



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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

December 20, 1997

MEMORANDUM

Subject: EPA Reg. No.: 62719-15
DP Barcode: D233219
Case No: 048009

From: Masih Hashim, Toxicologist *MHT JCR*
Technical Review Branch
Registration Division (7505C)

To: Tina Levine, PM 19
Insecticide-Rodenticide Branch
Registration Division (7505 C)

Applicant: DowElanco
9330 Zionville Road
Indianapolis, Indiana, 46268

FORMULATION FROM LABEL:

<u>Active Ingredient(s):</u>	<u>% by wt.</u>
059101 Chlorpyrifos	95.5
<u>Inert Ingredients</u>	<u>4.5</u>
Total	100%

2

BACKGROUND: DowElanco has submitted a set of acute toxicity studies in support of Dursban F Insecticidal Chemical. The MRID numbers are 442091-01 through 442091-05. Dynamac Corporation reviewed this package of tox studies. It was further reviewed and modified by TRB. All five studies were conducted at the Toxicology Research Laboratory at Dow Chemical Company.

RECOMMENDATION:

1. Each of the five studies is acceptable in accordance with the Subdivision F guidelines.
2. The Applicant has requested a waiver for the acute inhalation study due to the nature of the formulation. TRB grants the inhalation toxicity waiver request based on the following rationale: a) the waxy nature of technical chlorpyrifos; b) the low vapor pressure of technical chlorpyrifos (2×10^{-5} mm @ 25°C); 3) the results of a 90-day inhalation study (40013901 and 40166501) that indicate that a high vapor concentration could not be reached. This indicates that it is unlikely that concentrations would result from application of chlorpyrifos to cause a significant degree of acute toxicity in humans.

However, to be consistent with other Agency decisions for chlorpyrifos, TRB is bridging the data for the inhalation precautionary review language. In Accession No. 257590 the LC₅₀ for technical chlorpyrifos was greater than 0.2 mg/L in rats. This results in a Toxicity Category of II. This study was classified as Supplementary as only nominal concentrations of the test substance were measured.

The acute toxicology profile for the file symbol 62719-15 is as follows:

acute oral toxicity	II	acceptable
acute dermal toxicity	IV	acceptable
acute inhalation toxicity	II	waiver acceptable
primary eye irritation	IV	acceptable
primary skin irritation	IV	acceptable
dermal sensitization	not a sensitizer	acceptable

LABELING:

ID #: 062719-00015 DURSBAN F INSECTICIDAL CHEMICAL

SIGNAL WORD: WARNING

PRECAUTIONARY STATEMENTS:

May be fatal if swallowed or inhaled. Do not breathe dust. For handling activities, use

3
dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C). Wash thoroughly with soap and water after handling and before eating, drinking, or using tobacco. Remove contaminated clothing and wash clothing before reuse.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF SWALLOWED: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with a finger. If the person is unconscious, do not give anything by mouth and do not induce vomiting.

IF INHALED: Remove victim to fresh air. If not breathing, give artificial respiration, preferably mouth-to-mouth. Get medical attention.

ACUTE TOX ONE-LINER

1. PC CODE: 059101
2. CURRENT DATE: 12-27-97
3. TEST MATERIAL:

059101 chlorpyrifos 95.5 %

Study/Species/Lab/ Study#/Date	MRID No.	Results	Tox. Cat.	Core Grade
acute oral toxicity study/rat/Dow Labs/K-044793- 102A/11-27-96	442091-01	oral LD ₅₀ = 223 mg/kg	II	A
acute dermal toxicity study/rabbit/Dow Labs/K- 044793-102D/11-27-96	442091-02	dermal LD ₅₀ mg/kg >5000 mg/kg	IV	A
acute inhalation	-	waiver	II	A
primary eye irritation study /Dow Labs/K-044793-102C/11- 27-96	442091-03	minimal to mild irritant	IV	A
primary skin irritation /rabbit/Dow Labs/K044793- 102B/11-27-96	442091-04	mild irritant	IV	A
dermal sensitization study/guinea pigs/Dow Labs/K- 044793-102B/11-27-96	442091-05	not a sensitizer	-	A

Core Grade Key: A = Acceptable, S = Supplementary (upgradable)
U = Unacceptable, V = Self Validated

5

DATA EVALUATION RECORD

Dursban F Insecticidal Chemical
(chlorpyrifos)

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

Work Assignment No. 3-14 (D233219)

Prepared for

Registration 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:

Sudha R. Iyer, B.S.:

Project Manager:

Mary L. Menetrez, Ph.D.

