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WASHINGTON, D.C. 20460

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

Date: July 25, 2006

MEMORANDUM

Subject: Review of 7 acute toxicity studies with Rotenone.

PC Code: 071003
DP Barcode: D234462, D243239
TXR: 0053403

From: Elissa Reaves, Ph.D.
Reregistration Branch 2, HED (7509P)

Elissa R 7/25/06

Thru: Alan Nielsen, Branch Senior Scientist
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To: Katie Hall, Chemical Review Manager
Special Review and Reregistration Division (7508P)

The acute studies for rotenone (powder, resin, crystalline) have been reviewed. Please refer to the table below for the classification and conclusion for each study.

CONCLUSIONS

Study Description	MRID	Tox Category	Classification
Acute dermal toxicity-Rabbit-Rotenone Powder	44229901	IV	Acceptable/guideline
Acute dermal toxicity- Rabbit-Rotenone Resin	44229902	IV	Acceptable/guideline
Acute dermal toxicity-Rabbit-Rotenone Crystalline	44478301	IV	Acceptable/guideline
Acute Inhalation-Rat-Rotenone Crystalline	44478302	I	Acceptable/guideline
Primary Eye Irritation-Rabbit-Rotenone Crystalline	4478303	III	Acceptable/guideline
Primary Dermal Irritation-Rabbit-Rotenone Crystalline	44478304	IV	Acceptable/guideline
Skin Sensitization-Guinea Pig-Rotenone Crystalline	44478305	Not a dermal sensitizer	Acceptable/guideline

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DATA EVALUATION RECORD

Rotenone Powder

Study Type: Acute Dermal Toxicity (§81-2)

Work Assignment No. 1-1-11A (MRID 44229901)

Prepared for

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Crystal Mall II
Arlington, VA 22202

Prepared by

Pesticide Health Effects Group
Sciences Division
Dynamac Corporation
2275 Research Boulevard
Rockville, MD 20850-3268

Primary Reviewer:
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Signature: Kimberly Woodard
Date: 2-15-99

Project Manager:
Mary L. Menetrez, Ph.D.

Signature: Mary L Menetrez
Date: 2/19/99

Disclaimer

This Data Evaluation Record may have been altered by the Health Effects Division subsequent to signing by Dynamac Corporation personnel.

EPA Reviewer: Elissa Reaves, PhD Signature: Elissa R
Reregistration Branch 2 (7509C) Date: 7/25/06

EPA Work Assignment Manager: PV Shah, PhD Signature: P V Shah
Registration Action Branch 1 (7509C) Date: 7/25/06

TXR No.: 0053403

DATA EVALUATION RECORD

STUDY TYPE: Acute Dermal Toxicity - Rabbit
OPPTS Number: 870.1200 OPP Guideline Number: §81-2

DP BARCODE: D234462
P.C. CODE: 071003
EPA REC. NO.: 1439-236

TEST MATERIAL (PURITY): Rotenone Powder (5.57% AI)

SYNONYMS: Cube Powder

CITATION: Kuhn, J. (1997) Acute dermal toxicity study in rabbits. Stillmeadow, Inc. Sugar Land, TX. Laboratory Study Number 3250-97. February 13, 1997. MRID 44229901. Unpublished.

SPONSOR: TIFA LIMITED, Tifa Square, Millington, NJ.

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 44229901), five young adult New Zealand White rabbits/sex were dermally exposed to Rotenone Powder (5.57% AI) at 5,050 mg/kg (>2.5X limit dose) for 24 hours; the test substance was moistened with deionized water and applied to approximately 10% of the total body surface area. Animals were observed for clinical signs of toxicity and mortality for up to 14 days postdosing.

Dermal LD_{50} Males = >5,050 mg/kg (observed)
Females = >5,050 mg/kg (observed)

Rotenone Powder is classified as **TOXICITY CATEGORY IV** based on the observed LD_{50} values in both sexes.

All animals survived the 14-day observation period, with no treatment-related signs of toxicity nor dermal irritation. Although an effect on body weight was observed primarily during week one of the study, there were no toxicologically-significant decreases in body weight. Overall weight gain was noted in 9/10

animals (overall increases ranging between 5 and 17%). Necropsy after 14 days revealed no treatment-related gross abnormalities.

