated
Weight: 379-402 g
Source: Hazleton Res. Animals
Test Material: Cypermethrin (Cymbush) 2 EC 37% AI.
Positive Control Material: none
Quality Assurance (40 CFR §160.12): Satisfactory

Method: Modified Buehler.

Summary:
1. This product is / (is not a dermal sensitizer.)
2. Classification: Core minimum data (no + control expt.)

Procedure ~~(Deviation from §81-6)~~:

Induction - 0.3 ml to each of 20 Hill Top Chambers - Chambers applied to clipped dorsal sites of 20 g.p./secured c tape. Tape over chamber - 6 hr exposure - sites exposed, wiped. ~~Repeated~~ Repeated thrice, once/week, total 3 applications - 14 day rest period, all test animals challenged on a virgin site on the right shoulder. 10 additional animals (challenge only), each received 0.3 mls, for comparison - All patches removed 6 hrs later -

Test sites scored for irritation at 24 & 48 hrs, according to Draize (erythema/edema):

0 = insignificant
2 = significant
1 = equivocal

One index for incidence, and one for severity.

Results: All animals remained healthy.

The only scoring for irritation was 1/20 animals for the test material challenge, at 24 hours; a severity index (calculated to be 0.05), which was for a score of 1.0. No other irritation responses.

Conclusion: Cypermethrin 2EC did not sensitize guinea pigs.