Chlorpyrifos

Acute Oral Study (81-1)

EPA Reviewer: Masih Hashim TRB 7505C

MLH

DATA EVALUATION
RECORD

STUDY TYPE: Acute Oral Toxicity - Rat

OPPTS Number: 870.1100

OPP Guideline Number: §81-1

DP BARCODE: D233219

SUBMISSION CODE: S518298

P.C. CODE: 059101

TOX. CHEM. NO.:

EPA REG. NO.: 62719-15

TEST MATERIAL (PURITY): Dursban F Insecticidal Chemical (97.6% chlorpyrifos)

SYNONYMS: None specified

CITATION: Stebbins, K. (1996) Dursban F Insecticidal Chemical: Acute oral toxicity study in Fischer 344 rats. The Toxicology Research Laboratory, The Dow Chemical Company, Midland, MI. Laboratory Study Number K-044793-102A, K-044793-102A1. November 27, 1996. MRID 44209101. Unpublished.

SPONSOR: DowElanco, 9330 Zionsville Road, Indianapolis, IN.

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 44209101), groups of five young adult Fischer 344 rats/sex were given single oral doses of Dursban F Insecticidal Chemical (97.6% chlorpyrifos) at 50, 100, or 500 mg/kg. The test substance was administered as a suspension in 0.5% aqueous methocellulose. Animals were observed for clinical signs of toxicity and mortality for up to 14 days postdosing.

Oral LD₅₀ Males = 223 mg/kg (linear interpolation)
Females = 223 mg/kg (linear interpolation)

Dursban F Insecticidal Chemical is classified as TOXICITY CATEGORY II based on the calculated LD₅₀ values in both sexes.

Mortality occurred in 10/10 animals tested at 500 mg/kg between days 0 and 2 following administration. Clinical effects observed in decedent animals included, fecal soiling, salivation, lacrimation, urine soiling, decreased activity, and lateral recumbency. Effects observed in surviving animals were similar, and subsided from males by day 1 and from females by day 5. No treatment-related effects on body weight were observed. Gross necropsy of decedent animals revealed decreased ingesta and/or gas in the digestive tract, congestion in viscera, and hemolyzed blood in the stomach lumen. Necropsy of animals sacrificed after 14 days revealed no gross abnormalities.

This study is classified **acceptable (§81-1)** and satisfies the guideline requirement for an acute oral study 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: Dursban F Insecticidal Chemical
Description: Dark crystalline solid at room temperature
Lot/Batch #: 7299412
Composition: 97.6% Chlorpyrifos
CAS #: 2921-88-2
2. Vehicle: 0.5% Aqueous solution of methocellulose
3. Test animals: Species: Rat
Strain: Fischer 344
Age: Young adult
Weight: 176.1-186.9 g males; 122.7-130.4 g females
Source: Charles River Breeding Laboratories Inc., Raleigh NC
Acclimation period: At least 1 week
Diet: Purina Certified Rodent Chow (#5002), ad libitum
Water: Tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: April 17-May 1, 1996
2. Animal assignment and treatment: Prior to use, the test material was gently heated to liquefy. Animals were assigned to the test groups noted in Table 1. Following an overnight fasting period, young adult Fischer 344 rats were given a single oral dose of Dursban F Insecticidal Chemical by gavage. The test material was administered as a 3% suspension in 0.5% aqueous solution of methocellulose (dosing volume not specified). The rats were observed for signs of toxicity and/or mortality at 1, 2, 3, 5, 6, 7, and 8 hours following administration, and at least once daily thereafter for the remainder of the 14-day study. Body weights were recorded at days 0 (prior to dosing), 1, 7, and 14. After 14 days, the surviving animals were sacrificed, and all animals (upon death) were necropsied and examined for gross pathological changes.

