

US EPA ARCHIVE DOCUMENT

7-29-96

MEMORANDUM

Subject: EPA REG #: 1021-RAII
DPBarcode: D224863
Chemical ID #: 109701
Chemical Name: Permethrin
PRS Bean #: 5338
Type of Data: Toxicology, acute

TO: Rick Keigwin, PM # 10 Attn: Sheila Motes
Insecticide/Rodenticide Branch
Registration Division (7505C)

FROM: David L. Ritter, Toxicologist
Registration Support Branch
Precautionary Review Section
Registration Division (7505W)

DOR 7-29-96

Registrant: MGK Co.
8810 10th Ave. N.
Minneapolis MN 55427-4372

Action Requested:

Review acute toxicity data and precautionary labeling.

Background:

The data have been reviewed and the DERs are attached. The reviews were performed by Dynamac Corporation, 2275 Research Blvd., Rockville MD.

The primary reviewer is identified as C. E. Padova, B.S.

PRS Response:

The reviews were secondarily reviewed by the above-signed.

The Dynamac reviews are all acceptable in that they accurately reflect information found in the individual studies and that the conclusions drawn by the primary reviewer are consistent with the data.

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The acute oral, inhalation, eye and skin irritation studies were placed TOX category IV. The acute dermal study was placed in TOX category III and the dermal sensitization study showed that the product is not a dermal sensitizing agent in a modified Buehler assay.

All studies were classified as acceptable.

The studies are summarized below:

Acute Toxicity Data Requirements (40 CFR §158.340).
Pesticide Assessment Guidelines, Subdivision F. Hazard Evaluation: Human and Domestic Animals. (1982; revised 1984).

<u>Data Required</u>	<u>MRID #</u>	<u>Toxicity Category</u>	<u>Classification</u>
Acute Oral (§81-1)	439648-01	IV	A
Acute Dermal (81-2)	" -02	III	A
Acute Inhal. (81-3)	" -03	IV	A
Eye Irr. (§81-4)	" -04	IV	A
Dermal Irr. (§81-5)	" -05	IV	A
Dermal Sens. (§81-6)	" -06	Non-sens.	A

Precautionary Labeling Review:

See the attached LRS sheet.

ACUTE TOX ONE-LINER

1. PC CODE: 109701; permethrin
2. CURRENT DATE: 7/26/96
3. TEST MATERIAL: Multicide Mosquito Concentrate 2705
4. EPA Reg. #: 1021-RAII

Study/Species/Lab/ Study#/Date	MRID No.	Results	Tox. Cat.	Core Grade
Acute oral/rat /Biosearch/ 94-8104A/1-3-95	439648-01	LD ₅₀ m+f > 5000 mg/kg	IV	A
Acute derm./rabbit/ Biosearch/94-8104A/ 2-21-96	" -02	LD ₅₀ M+F > 2000 mg/kg	III	A
Acute inhal./rat/ Biosearch/84-8104A/ 2-21-96	" -03	LC ₅₀ M = 3.73 mg/l LC ₅₀ F > 6.21 mg/l	IV	A
Eye irr./rabbit/Bio search/94-8104A/ 1-3-95	" -04	Sl. irritant	IV	A
Skin irr./rabbit/ Biosearch/94-8104A/ 1-3-95	" -05	Sl. irritant	IV	A
Skin sensitization/ Guinea pig/Biosearch/ 94-8104A/1-3-95	" -06	Non-sens.	---	A

Core Grade Key:

- A = Acceptable
- U = Unacceptable
- S = Supplementary

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Date: 07/29/96

LABEL REVIEW SYSTEM

Page: 1

ID #: 001021-01688 MULTICIDE MOSQUITO ADULTICIDING CONCENTRATE 2705

SIGNAL WORD: CAUTION

PRECAUTIONARY STATEMENTS:

Harmful if absorbed through skin. 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.

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DATA EVALUATION RECORD

Multicide Mosquito Adulticiding Concentrate 2705
(PBO and Sumithrin)

Study Type: Acute Six Pack (81-1 through -6)

Work Assignment No. 1-51A (D224863)

Prepared for

Registration Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
Crystal Station 6H
2800 Crystal Drive
Arlington, VA 22202

Prepared by

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

Primary Reviewer:
Christie E. Padova, B.S.

