(10-2-96)

MEMORANDUM

EPA File Symbol: 11715-GRU Etofenprox Crawling Insect Killer I

DP Barcode: D227172

Chemical: 128965 Ethofenprox

Test Material: Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide)

From: Lawrence A. Fried, Biologist
Precautionary Review Section
Registration Support Branch (7505W)
Registration Division

Jan Fried
10-02-96

To: George LaRocca, PM, Team 13
Adam Heyward, Team Reviewer, Team 13

Applicant: 11715 Speer Products Inc.

FORMULATION FROM LABEL

Ingredient(s)	% by wt.
Tetramethrin	0.20
Etofenprox	1.00
Piperonyl Butoxide, Technical	1.00
Inerts	97.80
Total	100.00

BACKGROUND

Speer Products has submitted acute oral toxicity (MRID 440286-03), acute dermal toxicity (MRID 440286-06), acute inhalation toxicity (MRID 440286-08), primary eye irritation (MRID 440286-04), acute skin irritation (MRID 440286-05) and dermal sensitization (MRID 440286-07) studies on Etofenprox Crawling Insect Killer I. Primary review of the acute toxicity studies submitted was performed by Dynamac Corporation. Secondary review of the studies was performed by PRs.

RECOMMENDATION

81-1. Acute Oral: Category IV. The submitted study is acceptable.

81-2. Acute Dermal: Category IV. The submitted study is acceptable.

81-3. Acute Inhalation: Category IV. The submitted study is acceptable.

81-4. Eye Irritation: Category III. The submitted study is acceptable.

81-5. Skin Irritation: Category IV. The submitted study is acceptable.

81-6. Dermal Sensitization: Not a dermal sensitizer in guinea pigs. The submitted study is acceptable.

LABELING RECOMMENDATIONS: (Provided by the Label Review System)

CHILD RESISTANT PACKAGING REQUIRED

INGREDIENT LABELING: Contains Petroleum Distillate.

SIGNAL WORD: **CAUTION**

PRECAUTIONARY STATEMENTS:

Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash thoroughly with soap and water after handling.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF SWALLOWED: Call a physician or Poison Control Center. Do not induce vomiting. Do not give anything by mouth to an unconscious person. Avoid alcohol.

IF IN EYES: Flush eyes with plenty of water. Call a physician if irritation persists.

The proposed label should contain the following guidance:

May pose an aspiration pneumonia hazard.

ACUTE TOX ONE-LINER

ID No.: 11715-GRU Etofenprox Crawling Insect Killer I
DP Barcode: D227172
Chemical: 128965 Ethofenprox
Applicant: 11715 Speer Products Inc.
Test Material: Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% peperonyl butoxide)
Date: October 2, 1996

Study, Animal, Test Laboratory, Study #, Date	MRID No.	Results	Tox. Cat.	Core Grade
Acute Oral, Rat, Product Safety Labs, #4104, 12-22-95	440286-03	LD_{50}>5000 mg/kg	IV	A
Acute Dermal, Rat, Product Safety Labs, #4105, 01-19-96	440286-06	LD_{50}>5000 mg/kg	IV	A
Acute Inhalation, Rat, Product Safety Labs, #4108, 01-24-96	440286-08	LC_{50} >2.03 mg/L	IV	A
Eye Irritation, Rabbit, Product Safety Labs, #4106, 01-24-96	440286-04	Slight to moderate conjunctival effects at 24 hours.	III	A
Skin Irritation, Rabbit, Product Safety Labs, #4107, 01-24-96	440286-05	Very slight dermal irritation observed.	IV	A
Dermal Sensitization, Guinea Pig, Product Safety Labs, #4109, 01-24-96	440286-07	Not a dermal sensitizer in the guinea pig.	---	A

A = Acceptable

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EPA Reviewer: Fried, Date 10-02-96
Review Section __, Toxicology Branch __ (7505W)
EPA Secondary Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)

DATA EVALUATION RECORD

STUDY TYPE: Acute Oral Toxicity - Rat
OPPTS 870.1100 [§81-1]

DP BARCODE: D227172 SUBMISSION CODE: S507136
P.C. CODE: 128965, 069003, and 067501 TOX. CHEM. NO.:
EPA REG. NO.: 11715-GRU

TEST MATERIAL (PURITY): Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide)

SYNONYMS: Etofenprox Crawling Insect Killer I

CITATION: Wnorowski, G. (1995) Acute oral toxicity limit test. Product Safety Labs, East Brunswick, NJ. Laboratory Project Number 4104. December 22, 1995. MRID 44028603. Unpublished.

