MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 279-2459

Thiodan 2 C.O. EC Insecticide

FROM: Mary L. Waller
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)

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

APPLICANT: E. I. du Pont de Nemours & Co.

Agricultural Chemical Group

2000 Market Street

Philadelphia, PA 19103

FORMULATION FROM LABEL:

Active Ingredient(s):
Endosulfan: Hexachlorohexahydromethane-
2,4,5-triazines

% by wt.

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 elicit 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 irritation 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 LD50 of 50 mg/kg or less will be considered for classification as restricted use. This product has an LD50 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)  
MRID No.: 414005-01  
Testing Facility: FMC Toxicology Laboratory  
Author(s): Christine Freeman  
Species: Sprague-Dawley rats  
Age: Young adult  
Weight: 27.3 - 29.7 g  
Source: Taconic Farms, Germantown, NY  
Test Material: Thiodan 2 C.O.E.C. 10% W/V solution in H2O  
Quality Assurance (40 CFR §160.12): attached

Conclusion:
1. LD50 (mg/kg): Males = 194.4 (164.6 - 224.2) mg/kg; Females = 18.8 (40.7 - 61.5) mg/kg; Combined = 95% C.L.
2. The estimated LD50 is 194.4 mg/kg.
3. Tox. Category: I, Classification: Guideline Data

Procedure (Deviations From §81-1):

Results:

<table>
<thead>
<tr>
<th>DOSAGE (mg/kg)</th>
<th>(NUMBER KILLED/NUMBER TESTED)</th>
<th>Males</th>
<th>Females</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td></td>
<td>0/15</td>
<td>0/15</td>
<td>0/15</td>
</tr>
<tr>
<td>50</td>
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<tr>
<td>100</td>
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<td>175</td>
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<td>1/5</td>
</tr>
<tr>
<td>200</td>
<td></td>
<td>3/5</td>
<td>5/5</td>
<td>5/10</td>
</tr>
</tbody>
</table>

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: ( ) Reviewer: M. Waller
MRID No.: 41400602 Report Date: 11-7-89
Testing Laboratory: FMRC Toxicology Laboratory Report No. A89-2940
Author(s): Christine Freeman
Species: New Zealand White Rabbits
Sex: M & F Wt.: 2.01 - 2.84 kg
Quality Assurance (40 CFR §160.12): Attached

Summary:

1. LD50 (mg/kg): Males = 1076 (611 - 1541) mg/kg; Females = 920 (528 - 1331) mg/kg; Combined = 1000 (752 - 1249) mg/kg
2. The estimated LD50 is 1000 mg/kg.
3. Tox. Category: II. Classification: Guideline Data

Procedure (Deviations From §81-2): None

Results:

<table>
<thead>
<tr>
<th>DOSAGE (mg/kg)</th>
<th>(NUMBER KILLED/NUMBER TESTED)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
</tr>
<tr>
<td>500</td>
<td>0/5</td>
</tr>
<tr>
<td>1000</td>
<td>2/5</td>
</tr>
<tr>
<td>2000</td>
<td>5/5</td>
</tr>
</tbody>
</table>

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)  
MRID No.: 414006-03  
Testing Laboratory: FMD Toxicology Laboratory  
Author(s): Everett Mount  
Species: Sprague-Dawley rat  
Source: Taconic Farms, Germantown, NJ  
Test Material: Thiodan 2.0% EC  
Quality Assurance (40 CFR §160.12): attached

Summary:
1. LC50 (mg/kg): Males = \(0.4 \pm 0.1\) mg/L; Females = \(1.2 \pm 1.4\) mg/L; Combined \(\text{LC50}\) 
2. The estimated LC50 is 95\% C.L.
3. Mean Concentration: 
4. Tox. Category: II. Classification: Guideline Date

Procedure (Deviations From §81-2): None

Results:

<table>
<thead>
<tr>
<th>Exposure Concentration (mg/L)</th>
<th>REPORTED MORTALITY</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>(NUMBER KILLED/NUMBER TESTED)</td>
</tr>
<tr>
<td></td>
<td>Males</td>
</tr>
<tr>
<td>0.28 MMAD = 1.29</td>
<td></td>
</tr>
<tr>
<td>0.39 MMAD = 1.29</td>
<td></td>
</tr>
<tr>
<td>1.02 MMAD = 1.29</td>
<td>0/5</td>
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<tr>
<td>1.48 MMAD = 1.49</td>
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</tr>
<tr>
<td>1.96 MMAD = 1.54</td>
<td>5/5</td>
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</tbody>
</table>

Symptomology & Gross Necropsy Findings:

Toxic symptoms were hyperactivity, lacrimation, nasal discharge, tremors, squinting eyes, abdominal genital staining, and ataxia, chromodacryorrhea, unsteadiness and decreased feces.

No abnormalities were noted at necropsy.
DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: [15] Reviewer: M. Waller
MRID No.: 414005-04 Report Date: 7-25-89
Testing Laboratory: Free Toxicology Laboratory Report No. A89-2943
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 80221
Dosage: 0.1 ml
Test Material: Thiodan 2 EC Ref # F40021
Quality Assurance (40 CFR §160.12): attached

Summary:
Tox. Category: III Classification: Guideline Data

Procedure (Deviation From §81-4): None

Results:

<table>
<thead>
<tr>
<th>Observations</th>
<th>Cornea</th>
<th>Iris</th>
<th>Conjunctivae</th>
<th>Days</th>
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<tbody>
<tr>
<td></td>
<td>Opacity</td>
<td></td>
<td>Redness</td>
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<td></td>
<td>Chemosis</td>
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<td></td>
<td></td>
<td>Discharge</td>
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<tr>
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<td>1/6</td>
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</tbody>
</table>

Comments: An additional three animals were treated and received an eyewash after treatment.
DATA REVIEW FOR SKIN IRRITATION TESTING ($81-5$)

Product Manager: (15)  Reviewer: M. Waller
MRID No.: 414005-05  Report Date: 9-22-99
Testing Laboratory: FAA Toxicology Laboratory  Report No. A89-2943
Author(s): Christine Freeman
Species: New Zealand white rabbit
Age: Young and Adult
Sex: 3.67 and 3.9
Weight: 2.10 - 2.83 Kg
Dosage: 0.5 ml
Test Material: Thiodan 2 60. EC  Ref. # F4001
Quality Assurance (40 CFR §160.12): attached

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 ataxia, and thin skin thickening. Desquamation
started on day 7 and continued through day 14.

Special Comments:
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: Hazleton Research Animals Inc., Denver, PA
Test Material: Thiodan 2 C.C. EC Ref # F4001 95% w/w solution in H2O
Positive Control Material: DNAP 0.15% w/w solution in 80% EtOH—Induction
Quality Assurance (40 CFR §160.12): attached in acetone—challenge

Method: Büchner

Summary:
1. This product is not a dermal sensitization.
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.