Signature: Christie E. Padova
Date: 7-12-96

Project Manager:
William Spangler, Ph.D.

Signature: William J. Spangler
Date: 7/12/96

Disclaimer

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

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I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Multicide Mosquito Adulticiding Concentrate 2705
Description: Clear liquid
Lot/Batch #: Not clearly specified/Code #672-94
Purity: 9.80% PBO and 10.0% sumithrin
Density: 0.90 g/mL (temperature not specified)
CAS #: 51-03-6 (PBO) and 26046-85-5 (sumithrin)
2. Vehicle: None employed
3. Test animals: Species: Rat
Strain: Outbred Sprague-Dawley, albino
Age: Not specified
Weight: 220-231 g males; 200-228 g females
Source: Buckshire Corporation, Perkasie, PA
Acclimation period: \geq 5 days
Diet: Teklad Rodent Diet (#8604) ad libitum
Water: Tap water, ad libitum
Housing: Five/cage, by sex

B. STUDY DESIGN and METHODS:

1. In-life dates: October 12-26, 1994
2. Animal assignment and treatment: Following an overnight fasting period, five rats/sex were given a single oral dose of undiluted Multicide Mosquito Adulticiding Concentrate 2705 at 5,000 mg/kg (limit concentration) by gavage. The rats were observed for signs of toxicity and mortality frequently on the day of dosing, 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 LD₅₀ Males = >5,000 mg/kg (observed)
Females = >5,000 mg/kg (observed)

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- B. Clinical observations: Aside from ruffled fur on day 1, all animals appeared normal and healthy throughout the 14-day study.
- C. Body Weight: No significant treatment-related effect on body weight was observed, with overall (0-14 days) average increases of 54% for males and 16% for females.
- D. Necropsy: Necropsy after 14 days revealed no gross abnormalities.
- E. Deficiencies: Although the age of the test animals was not specified, based on the body weights provided, they were probably young adult animals at study initiation, and this deficiency is considered minor.

OK

OK
7-26-96

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

I. **MATERIALS AND METHODS**

A. MATERIALS:

1. Test Material: Multicide Mosquito Adulticiding Concentrate 2705
Description: Clear liquid
Lot/Batch #: Not clearly specified/Code #672-94 OK
Purity: 9.80% PBO and 10.0% sumithrin
Density: 0.90 g/mL (temperature not specified)
CAS #: 51-03-6 (PBO) and 26046-85-5 (sumithrin)
2. Vehicle: None employed
3. Test animals: Species: Rabbit
Strain: New Zealand White
Age: Adult
Weight: 2.51-2.73 kg males; 2.26-2.58 kg females OK
Source: Davidson Mill Farm, Jamesburg, NJ
Acclimation period: ≥5 days
Diet: Wayne 15% Rabbit Ration, unspecified amount/animal/day
Water: Tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: September 22-October 6, 1994
2. Animal assignment and treatment: Fur from the back areas of five New Zealand White rabbits/sex was clipped approximately 24 hours prior to dermal administration of undiluted Multicide Mosquito Adulticiding Concentrate 2705; the test substance was applied as received to approximately 10% of the total body surface area (200 cm²). Each treatment site was covered with a large gauze patch and wrapped with an occlusive plastic sheeting secured with elastic tape. The coverings were removed after 24 hours, and the test sites were washed with deionized water. The rabbits were observed for signs of toxicity, mortality, and/or dermal effects frequently on the day of dosing 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. Dermal effects were scored using the Draize method. At 14 days, the surviving animals were sacrificed, necropsied, and examined for gross pathological changes. OK

3. Statistics: Not applicable to this study.

II. **RESULTS AND DISCUSSION:**

A. Mortality: All animals survived the 14-day observation period.) o/r

Dermal LD₅₀ Males = >2,000 mg/kg (observed)
Females = >2,000 mg/kg (observed)

B. Clinical observations: No signs of systemic toxicity were observed during the study. ~~Very slight to well-defined erythema (scores of 1-2) and very slight to slight edema (scores of 1-2) were observed at all treatment sites; all dermal irritation subsided by day 7.~~ delete

C. Body Weight: No significant treatment-related effect on body weight was observed, with overall (0-14 days) average increases of 14-16% for both sexes.