SPONSOR: Speer Products, Inc., 4242 B.F. Goodrich Blvd., Memphis, TN

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 44028603), a group of five young adult Sprague-Dawley albino rats/sex were given a single oral dose of Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide) at 5,000 mg/kg (limit concentration); the test substance was administered as received. Animals were observed for clinical signs and mortality for up to 14 days postdosing.

Oral LD_{50} Males = >5,000 mg/kg (observed)
Females = >5,000 mg/kg (observed)

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

All animals survived the 14-day observation period. Ano-genital staining was observed in two male animals between days 1 and 2; otherwise, all animals appeared normal and healthy during the study. No treatment-related effect on body weight was observed, and necropsy of animals sacrificed after 14 days revealed no gross abnormalities.

This study is classified **acceptable**, and satisfies the guideline requirement for an acute oral study (81-1) in the rat.

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

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Etofenprox CIK I
   Description: White liquid
   Lot/Batch #: SPI #7421
   Purity: 1.0% Etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide
   CAS #: 80844-07-01, 7696-12-0, and 51-03-6, respectively
   pH: 7.0
   Specific gravity: 0.947 g/mL (temperature not specified)

2. Vehicle: None employed

3. Test animals: Species: Rat
   Strain: Sprague-Dawley derived, albino
   Age: Young adult
   Weight: 193-219 g males; 196-215 g females
   Source: Hilltop Lab Animals, Scottdale, PA
   Acclimation period: 20 days
   Diet: Purina Rodent Chow (#5012), unspecified amount/animal/day
   Water: Filtered tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: November 21-December 5, 1995

2. Animal assignment and treatment: Following a 19-hour fasting period, five young adult rats/sex were given a single oral dose of Etofenprox CIK I at 5,000 mg/kg (limit concentration) by gavage; the test substance was administered as received. The rats were observed for signs of toxicity and/or mortality at 1 and 3 hours following administration, and at least once daily thereafter for the remainder of the 14-day study; body weights were recorded at 0 (prior to dosing), 7, and 14 days. At 14 days, the surviving animals were sacrificed, necropsied, and examined for gross pathological changes.

3. Statistics: Not applicable to this study.

II. RESULTS AND DISCUSSION:

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

Oral LD_{50} Males = >5,000 mg/kg (observed)
Females = >5,000 mg/kg (observed)

B. Clinical observations: Ano-genital staining was observed in two male animals between days 1 and 2; otherwise, all animals appeared normal and healthy during the 14-day observation period.

C. Body Weight: No treatment-related effect on body weight was observed, with overall (0-14 days) average increases of 62% for males and 34% for females.

D. Necropsy: Gross necropsy revealed no treatment-related gross pathological changes.

E. Deficiencies: Although individual observations for the entire day of dosing were not conducted, this deficiency has no effect on the results of the study and is considered minor.

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[Etofenprox, Tetramethrin, and Piperonyl Butoxide] Primary Eye Irritation Study (81-4)

EPA Reviewer: Friel, Date 10-02-96
Review Section __, Toxicology Branch __ (7505W)
EPA Secondary Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)

DATA EVALUATION RECORD

STUDY TYPE: Primary Eye Irritation - Rabbit
OPPTS 870.2400 [§81-4]

DP BARCODE: D227172 SUBMISSION CODE: S507136
P.C. CODE: 128965, 069003, and 067501 TOX. CHEM. NO.:
EPA REG. NO.: 11715-GRU

TEST MATERIAL (PURITY): Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide)

SYNONYMS: Etofenprox Crawling Insect Killer I

CITATION: Wnorowski, G. (1996) Primary eye irritation. Product Safety Labs, East Brunswick, NJ. Laboratory Project Number 4106. January 24, 1996. MRID 44028604. Unpublished.

SPONSOR: Speer Products, Inc., 4242 B.F. Goodrich Blvd., Memphis, TN

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 44028604), 0.1-0.4 g of Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide) was sprayed (via an aerosol can) directly into the right eye of nine adult New Zealand White rabbits (four males and five females). The animals were observed for up to 72 hours following instillation, and eye irritation was scored using the Draize scale.

