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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MAR 30 1990

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 279-2659

Thiodan 2 C.O. EC Insecticide

FROM: Mary L. Waller Mary L. Waller E 3/30/90
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)

TO: George LaRocca (PM 15)
Insecticide-Rodenticide Branch
Registration Division (H75-05C)

APPLICANT: FMC Corporation
Agricultural Chemical Group
2000 Market Street
Philadelphia, PA 19103

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Endosulfan: Hexachlorohexahydromethano-2,4,3-benzodioxathiepin 3-oxide	23.1%
Inert Ingredient(s):	76.9%
Total	100.0%

/

BACKGROUND: The registrant has submitted an acute oral, acute dermal, acute inhalation, primary eye irritation, primary skin irritation, and dermal sensitization studies. The studies were conducted by FMC Toxicology Laboratory. The MRID numbers are 414005-01 through -06.

RECOMMENDATION: RSB/PRS findings are as follows:

1. All studies except the dermal sensitization study are acceptable.

2. The dermal sensitization study is classified as supplementary because the selected dose concentration may have been too dilute to ellicit sensitization. Dose selection was not discussed or determined as explained in the reference which the study cited (Ritz, H.L. and Buehler, E.V., Planning, Conduct and Interpretation of Guinea Pig Sensitization Patch Test). If the registrant can submit additional information to justify dose selection, the study classification will be reconsidered. If no additional information can be submitted, the registrant should reconduct the study using a higher concentration which, at a minimum, provokes minimal irritaion during the induction phase and the challenge concentration should be the highest nonirritating concentration as specified in the reference cited.

3. The signal word is "DANGER" based on the acute oral toxicity study.

NOTE TO PM:

This product meets the criteria established for classification as Restricted Use as defined in 40 CFR 152.170(b)(2)(i) which states that a pesticide, as formulated, which has an acute oral LD_{50} of 50 mg/kg or less will be considered for classification as restricted use. This product has an LD_{50} of 18.8 mg/kg for females.

LABELING:

1. Add the subheading "Re-Entry Statements" above the worker protection statements on page 2 of the draft label.

2. Revise Statement of Practical Treatment for oral and dermal exposure as follows:
IF SWALLOWED: Call a physician or Poison Control Center immediately. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger, or, if available, by administering syrup of ipecac. Do not induce vomiting or give anything by mouth to an unconscious or convulsing person.
IF ON SKIN: Wash with plenty of soap and water. Get medical attention.

3. Revise the sixth sentence under the Precautionary Statements as follows: "Wear protective clothing, waterproof rubber gloves, and a pesticide mask or respirator jointly approved by the . . ."

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

Product Manager: (15) Reviewer: M. Waller
MRID No.: 414005-01 Report Date: 11-3-89
Testing Facility: FMC Toxicology Laboratory Report No. A89-2939
Author(s): Christine Freeman
Species: Sprague-Dawley rats
Age: Young Adult Observation Days (Post Exposure): (14); other ( )
Weight: 273 - 297 g
Source: Taconic Farms, Germantown, NY
Test Material: Thiodan 2 C.O.E.C, 10% W/V solution in H_2O Ref# F4001
Quality Assurance (40 CFR §160.12): attached

Conclusion:

1. LD_{50} (mg/kg): Males = 194.4 (95% C.L. 164.6 - 224.2) mg/kg; Females = 18.8 (40.7 - 61.5) mg/kg; Combined = _____
2. The estimated LD_{50} is _____
3. Tox. Category: I. Classification: Guideline Data

Procedure (Deviations From §81-1): _____

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
25	/	0/5	0/5
50	/	4/5	4/5
100	0/5	5/5	5/10
150	0/5	/	0/5
175	1/5	/	1/5
200	3/5	5/5	8/10

Symptomology & Gross Necropsy Findings:

Toxic symptoms observed were clonic convulsions, diarrhea, tremors, rales, oral discharge, squinting eyes, and decreased locomotion.

No abnormalities were noted at necropsy.

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

Product Manager: (15) Reviewer: M. Waller
MRID No.: 41400502 Report Date: 11-7-89
Testing Laboratory: FMC Toxicology Laboratory Report No. A89-2940
Author(s): Christine Freeman
Species: New Zealand white rabbits
Sex: ♂ & ♀ Wt.: 2.01 - 2.84 kg
Test Material: Thiodan 2 C.O.EC.
Quality Assurance (40 CFR §160.12): attached

Summary:

1. LD_{50} (mg/kg): Males = 1076 (611 - 1541) mg/kg ; Females = 930 (528 - 1331) mg/kg ; Combined = 1000 (752 - 1249) mg/kg
2. The estimated LD_{50} is
3. Tox. Category: II . Classification: Guideline Data

Procedure (Deviations From §81-2): NONE

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
500 0/5	0/5	0/5	0/10
1000	2/5	3/5	5/10
2000	5/5	5/5	10/10

Symptomology & Gross Necropsy Findings:

Toxic symptoms were clonic convulsions, tremors, loss of muscle control, oral discharge, grinding teeth, and hypersensitivity to touch. Animals also exhibited eschar, fissuring, exfoliation, skin thickening and desquamation at test site.

