REVIEWER

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

005349

AUG 13 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

TO: Tim Gardner, PM # 17
Insecticide/Rodenticide Branch
Registration Division TS-767C

THRU: R. B. Jaeger, Section Head
Rev. Sec. # 1/Toxicology Branch
Hazard Evaluation Division TS-769C

FROM: D. Ritter, Toxicologist
Rev. Sec. # 1/Toxicology Branch
Hazard Evaluation Division TS-769C

Subject:

Dimilin - EPA Reg. # 37100-8/ER/1F2507/1H5301/37100-EUP-T

Dimilin 25 WP

Caswell #: 346A

TOX project numbers: 1522/23/24/25/26.

Action requested:

Review toxicity data submitted for citrus tolerance petition and fulfill Registration Standard requirements.

Our response:

1. Tolerances of 0.5 ppm in citrus, 0.3 ppm in dried citrus pulp, 20 ppm in citrus oil and 0.05 ppm in meat, milk and eggs were approved in the review of 4/29/85, R. Jaeger, PP # 1F2507. Data considered in support of those tolerances likewise support the present request.

2. A number of the toxicity studies submitted in this data package were previously submitted and evaluated in the S. Biscardi review of 9/26/77. We have attached DERs for those studies which have not been previously evaluated.

DATA EVALUATION REPORT

Dimilin (diflubenzuron)

STUDY: Acute Oral LD_{50} in the Mouse and Rat

LABORATORY: Duphar B. V., Weesp, The Netherlands.

STUDY NUMBER & DATE: 56645/3/77 April 1977. T.S.M. Koopman.

ACCESSION NUMBER: 261486

MATERIAL TESTED: Dimimlin 25 WP

ANIMALS: Male and female Wistar rats, 5 per sex per dose group, and male and female Wistar mice, 5 per sex per dose group.

METHODS:

Animals were given a single P.O. dose of test material in 1 % tragacanth solution. Animals were fasted 16 hours pre-exposure and for an additional 6 hours following treatment. Water was available ad lib. The test levels administered were 0, 1000, 2150, 4640 Or 10,000 mg/kg.

Animals were observed at 0 - 0.5, 1.5, 3, 6, 24 and 48 hours, and daily thereafter for mortality and toxic signs.

Body weights were obtained initially and on days 2, 7 and 14.

Gross examination was made on all animals expiring during the study and on all animals in the high dose group and the control group.

RESULTS:

Mortality - one control female mouse expired due to gavage error. There was no other mortality reported.

Toxic signs - none reported.

Body weights - no effect reported.

Gross necropsy - no evidence of effect.

CONCLUSIONS:

Rat Oral LD_{50} > 10,000 mg/kg. Mouse Oral LD_{50} > 10,000 mg/lg

CORE RATING: Guideline.

TOXICITY CATEGORY: III

DATA EVALUATION REPORT

Dimilin (Diflubenzuron)

STUDY: Acute Dermal LD_{50} in the Rabbit.

LABORATORY: Coromandel Indag Res. Ctre.

STUDY NUMBER & DATE: 81, 6/5/82 V.S. Rao.

ACCESSION NUMBER: 261486

MATERIAL TESTED: Dimilin 25 WP

ANIMALS: Himalayan albino rabbits.

METHODS:

Animals were housed and allowed access to feed and water according to stadard GLP.

More than 10 % of the total body surface area was clipped and washed with distilled water. The test material was applied as an aqueous slurry to the application site which was then occluded. Doses applied were 0, 2500, 5000 or 10000 mg/kg. The animals were mobilized for 24 hours, then the site was bared and the area cleansed with sunflower oil.

Observations were made for mortality and toxic effects at 1, 4 and 24 hours. then daily thereafter for 14 days.

Upon completion of the study the animals were necropsied grossly.

RESULTS:

Mortaility - there was no mortality reported.

Toxic signs - lethargy for the first day in several animals.

There was a mild dermal reaction (erythema) on day one only.

CONCLUSIONS:

The Dermal LD_{50} is > 10,000 mg/kg in this study.

CORE RATING: Guideline.

TOXICITY CATEGORY: III.