Based on the average irritation score of 9.7, ocular irritation was most severe in the treated unwashed eyes 1 hour following instillation, and included moderate to severe conjunctival redness in 6/6 eyes, very slight conjunctival chemosis in 4/6 eyes, and slight to severe conjunctival discharge in 6/6 eyes. At 24 hours, slight to moderate conjunctival redness and slight conjunctival discharge persisted in 3/6 eyes. No corneal or iridial changes were observed during the study, and all conjunctival effects subsided by 48 hours. Results in the treated washed eyes were comparable.

Based on the results of this study, **Etofenprox CIK I is a slight eye irritant**, and is classified as **TOXICITY CATEGORY III** for primary eye irritation based on the slight to moderate conjunctival effects which persisted in 3/6 eyes at 24 hours.

This study is classified **acceptable**, and satisfies the guideline requirement for a primary eye irritation study (81-4) 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: Etofenprox CIK I
   Description: Aerosol
   Lot/Batch #: SPI #7421
   Purity: 1.0% Etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide
   CAS #: 80844-07-01, 7696-12-0, and 51-03-6, respectively
   pH: 7.0

2. Vehicle and/or positive control: None employed

3. Test animals: Species: Rabbit
   Strain: New Zealand White
   Age: Adult
   Weight: Not specified
   Source: Davidson's Mill Farm, South Brunswick, NJ
   Acclimation period: 11 days
   Diet: Pelleted Purina Rabbit Chow (#5326), unspecified amount/animal/day
   Water: Filtered tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: December 12-22, 1995

2. Animal assignment and treatment: An approximately 1 second burst, equivalent to 0.1-0.4 g, of Etofenprox CIK I was sprayed from a pressurized can at a distance of 10 cm directly into the right eye of nine New Zealand White rabbits (four males and five females). Approximately 20-30 seconds following instillation, three of the treated eyes were irrigated with 30 mL of physiological saline. The remaining treated eyes were not rinsed, and the left eye of each animal served as an untreated control. The animals were observed for ocular irritation at 1, 24, 48, and 72 hours following instillation. At 24 hours, fluorescein dye was used to confirm the absence of corneal ulceration. Eye

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irritation was scored by the Draize scheme. In addition, each animal was observed for signs of toxicity and/or mortality at least once daily during the 3-day study.

II. RESULTS AND DISCUSSION:

A. Clinical observations: Based on the average irritation score of 9.7, ocular irritation was most severe in the treated unwashed eyes 1 hour following instillation, and included moderate to severe conjunctival redness (scores of 2-3) in 6/6 eyes, very slight conjunctival chemosis (score of 1) in 4/6 eyes, and slight to severe conjunctival discharge (scores of 1-3) in 6/6 eyes. At 24 hours, slight to moderate conjunctival redness (scores of 1-2) and slight conjunctival discharge (score of 1) persisted in 3/6 eyes. No corneal or iridial changes were observed during the study, and all conjunctival effects subsided by 48 hours. Based on the results of this study, Etofenprox CIK I is a slight eye irritant.

Results in the treated washed eyes were comparable. One hour following instillation, moderate to severe conjunctival redness (scores of 2-3) was observed in 2/3 eyes, very slight conjunctival chemosis (score of 1) was observed in 1/3 eyes, and severe conjunctival discharge (score of 3) was observed in 3/3 eyes. The average irritation score at 1 hour was 10. No corneal or iridial changes were observed during the study, and all conjunctival effects subsided by 48 hours.

All animals appeared normal and healthy during the 3-day study.

B. Deficiencies: Subdivision F guidelines specify that 0.1 mL or not more than 100 mg of a test substance should be instilled into the eye. In this study, 100-400 mg of a liquid test material were used per animal based on the weight of the aerosol can prior to and following use. Individual doses/animal were not specified, so comparisons of effects of the variable doses could not be assessed. Furthermore, it is not clear why an aerosol was provided to the laboratory by the sponsor, when a white liquid test material was used for concurrently-conducted acute studies in the same laboratory. However, this study represents a "worst case" scenario, and the data provided were adequate in establishing a Toxicity Category for Etofenprox CIK I. As a result, this deficiency is considered minor.