D. Necropsy: Necropsy after 14 days revealed no gross abnormalities. o/r

E. Deficiencies: None.

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decedent animals revealed dark red and/or mottled lungs (14/15) and dark red free-flowing liquid in cut surfaces of lungs (4/15). Gross necropsy of animals sacrificed after 14 days revealed dark red lungs in a single female from the 3.17-mg/L dose group; otherwise, no gross abnormalities were observed.

OK

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.

OK

I. **MATERIALS AND METHODS**

A. MATERIALS:

1. Test Material: Multicide Mosquito Adulticiding Concentrate 2705
 Description: Clear liquid
 Lot/Batch #: Not clearly specified/Code #672-94
 Purity: 9.80% PBO and 10.0% sumithrin
 Density: 0.90 g/mL (temperature not specified)
 CAS #: 51-03-6 (PBO) and 26046-85-5 (sumithrin)
2. Vehicle and/or positive control: None employed
3. Test animals: Species: Rat
 Strain: Outbred Sprague-Dawley, albino
 Age: Not specified
 Weight: 227-289 g males; 213-247 g females
 Source: Buckshire Corporation, Perkasie, PA
 Acclimation period: ≥5 days
 Diet: Teklad Rodent Diet (#8604) ad libitum, except during exposure
 Water: Tap water, ad libitum, except during exposure
 Housing: Five/cage, by sex

OK

B. STUDY DESIGN and METHODS:

1. In-life dates: October 7-November 22, 1994
2. Exposure conditions: A rectangular dynamic-flow exposure chamber (230 L) constructed of 1/2-inch thick acrylic sheet was used; animals were individually caged and elevated 2 inches above the chamber floor for whole-body exposure.

OK

Test atmosphere was generated by transferring measured test material via a Razel Model A Syringe Pump through an eight-jet Collision nebulizer; the

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generation system was operated using compressed air which had been passed through two silica gel drying traps prior to entering the test substance flask. The airflow, measured continuously during each exposure, ranged from 58 to 71 L/min (equivalent to 15.1 to 18.5 chamber turnovers/hour). The time required for 99% equilibration was not specified.

OK

The nominal test concentration was calculated at the end of each exposure period by dividing the total amount of test material delivered to the chamber (differential weight of the test substance flask) by the total air volume that passed through the chamber during the exposure time. The actual test atmosphere concentration was measured both gravimetrically (beginning at 15 minutes) and analytically (beginning at 60 minutes) once/hour during each exposure. Atmosphere from the breathing zone of the animals was collected either on Gelman Type A/E glass fiber filters (gravimetric analysis) or trapped in acetone (tandem midget impingers). Aliquots of the solvent were analyzed for each active ingredient (a.i.) component using high-performance liquid chromatography (HPLC); otherwise, details concerning the analytical analyses were not provided. The nominal and mean analytical and gravimetric test concentrations are presented in Table 1.

OK

Particle size was determined hourly during exposure using an Andersen Cascade Impactor. Samples were collected from the breathing zone of the animals at a rate of 28.3 L/min. The mass median aerodynamic diameter (MMAD), geometric standard deviation (GSD), and the percentage of particles <4.7 μm were calculated; in addition, the nominal gravimetric concentration was determined using the total mass collected during sampling. Mean results are presented in Table 1.

OK

TABLE 1. Exposure conditions

Nominal Conc. (mg/L)	Mean Anal. Conc. (mg/L)	Mean Gravimetric Conc. (mg/L)		MMAD (μm)	GSD (μm)	<4.7 μm (%)
		Filter	Impactor			
3.76	3.17	1.59	3.53	1.56	0.21	95.7
7.04	4.78	1.88	5.12	1.63	0.08	95.0
9.36	6.21	1.74	3.36	1.64	0.07	94.7

OK

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The temperature, relative humidity, and oxygen level were recorded every 30 minutes during each exposure period, and ranged from 20-23 °C (dry bulb), 61-83%, and 20.9%, respectively.

