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

March 3, 1998

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: EPA File Symbol: 33657-O Etofenprox Aerosol
DP Barcode: D216084
Case No: 007216

From: Byron T. Backus, Ph.D., Toxicologist
Technical Review Branch
Registration Division (7505C)

Byron T. Backus
3-MARCH-1998
BTB for JCR
3/3/98

To: Linda DeLuise, PM 03
Insecticide Branch
Registration Division (7505C)

Registrant: MTC America Inc.

FORMULATION (LABEL DECLARATION)

Active Ingredient(s):	% by wt.
128965 Etofenprox	1.00%
Inert Ingredient(s):	99.00%

BACKGROUND: The applicant has submitted six acute toxicity studies on this formulation (an oral LD50 study with rats, a dermal LD50 study with rabbits, an inhalation LC50 study with rats, a primary eye irritation study with rabbits, a primary dermal irritation study with rabbits, and a dermal sensitization study with guinea pigs). The MRID numbers are 436629-03 through 436629-08. All studies were conducted at Springborn Laboratories, Inc. (Spencerville, OH).

RECOMMENDATION: Each of the studies is acceptable. The acute toxicology profile for EPA File Symbol: 33657-O (Etofenprox Aerosol) is as follows:

acute oral toxicity	IV	acceptable
acute dermal toxicity	III	acceptable
acute inhalation toxicity	IV	acceptable
primary eye irritation	III	acceptable
primary skin irritation	III	acceptable
dermal sensitization	Non-Sensitizer	acceptable

LABELING: The following is the precautionary labeling for this product as obtained from the label review system:

Date: 03/03/98 LABEL REVIEW SYSTEM

ID #: 033657-00009 1% ETOFENPROX AEROSOL

SIGNAL WORD: CAUTION

PRECAUTIONARY STATEMENTS:

Harmful if absorbed through skin. Causes moderate eye irritation. Avoid contact with eyes, skin or clothing. Wash thoroughly with soap and water after handling.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF ON SKIN: Wash with plenty of soap and water. Get medical attention if symptoms persist.

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

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DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§81-1, 870.1100)

Product Manager: 03 **Reviewer:** Byron T. Backus, Ph.D.
MRID No.: 43662903 **Amended Study Completion Date:** January 17, 1995
Study No.: 3354.7

Testing Facility: Springborn Laboratories, Inc., Spencerville, OH
Author(s): Douds, D.A.
Quality Assurance (40 CFR §160.12): Included (p. 4)

Test Material: 1% Etofenprox, Lot no. 6831
Species: Rat; Albino, Sprague-Dawley Crl:CD®BR VAF/Plus®
Age: "Young adult"
Prefasting (Postfasting) Weights: M: 214-224 (188-198) g; F: 236-258 (216-235) g.
Source: Charles River, Portage, Michigan

Conclusion:

1. **LD_{50}:**
   Males >5000 mg/kg (no mortalities at this dose)
   Females >5000 mg/kg (no mortalities at this dose)
   Combined >5000 mg/kg (no mortalities at this dose)
2. **The estimated LD_{50} is** >5000 mg/kg
3. **Tox. Category:** IV **Classification:** Acceptable

Procedure (Including deviations from §81-1): Animals were fasted overnight; individual doses were calculated from fasted body weights. The test material was a liquid, with a density (measured by laboratory) of 0.96; the 5000 mg/kg dose was administered at 5.21 mL/kg. According to a certificate of analysis (Appendix B) the test material contained 1.55% Etofenprox, had a specific gravity of 0.974, and a pH (at 20°C) of 7.0.

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

Observations: One male and three females had soft stools (in most cases with fecal stain) days 0-1; one female had salivation and dark material around mouth. All animals were normal from day 2 to termination. "Body weight gain was noted for all animals during the test period."

Gross Necropsy: "No significant changes observed."

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DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2, 870.1200)

Product Manager: 03
MRID No.: 43662904

Reviewer: Byron T. Backus, Ph.D.
Amended Study Completion Date: January 17, 1995
Study No.: 3354.8

Testing Facility: Springborn Laboratories Inc., Spencerville, OH
Author(s): Douds, D.A.