Although individual observations for the entire day of dosing were not conducted, this deficiency does not alter the results of the study and is considered minor.

EPA Reviewer: Fried, Date 10-02-96
Review Section __, Toxicology Branch __ (7505W)
EPA Secondary Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)

DATA EVALUATION RECORD

STUDY TYPE: Primary Dermal Irritation - Rabbit
OPPTS 870.2500 [§81-5]

DP BARCODE: D227172 SUBMISSION CODE: S507136
P.C. CODE: 128965, 069003, and 067501 TOX. CHEM. NO.:
EPA REG. NO.: 11715-GRU

TEST MATERIAL (PURITY): Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide)

SYNONYMS: Etofenprox Crawling Insect Killer I

CITATION: Wnorowski, G. (1996) Primary skin irritation. Product Safety Labs, East Brunswick, NJ. Laboratory Project Number 4107. January 24, 1996. MRID 44028605. Unpublished.

SPONSOR: Speer Products, Inc., 4242 B.F. Goodrich Blvd., Memphis, TN

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 44028605), three adult New Zealand albino rabbits/sex were dermally exposed to 0.5 mL of Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide) for 4 hours. The test substance was applied to a single intact 6-cm^2 site/animal. Animals were observed for dermal irritation for up to 7 days following application, and irritation was scored by the Draize scheme.

Dermal irritation was most severe 1 hour following patch removal and included very slight to moderate/severe erythema and very slight to slight edema at 6/6 application sites. Well-defined erythema and very slight edema persisted at the application site of a single female animal at 72 hours, and desquamation was observed at that site at 7 days; otherwise, dermal irritation subsided from 5/6 sites by 72 hours. The Primary Dermal Irritation Index was 2.0.

Based on the results of this study, **Etofenprox CIK I is a very slight dermal irritant**, and is classified as **Toxicity Category IV** for primary dermal irritation based on the recovery of 5/6 application sites by 72 hours.

This study is classified **acceptable**, and satisfies the guideline requirement for a primary dermal irritation study (81-5) 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: Etofenprox CIK I
   Description: White liquid
   Lot/Batch #: SPI #7421
   Purity: 1.0% Etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide
   CAS #: 80844-07-01, 7696-12-0, and 51-03-6, respectively
   pH: 7.0

2. Vehicle: None employed

3. Test animals: Species: Rabbit
   Strain: New Zealand albino
   Age: Adult
   Weight: Not specified
   Source: Davidson's Mill Farm, South Brunswick, NJ
   Acclimation period: 8 days
   Diet: Pelleted Purina Rabbit Chow (#5326), unspecified amount/animal/day
   Water: Filtered tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: December 8-15, 1995

2. Animal assignment and treatment: Fur from the dorsal trunk areas of three adult animals/sex was clipped 1 day prior to dermal administration with 0.5 mL of Etofenprox CIK I. The test substance was applied as received to a single intact 6-cm^2 site/animal and covered with a 6.75-cm^2 adhesive-backed gauze patch. The entire trunk of each animal was wrapped with Micropore tape, and the animals were fitted with Elizabethan collars. The coverings and collars were removed 4 hours following application, and the sites were gently wiped with water and a clean towel. The rabbits were observed for dermal irritation at 1, 24, 48, and 72 hours and 7 days following patch removal. Erythema and edema

were scored separately using the Draize scheme. In addition, signs of toxicity and/or mortality were monitored at least once daily during the 7-day study.

II. RESULTS AND DISCUSSION:

A. Clinical observations: Dermal irritation was most severe 1 hour following patch removal and included very slight to moderate/severe erythema (scores of 1-3) and very slight to slight edema (scores of 1-2) at 6/6 application sites. Well-defined erythema (score of 2) and very slight edema (score of 1) persisted at the application site of a single female animal at 72 hours, and desquamation was observed at that site at 7 days; otherwise, dermal irritation subsided from 5/6 sites by 72 hours. The Primary Dermal Irritation Index (1 through 72 hours) was 2.0. Based on the results of this study, Etofenprox CIK I is a very slight dermal irritant.

All animals appeared normal and healthy during the 7-day study.

B. Deficiencies: Although individual observations for the entire day of dosing were not conducted, this deficiency does not alter the results of the study and is considered minor.