- 3. Animal assignment and treatment: Animals were assigned to the test groups noted in Table 2. Rats were exposed to Multicide Mosquito Adulticiding Concentrate 2705 via whole-body inhalation for 4 hours. Following exposure, the animals were rinsed with warm water and towel dried to reduce oral ingestion or dermal absorption. The animals were observed for gross toxicity and/or mortality frequently on the day of exposure, 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, and all animals were necropsied and examined for gross pathological changes. OK

Table 2. Mortality/animals treated

Mean Analytical Conc. (mg/L)	Male	Female	Combined
3.17	2/5	1/5	3/10
4.78	3/5	2/5	5/10
6.21	5/5	2/5	7/10

OK

- 4. Statistics: The acute inhalation LC₅₀ values (with 95% C.I.) for male animals and combined sexes were calculated using the Litchfield and Wilcoxon method [Litchfield, J., and F. Wilcoxon, J. Pharmacol. Exp. Ther. 96-99-115 (1949)].

II. RESULTS AND DISCUSSION:

- A. Mortality: Mortality data are presented in Table 2. Mortality occurred in 15/30 animals tested between 1 and 2 days following exposure.

Inhalation LC₅₀ Males = 3.73 (2.57-5.40) mg/L (95% C.I.)
 Females = ≥6.21 mg/L (observed)
 Combined = 4.55 (3.28-6.31) mg/L

OK

- B. Clinical observations: Clinical effects observed during

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the exposure period¹ included closed eyes, inactivity, and fur damp from test material. Additional effects observed included ruffled fur and oily fur, and a single female from the 6.21-mg/L exposure group exhibited dark ocular discharge on day 3. Surviving animals from all three dose groups recovered by day 8.

- C. Body Weight: No significant treatment-related effect on body weight was observed in surviving male animals, with overall (0-14 days) average increases of 28% (n=3) and 23% (n=2) for the 3.17- and 4.78-mg/L dose groups, respectively.

The body weights of 2/3 and 3/3 surviving females from the 4.78- and 6.21-mg/L dose groups, respectively, decreased either between 0 and 7 or 7 and 14 days following exposure. Overall, 9/10 surviving females from the three dose groups increased averages of 8.7-11%; a single female from the 6.21-mg/L dose group had an overall decrease in body weight of 2.6%.

- D. Necropsy: Gross necropsy of decedent animals revealed dark red and/or mottled lungs (14/15) and dark red free-flowing liquid in cut surfaces of lungs (4/15). Gross necropsy of animals sacrificed after 14 days revealed dark red lungs in a single female from the 3.17-mg/L dose group; otherwise, no gross abnormalities were observed.

- E. Deficiencies: None.

¹Observations were limited to the front five animals during exposure due to clouding of the atmosphere.

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[PBO and Sumithrin]

Primary Eye Irritation Study (81-4)

EPA Reviewer: _____, Date _____
 Review Section __, Toxicology Branch __ (7505W)
 EPA Secondary Reviewer: DR. J. J. J., Date 7-26-96
 Review Section __, Toxicology Branch __ (7505W)

DATA EVALUATION RECORD

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

<u>DP BARCODE:</u> D224863	<u>SUBMISSION CODE:</u>
<u>P.C. CODE:</u> 067501 and 069005	<u>TOX. CHEM. NO.:</u>
<u>EPA REG. NO.:</u> 1021-RAII	

TEST MATERIAL (PURITY): Multicide Mosquito Adulticiding Concentrate 2705 (9.80% PBO and 10.0% sumithrin)

OK

SYNONYMS: D-Phenothrin (sumithrin)

CITATION: Moore, G. (1995) Primary eye irritation - rabbits. Biosearch Inc., Philadelphia, PA. Laboratory Project Number 94-8104A. January 3, 1995. MRID 43964804. Unpublished.