Quality Assurance (40 CFR §160.12): Included (p. 4)

Test Material: 1% Etofenprox, Lot no. 6831
Species: Rabbit; Albino, New Zealand White
Age: "adult"
Weight: Males: 2782-3039 g; Females: 2639-2865 g
Source: Myrtle's Rabbitry, Thompson Station, TN

Dermal LD_{50} Testing: 24-hour occluded exposure at 2000 mg/kg

Conclusion:

1. **LD_{50} (mg/kg):**
   Males: > 2000 mg/kg (no mortalities)
   Females: > 2000 mg/kg (no mortalities)
   Combined: > 2000 mg/kg (no mortalities)
2. **The estimated LD_{50} is** > 2000 mg/kg
3. **Tox. Category:** III

Classification: Acceptable

Procedure (Including deviations from §81-2): The test material (a white liquid) was administered as received. The density (measured by laboratory) was 0.96. According to a certificate of analysis (Appendix B) the test material contained 1.55% Etofenprox, had a specific gravity of 0.974, and a pH (at 20°C) of 7.0.

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
2000	0/5	0/5	0/10

Observations: There were no signs of toxicity other than pronounced dermal irritation (erythema, edema, desquamation, eschar, and fissuring) with effects persisting in all animals through day 14.

Gross Necropsy: Necropsies of all animals were unremarkable.

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DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3, 870.1300)

Product Manager: 03
MRID No.: 43662905

Reviewer: Byron T. Backus, Ph.D.
Study Completion Date: March 2, 1995
Study No.: 3354.9

Testing Facility: Springborn Laboratories, Inc., Spencerville, OH
Author: Douds, D.A.

Quality Assurance (40 CFR §160.12): Included (p. 4)

Test Material: 1% Etofenprox, Lot no. 6831
Species: Rat; Albino, Sprague-Dawley Crl:CD®BR VAF/Plus®
Age: "Young adult"
Weight: Males: 281-297 g; Females: 241-259 g

Source: Charles River, Portage, Michigan

Conclusion:

1. **LC_{50} (mg/L):**
   Males: > 2.11 mg/L (0/5 died at this concentration)
   Females: > 2.11 mg/L (0/5 died at this concentration)
   Combined: > 2.11 mg/L (0/10 died at this concentration)
2. **The estimated LC_{50} is** > 2.11 mg/L
3. **Tox. Category:** IV

Classification: Acceptable

Procedure (Including deviations from §81-3): "The volatility of the test article relative to a distilled water standard was determined prior to study initiation. This...was...to determine if the test article had sufficiently low volatility to allow for an accurate gravimetric determination of the aerosol concentration. A known quantity of the test article was placed on a preweighed filter disk and was allowed to evaporate...results of this volatility trial indicated that the test article evaporation rate (0.85 mg/minute) was only slightly greater than the...distilled water evaporation rate (0.55 mg/minute). Therefore, standard gravimetric sampling techniques would be acceptable for this test article."

Exposure was whole body.

Results:

Exposure Concentration ± S.D. mg/L (Gravimetrically Determined)	Number of Deaths/Number Tested		
	Males	Females	Combined
2.11 ± 0.08	0/5	0/5	0/10

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Clinical Observations: "The most notable clinical abnormalities observed during the study included urine stain, dark material around the facial area, rough haircoat, and swollen eyelids." These symptoms were generally gone by day 4. One rat had hairloss on both forelimbs days 6-12, but it is uncertain whether this was related to exposure to the test material.

Gross Necropsy Findings: "No significant gross internal findings were observed at necropsy on study day 14."

Chamber Atmosphere		
Grav. Conc.	MMAD	GSD
2.11 ± 0.08 mg/L	3.1 µm	2.6

Other Information: The nominal concentration was 51.91 mg/L. A mean of 61% of the particles had an effective cutoff diameter of 4.0 µm. According to a certificate of analysis (Appendix B) the test material contained 1.55% Etofenprox.