EPA Reviewer: Field, Date 10-02-96
Review Section __, Toxicology Branch __ (7505W)
EPA Secondary Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)

DATA EVALUATION RECORD

STUDY TYPE: Acute Dermal Toxicity - Rat
OPPTS 870.1200 [§81-2]

DP BARCODE: D227172 SUBMISSION CODE: S507136
P.C. CODE: 128965, 069003, and 067501 TOX. CHEM. NO.:
EPA REG. NO.: 11715-GRU

TEST MATERIAL (PURITY): Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide)

SYNONYMS: Etofenprox Crawling Insect Killer I

CITATION: Wnorowski, G. (1996) Acute dermal toxicity limit test. Product Safety Labs, East Brunswick, NJ. Laboratory Project Number 4105. January 19, 1996. MRID 44028606. Unpublished.

SPONSOR: Speer Products, Inc., 4242 B.F. Goodrich Blvd., Memphis, TN

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 44028606), five young adult Sprague-Dawley albino rats/sex were dermally exposed to Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide) at 5,000 mg/kg (>2X limit concentration) for 24 hours; the test substance was applied as received to approximately 10% of the total body surface area. Animals were observed for clinical signs and mortality for up to 14 days postdosing.

Dermal LD_{50} Males = >5,000 mg/kg (observed)
Females = >5,000 mg/kg (observed)

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

All animals survived and appeared normal and healthy during the 14-day observation period; erythema (not graded) was observed at the treatment sites of three animals/sex upon patch removal, and persisted at two sites through 14 days. No treatment-related effects on body weight were observed, and necropsy of animals sacrificed after 14 days revealed no gross abnormalities.

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

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

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Etofenprox CIK I
   Description: White liquid
   Lot/Batch #: SPI #7421
   Purity: 1.0% Etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide
   CAS #: 80844-07-01, 7696-12-0, and 51-03-6, respectively
   pH: 7.0
   Specific gravity: 0.947 g/mL (temperature not specified)

2. Vehicle: None employed

3. Test animals: Species: Rat
   Strain: Sprague-Dawley derived, albino
   Age: Young adult
   Weight: 203-230 g males; 210-222 g females
   Source: Hilltop Lab Animals, Scottdale, PA
   Acclimation period: 9 days
   Diet: Purina Rodent Chow (#5012), unspecified amount/animal/day
   Water: Filtered tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: December 1-15, 1995

2. Animal assignment and treatment: Fur from the dorsal trunk areas of five animals/sex was clipped 1 day prior to dermal administration of Etofenprox CIK I at 5,000 mg/kg (>2X limit concentration). The test substance was applied as received and spread evenly over an area of approximately 6-in^2 (10% of the total body surface area). Each application site was covered with an 6.75-in^2 adhesive-backed gauze patch, and the entire trunk of each animal was wrapped with Durapore tape. The coverings were removed 24 hours following application, and the test sites were gently wiped with water and a clean towel. The rats were observed for signs of toxicity

and/or mortality at 1 and 6 hours following application, and at least once daily thereafter for the remainder of the 14-day study; body weights were recorded at 0 (prior to dosing), 7, and 14 days. At 14 days, surviving animals were sacrificed, necropsied, and examined for gross pathological changes.

3. Statistics: Not applicable to this study.

II. RESULTS AND DISCUSSION:

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

Dermal LD_{50} Males = >5,000 mg/kg (observed)
Females = >5,000 mg/kg (observed)

B. Clinical observations: All animals appeared normal and healthy during the 14-day observation period. Erythema (not graded) was observed at the treatment sites of three animals/sex upon patch removal, and persisted at two sites (one animal/sex) through 14 days.

C. Body Weight: No treatment-related effect on body weight was observed, with overall (0-14 days) average increases of 53% for males and 12% for females.

D. Necropsy: Gross necropsy revealed no treatment-related gross pathological changes.

E. Deficiencies: Although individual observations for the entire day of dosing were not conducted and the study was terminated before treatment site irritation had subsided in all animals, these deficiencies have no effect on the results of the study and are considered minor.