This study is classified **acceptable/guideline (§81-2)** and satisfies the guideline requirement for an acute dermal study in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Rotenone Powder
   Description: Fine tan powder
   Lot/Batch #: Tifa Ref# AF-3/12/96
   Purity: 5.57% Rotenone
   CAS #: 83-79-4

2. Vehicle: Deionized water, 2.06 mL/g substance

3. Test animals: Species: Rabbit
   Strain: New Zealand White
   Age: Young adult
   Weight: 2.800-3.075 kg males; 2.900-3.150 kg females
   Source: Ray Nichols Rabbitry; Lumberton, TX
   Acclimation period: 5 Days
   Diet: Purina Mills, Inc. Lab Rabbit Chow (#5321), unspecified measured amount/animal/day
   Water: Tap water, ad libitum
   Housing: One animal/cage
   Environmental conditions:
   Temperature: 72 ± 5°F
   Humidity: 30-80%
   Air changes: 10-12 air changes/hour
   Photoperiod: 12-hour light/dark cycle

B. STUDY DESIGN and METHODS:

1. In-life dates: January 9-23, 1997

2. Animal assignment and treatment: Fur from the dorsal surface of the trunk of five young adult New Zealand White rabbits/sex was clipped 1 day prior to dermal administration of Rotenone Powder at 5,050 mg/kg (>2.5X limit dose). The test substance was moistened with

deionized water and evenly applied to the clipped surface. Each test site was covered with an 8 x 4 inch surgical gauze patch and secured with non-irritating adhesive tape. The trunk of each animal was then wrapped with an orthopedic stockinette and secured in place with non-irritating adhesive tape. Following a 24-hour exposure period, the coverings were removed and the test sites were gently washed with room temperature tap water and a clean cloth. The rabbits were observed for signs of toxicity and/or mortality at least three times on the day of dosing and at least once daily thereafter for up to 14 days. Dermal effects were observed at approximately 60 minutes after removal of wrappings (Day 1) and on Days 4, 7, 10, and 14. Body weights were recorded at Days 0 (prior to exposure), 7, and 14. At 14 days, surviving animals were euthanized, necropsied, and examined for gross pathological changes.

3. Statistics: No statistical analyses were conducted.

II. **RESULTS AND DISCUSSION:**

A. Mortality: All animals survived the 14-day observation period.

Dermal LD_{50} Males = >5,050 mg/kg (observed)
Females = >5,050 mg/kg (observed)

B. Clinical observations: No treatment-related signs of toxicity nor dermal irritation were observed.

C. Body Weight: Treatment-related effects on body weight were observed in animals of both sexes. Between 0 and 7 days, the body weights of 3/5 males and 2/5 females either decreased or remained unchanged, and between 7 and 14 days, 2/5 females either decreased or remained unchanged. Overall (0-14 days), 9/10 animals gained weight, ranging between 5 and 17%. A single female exhibited no net change during the 14-day study.

D. Necropsy: Necropsy of animals sacrificed after 14 days revealed no treatment-related gross abnormalities.

E. Deficiencies: There were no deficiencies that affected the results of this study.

DATA EVALUATION RECORD

Rotenone Resin

Study Type: Acute Dermal Toxicity (§81-2)

Work Assignment No. 1-1-11B (MRID 44229902)

Prepared for

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Crystal Mall II
Arlington, VA 22202

Prepared by

Pesticide Health Effects Group
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Primary Reviewer:
Kimberly Woodard, B.S.

Signature: Kimberly Woodard
Date: 2-15-99

Project Manager:
Mary L. Menetrez, Ph.D.

Signature: Mary L Menetrez
Date: 2/19/99

Disclaimer

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EPA Reviewer: Elissa Reaves, PhD Signature: Elissa Reaves
Reregistration Branch 2 (7509C) Date: 7/25/06
EPA Work Assignment Manager: PV Shah, PhD Signature: PV Shah
Registration Action Branch 1 (7509C) Date: 7/25/06

TXR No.: 0053403

DATA EVALUATION RECORD

STUDY TYPE: Acute Dermal Toxicity - Rabbit
OPPTS Number: 870.1200 OPP Guideline Number: 81-2

DP BARCODE: D234462
P.C. CODE: 071003
EPA REG. NO.: 1439-259

TEST MATERIAL (PURITY): Rotenone Resin (39.97% AI)

SYNONYMS: None specified

CITATION: Kuhn, J. (1997) Acute dermal toxicity study in rabbits. Stillmeadow, Inc. Sugar Land, TX. Laboratory Study Number 3248-97. February 20, 1997. MRID 44229902. Unpublished.

SPONSOR: TIFA LIMITED, Tifa Square, Millington, NJ.