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DATA EVALUATION REPORT

Dimilin (Diflubenzuron)

STUDY: Primary Eye Irritiation in the Rabbit.

LABORATORY: Coromandel Indag.

STUDY NUMBER & DATE: 32, 12/31/81. V.R. Chandran

ACCESSION NUMBER: 261486

MATERIAL TESTED: Dimilin 25 WP.

ANIMALS: Himalayan albino rabbits

METHODS:

Six animals with healthy eyes were used. 100 mg of test material was introduced neat into the left conjunctiva of each animal, the right eye serving as control. The sites were not washed. The eyes were examined for injury at 4, 24, 48 and 72 hours and on days 4, 7, 10 and 14 after Draize.

Husbandry and feed and water availability was according to standard GLP.

RESULTS:

Corneal opacity, iridial inflamation and conjunctival irritation were reported for the first 2 days following exposure. Total Draize score was calculated to be 23.3/110. The reaction involves reversible corneal damage that clears within 21 days.*

CONCLUSIONS:

A reversible eye irritant.

CORE RATING: Guideline.

TOXICITY CATEGORY: II.

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* Criteria & Policy Notice # 2161.2, 3/31/81.

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DATA EVALUATION REPORT

Dimilin (Diflubenzuron)

STUDY: Acute Oral, Percutaneous and Subcutaneous Toxicity in the Mouse and Rat

LABORATORY: Jap. Dept. Environ. Biol. Nat. Envirn. Control Cntre.

STUDY NUMBER & DATE: DCP 895 (Sei. 51-128-2) 4/30/77.

ACCESSION NUMBER: 216486

MATERIAL TESTED: Technical Dimilin and Dimilin 25 WP.

ANIMALS: Rats and Mice of unstated strain.

CORE RATING:

This study is rated Invalid for the following reasons:

1. No detailed analytical data.

2. Observation period was only 7 days, not the required 14.

Not repairable.

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DATA EVALUATION REPORT

Dimilin (Diflubenzuron)

STUDY: Oral LD_{50} in the Rat.

LABORATORY: Coromandel Indag Res. Ctre.

STUDY NUMBER & DATE: 119, 10/30/82 V.S. Rao.

ACCESSION NUMBER: 261486

MATERIAL TESTED: Dimilin 25 WP

ANIMALS: Albino rats (strain not stated). 5 males and 5 females per sex per group.

CORE RATING:

This study is rated CORE Invalid for the following reasons:

1. No detailed analytical data.

2. No post-mortem examination although mortality was reported.

Repairability: Submit detailed analytical data and results of Post-mortem examination.

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DATA EVALUATION REPORT

Dimilin (Diflubenzuron)

STUDY: Oral LD_{50} in the Mouse.

LABORATORY: Coromandel Indag Res. Ctre.

STUDY NUMBER & DATE: 114, 10/10/82 V.S. Rao.

ACCESSION NUMBER: 261486

MATERIAL TESTED: Dimilin 25 WP

ANIMALS: Albino Mice,strain not stated, 5 per sex per dose.

METHODS:

Feed and water ad libitum. Husbandry - Standard GLP.

Dosed by gavage at levels of 0, 8000, 10000, 12000, 14000 and 16000 mg/kg in distilled water. Animals were observed daily for mortality and toxic symptoms.

RESULTS:

No mortality was reported in the 8000 mg/kg groups. 60% mortality was reported in the 10000 mg/kg animals; 50% in the 12000 mg/kg animals; 80% mortality in the 14000 and 16000 mg/kg groups each.

CONCLUSIONS:

The Oral LD_{50} in mice in this study is 11,307 mg/kg (9,038 - 14,141).

CORE RATING:

Supplementary: No post-mortems were reported.

Repairability: Supply results of post-mortem examination.

TOXICITY CATEGORY:

III.

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DATA EVALUATION REPORT

Dimilin (diflubenzuron)

STUDY: Acute Dermal LD_{50} in the Rabbit.

LABORATORY: Duphar B. V., Weesp, The Netherlands.

STUDY NUMBER & DATE: 56645/6/77 April 1977. T.S.M. Koopman.

ACCESSION NUMBER: 261486

MATERIAL TESTED: Dimimlin 25 WP

ANIMALS: New Zealand White rabbits, 4 per sex per dose.