[Etofenprox, Tetramethrin, and Piperonyl Butoxide] Dermal Sensitization Study (81-6)

EPA Reviewer: Friel, Date 10-02-96
Review Section __, Toxicology Branch __ (7505W)
EPA Secondary Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)

DATA EVALUATION RECORD

STUDY TYPE: Dermal Sensitization - Guinea pig
OPPTS 870.2600 [§81-6]

DP BARCODE: D227172 SUBMISSION CODE: S507136
P.C. CODE: 128965, 069003, and 067501 TOX. CHEM. NO.:
EPA REG. NO.: 11715-GRU

TEST MATERIAL (PURITY): Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide)

SYNONYMS: Etofenprox Crawling Insect Killer I

CITATION: Wnorowski, G. (1996) Dermal sensitization test - Buehler method. Product Safety Labs, East Brunswick, NJ. Laboratory Project Number 4109. January 24, 1996. MRID 44028607. Unpublished.

SPONSOR: Speer Products, Inc., 4242 B.F. Goodrich Blvd., Memphis, TN

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 44028607) conducted with Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide), ten young adult Hartley albino guinea pigs were tested using methods based on those derived by Buehler. A concurrent positive control study was conducted in the same manner using 1-chloro-2,4-dinitrobenzene.

Very faint erythema was observed at 1/10 sites 24 and 48 hours following the single challenge treatment to previously-induced animals. No dermal irritation was observed 24 or 48 hours following challenge to naive control animals. Acceptable positive control data were provided to validate the test methodology. Based on the results of this study, **Etofenprox CIK I does not appear to be a dermal sensitizer.**

This study is classified **acceptable**, and satisfies the guideline requirement for a dermal sensitization study (81-6) in the guinea pig.

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

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Etofenprox CIK I
   Description: White liquid
   Lot/Batch #: SPI #7421
   Purity: 1.0% Etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide
   CAS #: 80844-07-01, 7696-12-0, and 51-03-6, respectively
   pH: 7.0

2. Vehicle and positive control: No vehicle was employed in the definitive study.

   0.08% 1-Chloro-2,4-dinitrobenzene (DNCB; ≥98% purity) in 80% aqueous ethanol (induction phase) or 0.04% DNCB in acetone (challenge phase) was used for concurrent positive control data.

3. Test animals: Species: Guinea pig
   Strain: Hartley albino
   Age: Young adult
   Weight: 305-383 g males; 373 g female (one only)
   Source: Davidson's Mill Farms, South Brunswick, NJ
   Acclimation period: 5 days
   Diet: Pelleted Purina Guinea Pig Chow, unspecified amount/animal/day
   Water: Filtered tap water, ad libitum
   Housing: Group (not further specified)

B. STUDY DESIGN and METHODS:

1. In-life dates: December 5, 1995-January 4, 1996

2. Animal assignment and treatment: The study was conducted using methods based on those derived by Buehler [Robinson, M., et al., Toxicology, 61:91-107 (1990); Ritz, H. and E. Buehler, Current Concepts in Cutaneous Toxicity, p. 25-40: Academic Press, NY (1980)]. Preliminary testing was conducted using either 0.4 mL of Etofenprox CIK I as received (100%) or 0.4 mL of 25, 50, or 75% (w:w) dilutions in distilled water. As a result, the test substance was used as received (100%) for both phases of the definitive study.

   For the induction phase, fur on the dorsal and flank areas of ten young adult male animals was clipped 1 day prior to dermal administration of 0.4 mL of

Etofenprox CIK I. The test substance was applied as received to the left side of each animal using an occlusive 25-mm Hill Top Chamber secured with Durapore adhesive tape. An additional ten male animals were treated in the same manner as described using 0.4 mL of 0.08% DNCB. Following a 6-hour exposure period, the chambers were removed, and any excess test substance was removed from the skin by gently wiping with water and clean towels. Application of the test substance was repeated once weekly for 2 consecutive weeks (three total applications).

For the challenge treatment, 0.4 mL of either Etofenprox CIK I or 0.04% DNCB in acetone was applied in the same manner as described, to previously untreated sites on the right side of each animal 14 days following the final induction treatment. To serve as naive controls, an additional five animals/test substance or positive control were included for the challenge treatment.