SPONSOR: McLaughlin Gormley King Company, 8810 Tenth Avenue North, Minneapolis, MN

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 43964804), 0.1 mL of Multicide Mosquito Adulticiding Concentrate 2705 (9.80% PBO and 10.0% sumithrin) was instilled into the conjunctival sac of one eye of six female New Zealand White rabbits. The treated eyes were not rinsed. The animals were observed for up to 7 days following instillation, and eye irritation was scored using the Draize scale.

OK

Based on the average ocular irritation score of 5.0, irritation was most severe 1 hour following instillation and included slight to moderate conjunctival redness in 6/6 treated eyes, and slight conjunctival discharge in 5/6 eyes. No corneal or iridial irritation was observed during the study; conjunctival irritation subsided in 4/6 treated eyes by 24 hours, and all treated eyes by 48 hours.

Based on the results of this study, **Multicide Mosquito Adulticiding Concentrate 2705 is a very slight eye irritant**, and is classified as **TOXICITY CATEGORY IV** for primary eye irritation based on the conjunctival effects which subsided in 4/6 treated eyes by 24 hours.

OK

This study is classified **acceptable**, and satisfies the guideline requirement for a primary eye irritation study (81-4) in the rabbit.

OK

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

OK

I. **MATERIALS AND METHODS**

A. MATERIALS:

1. Test Material: Multicide Mosquito Adulticiding Concentrate 2705
Description: Clear liquid
Lot/Batch #: Not clearly specified/Code #672-94
Purity: 9.80% PBO and 10.0% sumithrin
Density: 0.90 g/mL (temperature not specified)
CAS #: 51-03-6 (PBO) and 26046-85-5 (sumithrin)
2. Vehicle and/or positive control: None employed
3. Test animals: Species: Rabbit
Strain: New Zealand White
Age: Not specified
Weight: 2.24-2.71 kg (all female)
Source: Davidson Mill Farm, Jamesburg, NJ
Acclimation period: ≥5 days
Diet: Wayne 15% Rabbit Ration, unspecified amount/animal/day
Water: Tap water, ad libitum

OK

B. STUDY DESIGN and METHODS:

1. In-life dates: September 26-October 3, 1994
2. Animal assignment and treatment: A 0.1-mL aliquot of Multicide Mosquito Adulticiding Concentrate 2705 was instilled into the conjunctival sac of one eye of six female New Zealand White rabbits. The treated eyes were held together for approximately 1 second to prevent loss of material, and were not rinsed. The other eye of each animal served as an untreated control. The animals were observed for ocular irritation at 1, 24, 48, and 72 hours and 4 and 7 days following instillation. At 24 hours, fluorescein dye was used to confirm the absence of corneal ulceration. Eye irritation was scored by the Draize scheme.

OK

II. **RESULTS AND DISCUSSION**:

- A. Clinical observations: Based on the average ocular irritation score of 5.0, irritation was most severe 1 hour following instillation and included slight to

OK

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moderate conjunctival redness (scores of 1-2) in 6/6 treated eyes, and slight conjunctival discharge (score of 1) in 5/6 eyes. No corneal or iridial irritation was observed during the study; conjunctival irritation subsided in 4/6 treated eyes by 24 hours, and all treated eyes by 48 hours. Based on the results of this study, Multicide Mosquito Adulticiding Concentrate 2705 is a very slight eye irritant. O/K

- B. Deficiencies: Although individual observations for the entire day of dosing and individual daily observations were not conducted, these deficiencies do not alter the results of the study and are considered minor. O/K

Although the age of the test animals was not specified, based on the body weights provided, the animals were most likely young adult, and this deficiency is considered minor. O/K

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I. MATERIALS AND METHODS

A. MATERIALS:

- 1. Test Material: Multicide Mosquito Adulticiding Concentrate 2705
 Description: Clear liquid
 Lot/Batch #: Not clearly specified/Code #672-94
 Purity: 9.80% PBO and 10.0% sumithrin
 Density: 0.90 g/mL (temperature not specified)
 CAS #: 51-03-6 (PBO) and 26046-85-5 (sumithrin)
- 2. Vehicle and/or positive control: None employed
- 3. Test animals: Species: Rabbit
 Strain: New Zealand White
 Age: Not specified
 Weight: 2.11-2.60 kg (all female)
 Source: Davidson Mill Farm, Jamesburg, NJ
 Acclimation period: >=5 days
 Diet: Wayne 15% Rabbit Ration, unspecified amount/animal/day
 Water: Tap water, ad libitum