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 44229902), five young adult New Zealand White rabbits/sex were dermally exposed to Rotenone Resin (39.97% AI) at 5,050 mg/kg (>2.5X limit dose) for 24 hours; the test substance was moistened with deionized water and applied to approximately 10% of the total body surface area. Animals were observed for clinical signs of toxicity and mortality for up to 14 days postdosing.

Dermal LD_{50} Males = >5,050 mg/kg (observed)
Females = >5,050 mg/kg (observed)

Rotenone Resin is classified as **TOXICITY CATEGORY IV** based on the observed LD_{50} values in both sexes.

All animals survived the 14-day observation period, and aside from decreased defecation in one male on Day 5, appeared normal during the study. Slight erythema was observed at all test sites upon patch removal on Day 1; irritation subsided from all sites by day 4. No significant effect on body weight was observed in females; 2/5 males, however, exhibited slight decreases in weight

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between 4 and 7 days. All animals exhibited overall weight gains during the study, ranging from 6.6 to 14%. Necropsy after 14 days revealed no treatment-related gross abnormalities.

This study is classified **acceptable/guideline (§81-2)** and satisfies the guideline requirement for an acute dermal study in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Rotenone Resin
   Description: Gray and yellow chunks with yellow powder residue
   Lot/Batch #: Tifa Ref# 76819
   Purity: 3 9.97% Rotenone
   CAS #: 83-79-4

2. Vehicle: Deionized water, 0.599 mL/g substance

3. Test animals: Species: Rabbit
   Strain: New Zealand White
   Age: Young adult
   Weight: 3.300-3.750 kg males; 2.700-3.150 kg females
   Source: Ray Nichols Rabbitry; Lumberton, TX
   Acclimation period: 5 Days
   Diet: Purina Mills, Inc. Lab Rabbit Chow (#5321), unspecified measured amount/animal/day.
   Water: Tap water, ad libitum
   Housing: One animal/cage
   Environmental conditions:
   Temperature: 72 ± 5°F
   Humidity: 30-80%
   Air changes: 10-12 air changes/hour
   Photoperiod: 12-hour light/dark cycle

B. STUDY DESIGN and METHODS:

1. In-life dates: January 23, 1997 - February 6, 1997

2. Animal assignment and treatment: Fur from the dorsal surface of the trunk of five young adult New Zealand White rabbits/sex was clipped 1 day prior to dermal

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administration of Rotenone Resin at 5,050 mg/kg (>2.5X limit dose). The test substance was moistened with deionized water and evenly applied to the clipped surface. Each test site was covered with an 8 x 4 inch surgical gauze patch and secured with non-irritating adhesive tape. The trunk of each animal was then wrapped with a stockinette and secured in place with non-irritating adhesive tape. Following a 24-hour exposure period, the coverings were removed and the test sites were gently washed with room temperature tap water and a clean cloth. The rabbits were observed for signs of toxicity and/or mortality at least three times on the day of dosing and at least once daily thereafter for up to 14 days. Dermal effects were observed at approximately 60 minutes after removal of wrappings (Day 1) and on Days 4, 7, 10, and 14. Body weights were recorded at Days 0 (prior to exposure), 7, and 14. At 14 daybs, surviving animals were euthanized, necropsied, and examined for gross pathological changes.

3. Statistics: No statistical analyses were conducted.

II. RESULTS AND DISCUSSION:

A. Mortality: All animals survived the 14-day observation period.

Dermal LD_{50} Males = >5,050 mg/kg (observed)
Females = >5,050 mg/kg (observed)

B. Clinical observations: No treatment-related signs of toxicity were observed with the exception of one male which, on Day 5, was noted for decreased defecation. Very slight erythema (scores of 1) along with yellow staining of the test site was observed in 5/5 rabbits/sex on Day 1. Yellowing of the test site was also observed in 1/5 female rabbits on Days 4 and 7 also.

C. Body Weight: Treatment-related effects on body weight were observed in male rabbits. Between 0 and 7 days, the body weights of 2/5 males decreased; however, between 7 and 14 days all males exhibited weight increases. No treatment-related effects on body weight were observed in females. Both sexes exhibited overall (0-14 days) group average increases of 8.3% for males and 11% for females (individual weight increases ranging between 6.6 and

14).

D. Necropsy: Necropsy of animals sacrificed after 14 days revealed no treatment-related gross abnormalities.

E. Deficiencies: There were no deficiencies that affected the results of this study.

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