The guinea pigs were observed for dermal irritation 24 and 48 hours following each induction and challenge exposure. Skin reactions were scored according to the following scale:

0 - No reaction
0.5 - Very faint erythema, usually non-confluent
1 - Faint erythema usually confluent
2 - Moderate erythema
3 - Severe erythema with or without edema

Body weights of each animal were recorded prior to the first induction treatment and on the day following the challenge treatment.

II. RESULTS AND DISCUSSION:

A. Induction reactions and duration: The incidence of dermal irritation increased with each successive application of Etofenprox CIK I, and generally lessened from the 24- to 48-hour observation intervals. Twenty-four hours following the first two induction treatments, very faint erythema (score of 0.5) was observed at 0/10 and 2/10 sites, respectively. Twenty-four hours following the third treatment, very faint to faint erythema (scores of 0.5-1) was observed at 5/10 sites.

B. Challenge reactions and duration: Twenty-four and 48 hours following the single challenge treatment to previously-induced animals, very faint erythema (score of 0.5) was observed at 1/10 sites. No dermal irritation was observed 24 or 48 hours following challenge to naive control animals. Based on the results of this study, Etofenprox CIK I does not appear to be a dermal sensitizer.

No significant treatment-related effect on body weight was observed between test and naive control animals, with overall (approximately 29 days) average increases of 61% for test animals (all male) and 75% for naive control males animals and 31% for the single naive control female animal.

C. Positive control: The incidence and severity of dermal irritation increased with each successive application of DNCB. Irritation was generally more severe 24 hours following treatment. Twenty-four hours following the first induction treatment, very faint erythema (score of 0.5) was observed at 6/10 sites, and 24 hours following the third induction treatment, faint to severe erythema (scores of 1-3) was observed at 10/10 sites.

Twenty-four hours following the single challenge treatment to previously-induced animals, faint to moderate erythema (scores of 1-2) was observed at 10/10 sites; the degree of irritation worsened by 48 hours to faint to severe erythema at 10/10 sites. In contrast, 24 and 48 hours following treatment to naive control animals, very faint erythema was observed at 2/5 and 0/5 sites, respectively. These data confirm the adequacy of the test species and method employed.

D. Deficiencies: There were no deficiencies that affected the validity of the study results.

EPA Reviewer: Fred, Date 10-02-96
Review Section __, Toxicology Branch __ (7505W)
EPA Secondary Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)

DATA EVALUATION RECORD

STUDY TYPE: Acute Inhalation Toxicity - Rat
OPPTS 870.1300 [§81-3]

DP BARCODE: D227172 SUBMISSION CODE: S507136
P.C. CODE: 128965, 069003, and 067501 TOX. CHEM. NO.:
EPA REG. NO.: 11715-GRU

TEST MATERIAL (PURITY): Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide)

SYNONYMS: Etofenprox Crawling Insect Killer I

CITATION: Wnorowski, G. (1996) Acute inhalation toxicity limit test. Product Safety Labs, East Brunswick, NJ. Laboratory Project Number 4108. January 24, 1996. MRID 44028608. Unpublished.

SPONSOR: Speer Products, Inc., 4242 B.F. Goodrich Blvd., Memphis, TN

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 44028608), five young adult Sprague-Dawley albino rats/sex were exposed by whole-body inhalation to Etofenprox CIK I (1.0% etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide) at 2.03 mg/L (limit concentration) for 4 hours. Animals were observed for clinical signs and mortality for up to 14 days following exposure.

Inhalation LC_{50} Males = >2.03 mg/L (observed)
Females = >2.03 mg/L (observed)

Etofenprox CIK I is classified as **TOXICITY CATEGORY IV** based on the observed LC_{50} values in both sexes.

All animals survived the 4-hour exposure and 14-day observation periods. Clinical effects observed upon chamber removal included test substance on fur, hunched posture, irregular respiration, and hypoactivity. Effects subsided from all animals by day 2. No treatment-related effects on body weight were observed, and necropsy revealed no treatment-related gross pathological changes.

This study is classified **acceptable**, and satisfies the guideline requirement for an acute inhalation study (81-3) in the rat.