G/K

OK

B. STUDY DESIGN and METHODS:

- 1. In-life dates: September 20-23, 1994
- 2. Animal assignment and treatment: Fur from the dorsal trunk area of six female animals was clipped approximately 24 hours prior to dermal administration with 0.5 mL of Multicide Mosquito Adulticiding Concentrate 2705. The test substance was applied as received to a single, 6-cm² intact site/animal; an adjacent untreated site served as a control. The treated and control areas were covered with gauze patches secured with non-irritating adhesive tape, then the entire trunk of each animal was wrapped with gauze and overwrapped with elastic tape. The coverings were removed 4 hours following application, and the test sites were gently washed with deionized water. The rabbits were observed for dermal irritation at 0.5/1, 24, 48, and 72 hours following patch removal. Erythema and edema were scored separately using the Draize scale.

OK

II. RESULTS AND DISCUSSION:

- A. Clinical observations: Very slight erythema (score of 1) was observed at 1/6 application sites within 1 hour of patch removal; otherwise, no dermal irritation was

G/K

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observed during the 72-hour observation period. In this study, Multicide Mosquito Adulticiding Concentrate 2705 is not a dermal irritant.

- B. Deficiencies: Although individual observations for the entire day of dosing and individual daily observations were not conducted, these deficiencies do not alter the results of the study and are considered minor.

The age of the test animals was not specified. Based on the provided weights, the animals were most likely young adult, and this deficiency is considered minor.

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[PBO and Sumithrin]

Dermal Sensitization Study (81-6)

EPA Reviewer: _____, Date _____
 Review Section __, Toxicology Branch __ (7505W)
 EPA Secondary Reviewer: DLR, Date 7-26-96
 Review Section __, Toxicology Branch __ (7505W)

DATA EVALUATION RECORD

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

<u>DP BARCODE</u> : D224863	<u>SUBMISSION CODE</u> :
<u>P.C. CODE</u> : 067501 and 069005	<u>TOX. CHEM. NO.</u> :
<u>EPA REG. NO.</u> : 1021-RAII	

OK

TEST MATERIAL (PURITY): Multicide Mosquito Adulticiding Concentrate 2705 (9.80% PBO and 10.0% sumithrin)

SYNONYMS: D-Phenothrin (sumithrin)

CITATION: Moore, G. (1996) Guinea pig dermal sensitization, 9 induction applications - modified Buehler method. Biosearch Inc., Philadelphia, PA. Laboratory Project Number 94-8104A. February 21, 1996. MRID 43964806. Unpublished.

SPONSOR: McLaughlin Gormley King Company, 8810 Tenth Avenue North, Minneapolis, MN

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 43964806) conducted with Multicide Mosquito Adulticiding Concentrate (9.80% PBO and 10.0% sumithrin), ten male 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.

OK

Very slight erythema was observed at 1/10 sites 24 hours following a single challenge treatment to either previously-induced or naive control animals. Based on the results of this study, **Multicide Mosquito Adulticiding Concentrate 2705 is not a dermal sensitizer.** Acceptable positive control data were provided to validate the test methodology.