Chamber Environment	
Chamber Volume	100 liters
Airflow	45.3 Lpm
Temperature	66.4-69.8°F
Relative Humidity	74.2-94.6%

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DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)

Product Manager: 03
MRID No.: 43662906

Reviewer: Byron T. Backus, Ph.D.
Amended Study Completion Date: March 13, 1995
Study No.: 3354.10

Testing Facility: Springborn Laboratories, Inc., Spencerville, OH
Author: Douds, D.A.

Quality Assurance (40 CFR §160.12): Included (p. 4)

Test Material: 1% Etofenprox, Lot no. 6831 (Aerosol Can)
Dosage: "Approximate 1 second burst...in the right eye." 0.7-1.4 g
Species: Rabbits; Albino, New Zealand White
Age: "Adult"
Weight: not given

Source: Myrtle's Rabbitry, Thompson Station, TN

Conclusion:

1. **Toxicity Category:** III (Iritis in 5/6 at 1 hr, 1/6 at 24 hrs; all eyes clear by 48 hours)
2. **Classification:** Acceptable

Procedure (Including deviations from §81-4): "The test article was sprayed directly into the right eye of each animal for an approximate 1 second burst from a distance of approximately 10 cm."

Observations	Number of "positive"/number tested					
	Hours				Days	
	1	24	48	72	4	7
Corneal Opacity	0/6	0/6	0/6	0/6	nd	nd
Iritis	5/6	1/6	0/6	0/6	nd	nd
Conjunctivae:						
Redness*	3/6	0/6	0/6	0/6	nd	nd
Chemosis*	0/6	0/6	0/6	0/6	nd	nd
Discharge	3/6	0/6	0/6	0/6	nd	nd

*Score of 2 or more required to be considered "positive."

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DATA REVIEW FOR PRIMARY DERMAL IRRITATION TESTING (§81-5, 870.2500)

Product Manager: 03
MRID No.: 43662907

Reviewer: Byron T. Backus, Ph.D.
Amended Study Completion Date: Jan. 16, 1995
Study No.: 3354.11

Testing Facility: Springborn Laboratories, Inc., Spencerville, OH
Author: Douds, D.A.

Quality Assurance (40 CFR §160.12): Included (p. 4)

Test Material: 1% Etofenprox, Lot no. 6831
Dosage: 0.5 mL/site; 4-hour semi-occluded exposure
Species: Rabbits; Albino, New Zealand White
Age: "Adult"
Weight: 2.355-2.562 kg

Source: Myrtle's Rabbitry, Thompson Station, TN

Summary:

1. **Toxicity Category:** III (moderately irritating; PII = 4.25)
2. **Classification:** Acceptable

Procedure (Including deviations from §81-5): Test article was applied to a 1" x 1" patch of skin.

Results: One hour after patch removal, well-defined erythema (scores 2-4) and edema (scores 2-3) were observed at all treated sites. Mean irritation score at 24 hrs: 3.83; at 48 hrs: 3.83; at 7 days: 3.83; but 5/6 scored zero at 14 days (the remaining rabbit had a score of 1 for erythema).

Special Comments: No indication of permanent skin damage. According to a certificate of analysis (Appendix B) the test material contained 1.55% Etofenprox.

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DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6, 870.2600)

Product Manager: 03
MRID No.: 43662908

Reviewer: Byron T. Backus, Ph.D.
Study Completion Date: March 2, 1995
Study No.: 3354.12

Testing Facility: Springborn Laboratories, Inc., Spencerville, OH
Author: Douds, D.A.

Quality Assurance (40 CFR §160.12): Included (p. 4)

Test Material: 1% Etofenprox, Lot no. 6831
Positive Control Material: Dinitrochlorobenzene (DNCB), Lot. No. 12423MZ
Species: Guinea pig; Hartley-derived albino
Age: "Young adult"
Weight: Males: 365-431 g; Females: 330-390 g
Source: Harlan Sprague Dawley, Inc., Haslett, Michigan
Method: "Modified" Buehler

Conclusion:

1. **The results indicate that this product is not a dermal sensitizer.**
2. **Classification:** Acceptable