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

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Etofenprox CIK I
   Description: White liquid
   Lot/Batch #: SPI #7421
   Purity: 1.0% Etofenprox, 0.3% tetramethrin, and 1.0% piperonyl butoxide
   CAS #: 80844-07-01, 7696-12-0, and 51-03-6, respectively
   pH: 7.0
   Specific gravity: 0.947 g/mL (temperature not specified)

2. Vehicle and/or positive control: None employed

3. Test animals: Species: Rat
   Strain: Sprague-Dawley derived, albino
   Age: Young adult
   Weight: 238-253 g males; 214-229 g females
   Source: Hilltop Lab Animals, Scottdale, PA
   Acclimation period: 23 days
   Diet: Purina Rodent Chow (#5012), unspecified amount/animal/day, except during exposure
   Water: Tap water, ad libitum, except during exposure

B. STUDY DESIGN and METHODS:

1. In-life dates: December 15-29, 1995

2. Exposure conditions: A rectangular dynamic-flow perspex exposure chamber (150 L) was used; aside from "whole body", animal orientation within the chamber was not described.

   Test atmosphere was generated using a Spraying Systems 0.25-inch JCO atomizer operated using dry, compressed air. Measured test material was pumped via a Master Flex Pump into the atomization nozzle. The resultant aerosol was diluted with filtered, "conditioned" room air prior to entering the exposure chamber. The mean chamber airflow averaged 45.8 L/min (equivalent to 18.3 turnovers/hour). The times required for 90 and 99% equilibration were 7.5 and 15.1 minutes, respectively.

The nominal test atmosphere concentration was determined at the end of the exposure period by dividing the total amount of test material delivered to the chamber by the total air volume that passed through the chamber during the exposure time. The actual test atmosphere concentration was determined gravimetrically six times during the exposure period by drawing 12-L samples from the breathing zone of the animals through 25-mm Whatman glass fiber filters. The nominal and average gravimetric test concentrations were 39.06 and 2.03 mg/L, respectively.

Particle size was determined twice (at unspecified intervals) during the exposure period using an eight-stage Andersen cascade impactor. Samples (volume not specified) were collected from the breathing zone of the animals. The calculated average mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) were 2.6 and 1.76 μm. The average percentage of particles <4.7 μm was 88.8%.

During exposure, the temperature was 70-73°F, and the relative humidity was 54-100%. Although the oxygen level was not measured, the turnover rate ensured a concentration of ≥19%.

3. Animal assignment and treatment: Five young adult albino rats/sex were exposed via whole-body inhalation to Etofenprox CIK I at 2.03 mg/L (limit concentration) for 4 hours. The animals were observed for signs of toxicity and/or mortality at least every 30 minutes during exposure, upon chamber removal, and at least once daily thereafter for the remainder of the 14-day study. Body weights were recorded at 0 (prior to exposure), 7, and 14 days. After 14 days, the surviving animals were sacrificed, necropsied, and examined for gross pathological changes.

4. Statistics: Not applicable to this study.

II. RESULTS AND DISCUSSION:

A. Mortality: All animals survived the 4-hour exposure and 14-day observation periods.

Inhalation LC_{50} Males = >2.03 mg/L (observed)
Females = >2.03 mg/L (observed)

B. Clinical observations: Clinical effects observed upon chamber removal included test substance on fur (10/10), hunched posture (4/10), irregular respiration (2/10), and hypoactivity (1/10). Effects subsided from all animals by day 2.

C. Body Weight: No treatment-related effect on body weight was observed, with overall (0-14 days) average increases of 41% for males and 18% for females.

D. Necropsy: Necropsy revealed no treatment-related gross pathological changes.

E. Deficiencies: The actual test atmosphere concentration was determined gravimetrically, which is considered an unacceptable method for liquid aerosols. However, since gravimetrically-determined concentrations are typically biased-low (because they usually do not account for volatilization of a test substance), and since no mortality occurred in this study at the calculated concentration of 2.03 mg/L (limit concentration), this deficiency does not alter the observed LC_{50} values or subsequent Toxicity Category of Etofenprox CIK I and is considered minor.

The aerodynamic particle size should have been determined hourly during the exposure. This deficiency is considered minor since the size was determined once every 2 hours, and since the individual MMAD and GSD values were comparable and within the ideal respirable range of 1-4 μm.

Although individual observations for the entire day of dosing were not conducted, this deficiency has no effect on the results of the study and is considered minor.

Although humidity levels ranged from 54-100%, exceeding the 40-60% limits set forth in Subdivision F guidelines, the test substance is an aqueous formulation, and this deficiency is considered minor.