OK

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

OK

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

OK

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I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Multicide Mosquito Adulticiding Concentrate 2705
Description: Clear liquid
Lot/Batch #: Not clearly specified/Code #672-94
Purity: 9.80% PBO and 10.0% sumithrin
Density: 0.90 g/mL (temperature not specified)
CAS #: 51-03-6 (PBO) and 26046-85-5 (sumithrin) OK

2. Vehicle and positive control: Polyethylene glycol was used as a test substance vehicle.

0.1% (w:v) 1-Chloro-2,4-dinitrobenzene (DNCB; purity not specified) in 50% ethanol:0.9% saline solution (induction phase) and 0.07% (w:v) DNCB in acetone (challenge phase) was used for concurrent positive control data. OK

3. Test animals: Species: Guinea pig
Strain: Hartley albino
Age: Not specified
Weight: 281-399 g (all male/definitive study) and 286-420 g (all male/positive control study)
Source: Davidson Mill Farm, Jamesburg, NJ
Acclimation period: ≥7 days
Diet: Wayne Guinea Pig Formula, ad libitum
Water: Tap water, ad libitum
Housing: 2-3 Animals/cage OK

B. STUDY DESIGN and METHODS:

1. In-life dates: September 30-November 4, 1994

2. Animal assignment and treatment: The study was conducted using methods derived by Buehler [Ritz, H. and E. Buehler, Current Concepts in Cutaneous Toxicity, Academic Press (1980)]. Based on the results of preliminary experiments conducted with 0.4 mL of either Multicide Mosquito Adulticiding Concentrate 2705 as received (100%) or diluted to 10, 25, or 50% (v:v) in polyethylene glycol, the test substance was administered at 50% for the induction phase and at 10% for the challenge application. Due to the moderate erythema observed following the second induction application, the test concentration was reduced to 25% for the remaining induction treatments. OK

For the induction phase, fur on the left flank of

each animal was clipped 1 day prior to dermal administration with 0.4 mL of a solution containing 50 or 25% (v:v) Multicide Mosquito Adulticiding Concentrate 2705 in polyethylene glycol. The test solution was applied using a gauze patch that had been secured to dental dam. Once the gauze was positioned, the dental dam was wrapped around the animal and secured with elastic tape. An additional ten male animals were treated in the same manner using 0.4 mL of 0.1% DNCB. Following a 6-hour exposure period, the coverings were removed, and the test sites were gently washed with deionized water. Application was repeated in the same manner to the same site three times weekly for 3 weeks (nine total applications). When necessary, the application sites for the test and positive control substances were adjusted slightly toward the midline to prevent application to necrotic skin.

Two weeks following the final induction treatment, a single challenge treatment was performed using 0.4 mL of either a 10% Multicide Mosquito Adulticiding Concentrate 2705 solution or a 0.07% DNCB solution to the previously untreated right flank of each animal and otherwise in the same manner as described. The guinea pigs were observed for dermal irritation 24 hours following each induction treatment and 24 and 48 hours following the challenge treatment. Skin reactions were scored according to the following scale:

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

Body weights of each animal were recorded at days -1 (day prior to first induction application) and 36 (study termination).

II. RESULTS AND DISCUSSION:

- A. Induction reactions and duration: Very faint to moderate erythema (scores of 0.5-2) was observed at 8/10 to 10/10 application sites 24 hours following the each induction treatment. In addition, dry flaky skin was observed at 8/10 sites during the induction phase.
- B. Challenge reactions and duration: Very slight erythema (score of 0.5) was observed at 1/10 sites 24 hours

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following a single challenge treatment to either previously-induced or naive control animals. Based on the results of this study, Multicide Mosquito Adulticiding Concentrate 2705 is not a dermal sensitizer.

No treatment-related effect on body weight was observed during the study, with overall (-1 to 36 days) average increases of 80-83% for previously-induced and naive control animals.

OK

- C. Positive control: The incidence and severity of irritation increased with each successive induction application; 24 hours following the sixth through ninth induction application, faint to severe erythema (scores of 1-3), eschar formation, and/or dry, flaky skin was observed at 10/10 test sites.

OK

Twenty-four hours following the single challenge treatment to previously-induced animals, very faint to moderate erythema (scores of 0.5 to 2) was observed at 9/10 sites. In contrast, 24 hours following treatment to naive control animals, very faint erythema (score of 0.5) was observed at 1/5 test sites. These data confirm the adequacy of the test species and method employed.

- D. Deficiencies: Although the age of the test animals was not specified, based on the body weights provided, they were probably young adult animals at study initiation, and this deficiency is considered minor.

① Id of PEG not given

② Needs Vehicle Control ?