METHODS:

Group 1 was administered 1 % tragacanth only.

Group 2 received 3840 mg/kg of the formulation without the AI.

Group 3 received 2150 mg test material.

Group 4 received 4640 mg/kg test material.

Animals' trunks were clipped free of hair. Half the animals recieved dermal abrasions into the stratum corneum. an occlusive dressing ca. 11 x 27 cm was applied and the test substance was introduced under this by a blunt needle. 24 hours later the patch was removed and the area was cleansed and dried. The animals were observed daily for mortality and signs of toxicity. Animals were weighed initially and on days 2, 7 and 14 thereafter. Gross post mortem examination was performed on all animals dying during the study and on all control and high dose animals.

RESULTS:

There was no mortality nor any reported signs of toxicity. Body weights were not adversely affected by exposure to the test materials. No gross abnormality attributable to test material were reported.

CONCLUSIONS:

The Dermal LD_{50} inthis study is > 4640 mg/kg.

CORE RATING: Supplemental. Repairable by supplying detailed analytical data.

TOXICITY CATEGORY: III.

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DATA EVALUATION REPORT

Dimilin (diflubenzuron)

STUDY: Acute Dermal LD_{50} in the Rabbit.

LABORATORY: Duphar B. V., Weesp, The Netherlands.

STUDY NUMBER & DATE: 56645/17/73 December 1973 A. van Eldik

ACCESSION NUMBER: 261486

MATERIAL TESTED: Dimimlin 25 WP

ANIMALS: New Zealand White rabbits, 4 per sex per dose.

CORE RATING:

Invalid. No detailed data, or other numerical information such as tables, etc. This is a summary only.

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DATA EVALUATION REPORT

Dimilin (Diflubenzuron)

STUDY: Primary Skin Irritation in the Rabbit.

LABORATORY: Coromandel Indag Res. Ctre.

STUDY NUMBER & DATE: 31, 12/31/81 V.R. Chandran.

ACCESSION NUMBER: 261486

MATERIAL TESTED: Dimilin 25 WP

ANIMALS: Himalayan Albino rabbits 3 males and 3 females.

METHODS:

Husbandry: Standard GLP.

Two 5 cm^2 areas of the back of each animal was shaved. Abrasion through the stratum corneum were made. 500 mg/kg test material was mixed with a small amount of water to form a slurry; this was spread over the test sites. Occlusive dressings were applied and left in situ for 24 hours. The sites were then scored after Draize (1959) at 24 and 72 hours.

RESULTS:

Some erythema was noted in all animals at 24 hours at the abraded sites; two rabbits exhibited a mild erythematous response at 72 hours. Intact sites responded only slightly. No edema was reported.

CONCLUSIONS:

The calculated PIS was 0.42.

CORE RATING:

Minimum data.

TOXICITY CATEGORY:

III.

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DATA EVALUATION REPORT

Dimilin (Diflubenzuron)

STUDY: Dermal Sensitization in the Guinea Pig

LABORATORY: Huntingdon Research Ctr.

STUDY NUMBER & DATE: 56645/13/78 5/5/78. S. R. Kynoch

ACCESSION NUMBER: 261486

MATERIAL TESTED: Dimilin 25 WP.

ANIMALS: Ten female Hartley-Dunkin strain guinea pigs.

METHODS:

Induction Phase:

Intradermal -

A 4 x 6 cm area was clipped free of hair. Three pairs of intradermal injections were made consisting of 1) 50-50 v/v of Freunds adjuvant; 2) 1% in distilled water and a mixture of 1) and 2), 50:50. Total volume was 0.1 ml for each pair of injections.

Topical -

A week later the same exposure was reclipped and 0.4 ml of a 50 % solution was applied via a 3 x 6 cm square of filter paper which was then occluded for 48 hours.

Challenge Phase:

Two weeks after the challenge phase the animals were again clipped free of hair and 0.1 ml of test material (10 %) was applied on a 2 x 2 cm filter paper and occluded for 24 hours.

The dermal response was evaluated for erthematous and edematous response at 24, 48 and 72 hours after the patch was removed.

CORE Rating: Invalid. No positive control was used. Not repairable.