Gross necropsy revealed blood in stomach, blanching of the intestines, and ulcerated stomach.

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

Product Manager: (15) Reviewer: M. Waller
MRID No.: 414005-03 Report Date: 1-5-90
Testing Laboratory: FMC Toxicology Laboratory Report No. A89-2941
Author(s): Everett Mount
Species: Sprague-Dawley rat
Sex: ♂ + ♀ Weight: ♂: 230-300 g; ♀: 226-300 g
Source: Taconic Farms, Germantown, NJ
Test Material: Thiodan 2 C.O. EC Ref. # F4001
Quality Assurance (40 CFR §160.12): attached

Summary:

1. LC_{50} (mg/kg): Males = 1.2 (1.0 - 1.4) mg/L (95% C.L.); Females = 0.4 (0.1 - 0.6) mg/L; Combined =
2. The estimated LC_{50} is
3. Mean Concentration:
4. Tox. Category : II . Classification: Guideline Data

Procedure (Deviations From §81-2): NONE

Results:

Exposure Concentration (mg/L)	Reported Mortality (NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
0.28 MMAD = 1.29	—	0/5	0/5
0.39 MMAD = 1.29	—	4/5	4/5
1.02 MMAD = 1.29	0/5	5/5	5/10
1.48 MMAD = 1.49	5/5	—	5/5
1.96 MMAD = 1.54	5/5	5/5	10/10

Symptomology & Gross Necropsy Findings:

Toxic symptoms were hypoactivity, lacrimation, nasal discharge, tremors, squinting eyes, abdominogenital staining, ~~and~~ ataxia, chromorhinorrhea, unthriftiness and decreased feces.

No abnormalities were noted at necropsy.

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

Product Manager: (15)
MRID No.: 414005-04
Testing Laboratory: FMC Toxicology Laboratory
Author(s): Christine Freeman
Species: New Zealand white rabbits
Sex: 4♂ + 5♀ Weight: 2.19-2.62 Kg
Source: Hazelton Research Animals, Inc. Denver, PA
Dosage: 0.1 ml
Test Material: Thiodan 2 C.O. EC Ref # F4008#1
Quality Assurance (40 CFR §160.12): Attached

Reviewer: M. Waller
Report Date: 7-25-89
Report No. A89-2942

Summary:

Tox. Category: III Classification: Guideline Data

Procedure (Deviation From §81-4): None

Results:

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

Comments: An additional three animals were treated and received an eyewash after treatment.

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

Product Manager: (15)
MRID No.: 414005-05
Testing Laboratory: FMC Toxicology Laboratory
Author(s): Christine Freeman
Species: New Zealand white rabbit
Age: Young Adult
Sex: 3♂ and 3♀
Weight: 2.10 - 2.83 Kg
Dosage: 0.5 ml
Test Material: Thiodan 2 C.O.EC Ref. # F4001
Quality Assurance (40 CFR §160.12): attached

Reviewer: M. Waller
Report Date: 9-22-89
Report No. A89-2943

Summary:

The Primary Irritation Index = _____

Toxicity Category: III

Classification: Guideline Data

Procedure (Deviations From §81-5): None

Results:

At 72 hours, 2/6 animals exhibited well-defined erythema, 2/6 animals exhibited very slight erythema. Animals also exhibited atonia, and ~~thin~~ skin thickening. Desquamation started on day 7 and continued through day 14.

Special Comments:

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

Product Manager: (15)
MRID No.: 414005-06
Testing Laboratory: FMC Toxicology Laboratory
Author(s): Christine Freeman
Species: Guinea Pigs, Hartley
Sex: ♂ and ♀ Weight: 311-393 g
Source: Hazelton Research Animals Incorp., Denver, PA
Test Material: Thiodan 2 C.O.EC Ref # F4001 25% w/v solution in H_2O
Positive Control Material: DNCB 0.15% w/v solution in 80% ETOH - Induction in acetone - challenge
Quality Assurance (40 CFR §160.12): attached

Reviewer: M. Waller
Report Date: 9-29-89
Report No. A89-2944

Method: Buehler

Summary:
1. ~~This product is / is not a dermal sensitizer.~~
2. Classification: Supplementary

Procedure (Deviation From §81-6): Selected concentration may have been too dilute to elicit sensitization.

Results: The test group and the challenge control group did not exhibit any irritation during the test.

The positive control group exhibited very slight to well-defined erythema after the first induction treatment. Irritation increased in severity and number of animals involved. At challenge, positive control animals exhibited well-defined to severe erythema and very slight edema.