Procedure (Including deviations from §81-6): In preliminary range-finding testing, the test article was evaluated at 2.5%, 5%, 10%, 15%, 25%, 50%, 75% and 100% w/v. Five male and 5 female guinea pigs were topically treated (6-hr occluded exposure) on their left sides with 0.4 mL 100% 1% Etofenprox, once per week, for three consecutive weeks. The induction sites were graded at 24 and 48 hrs after application. Following a two-week period, the 10 previously exposed (induced) animals, as well as 10 naive animals, were treated with 5% w/v 1% Etofenprox in distilled water. After seven days, rechallenges (10% and 15% w/v 1% Etofenprox in distilled water) were performed at two sites on each of the 10 animals that had gone through the induction procedure, as well as a second new group of 10 naive controls. A group of six animals were similarly induced with 0.5% w/v DNCB in an acetone/ethanol vehicle, and were challenged (along with 4 naive controls) with 0.1% and 0.2% w/v DNCB in acetone/ethanol for challenge.

Results: During the induction phase, there was a considerable variation in the degree of dermal irritation. Following the first induction, scores of ± to 1 were observed (both at 24 and 48 hours); following the second induction, scores ranged from 0 to 3 at both 24 and 48 hours; following the third induction, scores ranged from 0 to 1, and the two animals which had scored 3 following the second induction scored 1 and ±. No irritation

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was observed following the first challenge (with a solution containing 0.05% Etofenprox); following rechallenge, scores of 0 to ± (at both 24 and 48 hours) for 0.1% Etofenprox were observed in both the previously induced animals as well as those which had not been previously exposed; and scores of 0 to 1 in those animals (previously induced and naive) exposed to 0.15% Etofenprox. The appropriate response occurred in induced positive control animals.

Special Comment: One concern of this reviewer involves the use of the 100% (undiluted) 1% Etofenprox product in induction treatment, and use of only a 5% dilution of the product (resulting in a 0.05% Etofenprox-containing solution) for the initial challenge. However, the laboratory subsequently rechallenged with 10% and 15% (0.10% and 0.15% Etofenprox-containing solutions, respectively).

A second concern is the occurrence of scores of 3 (at both 24 and 48 hours) in two females following the second induction treatment. However, scores for the remaining animals were generally in the range of 0 to 1 (one female had a score of 2 at 24 hours following the second induction), and scores in all animals (including those with scores of 3 following the second induction) ranged from 0 to 1 following the third induction treatment.

While this reviewer has reservations with the choice of undiluted product for purposes of induction (in the primary skin irritation study in rabbits - MRID 43662907 - the primary irritation index was 4.25, near the high end for a "moderate" irritant [scores ranging from 2.00 to 5.00]), there was no indication of any dermal sensitization reaction in guinea pigs that were exposed to it.

ACUTE TOX ONE-LINERS

1. **PC CODE:** 128965
2. **CURRENT DATE:** March 3, 1998
3. **TEST MATERIAL**: 1% Ethofenprox Aerosol
   Ethofenprox - 1%

Study/Species/Lab Study #/Date	MRID No.	Results	Tox. Cat.	Core Grade
Acute oral toxicity rat/Springborn Laboratories/ 3354.7/17-JAN-95	43662903	LD_{50} > 5000 mg/kg (no deaths at this dose)	IV	A
Acute dermal toxicity rabbit/Springborn Laboratories/3354.8/ 17-JAN-95	43662904	LD_{50} > 2000 mg/kg	III	A
Acute inhalation toxicity rat/ Springborn Laboratories/ 3354.9/2-MAR-95	43662905	LC_{50} > 2.11 mg/L (0/10 died at this concentration)	IV	A
Primary eye irritation rabbit/Springborn Laboratories/3354.10/ 13-MAR-95	43662906	Iridial irritation in 5/6 at 1 hr; 1/6 at 24 hrs; all irritation clear by day 7	III	A
Primary dermal irritation rabbit/Springborn Laboratories/3354.11/ 16-JAN-95	43662907	PII = 4.25; mean irritation score at 7 days: 3.83, but 5/6 scored zero by day 14 and no indication of permanent damage.	III	A
Dermal sensitization/ guinea pig/Springborn Laboratories/3354.12/ 2-MAR-95	43662908	Not a sensitizer	–	A

Core Grade Key: **A = Acceptable**

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