Table 1. Doses, mortality/animals treated

Dose, mg/kg	Males	Females	Combined
50	0/5	0/5	0/10
100	0/5	0/5	0/10
500	5/5	5/5	10/10

3. Statistics: The acute oral LD₅₀ values were calculated by linear interpolation [Stephan, C. ASTM STP 634:65-84 (1977)].

II. RESULTS AND DISCUSSION:

- A. Mortality: Mortality data are provided in Table 1. Mortality occurred in 10/10 animals tested at 500 mg/kg between days 0 and 2 following administration.

Oral LD₅₀ Males = 223 mg/kg (linear interpolation)
 Females = 223 mg/kg (linear interpolation)

- B. Clinical observations: Clinical effects observed in decedent animals included salivation (9/10), fecal soiling (7/10), lacrimation (6/10), urine soiling (6/10), decreased activity (4/5; females), and lateral recumbency (4/5; females).

Effects observed in surviving animals (from the lower dose groups) included urine soiling (9/20), lacrimation (7/20), salivation (6/20), decreased activity (6/20), and fecal soiling (5/20). Surviving males and females recovered by days 1 and 5, respectively.

- C. Body Weight: No significant treatment-or concentration-related effects on body weight were observed in the surviving animals during the study; animals exhibited overall (0-14 days) average increases of 18-25% for males and 13-15% for females.
- D. Necropsy: Gross necropsy of decedent animals revealed congestion in viscera (6/10), decreased ingesta and/or gas in the digestive tract (4/10), and hemolyzed blood in the stomach lumen (3/10; females). Necropsy of animals sacrificed after 14 days revealed no gross abnormalities.
- E. Deficiencies: There were no deficiencies that affected the validity of the study results.

9
EPA Reviewer: Masih Hashim, TRB 7505C

MHT

DATA EVALUATION
RECORD

STUDY TYPE: Acute Dermal Toxicity - Rabbit

OPPTS Number: 870.1200

OPP Guideline Number: §81-2

DP BARCODE: D233219

SUBMISSION CODE: S518298

P.C. CODE: 059101

TOX. CHEM. NO.:

EPA REG. NO.: 62719-15

TEST MATERIAL (PURITY): Dursban F Insecticidal Chemical (97.6% chlorpyrifos)

SYNONYMS: None specified

CITATION: Stebbins, K. (1996) Dursban F Insecticidal Chemical: Acute dermal toxicity study in New Zealand White rabbits. The Toxicology Research Laboratory, The Dow Chemical Company, Midland, MI. Laboratory Study Number K-044793-102D, K-044793-102D1. November 27, 1996. MRID 44209102. Unpublished.

SPONSOR: DowElanco, 9330 Zionsville Road, Indianapolis, IN.

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 44209102), groups of five young adult New Zealand White rabbits/sex were dermally exposed to Dursban F Insecticidal Chemical (97.6% chlorpyrifos) at 2,000 (limit dose) or 5,000 mg/kg for 24 hours. The test substance was heated to liquefy 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 LD₅₀ Males = >5,000 mg/kg (observed)
Females = >5,000 mg/kg (observed)

Dursban F Insecticidal Chemical is classified as TOXICITY CATEGORY IV based on the observed LD₅₀ values in both sexes.

All animals survived the 14-day observation period. Fecal soiling was observed in 2/10 animals in the 5,000 mg/kg dose group up through day 1. No other systemic effects were observed. Erythema, edema, scaling, and fissuring of the test sites were observed in animals from the 5,000 mg/kg dose group, and erythema and scaling of the test sites were observed in animals from the 2,000 mg/kg dose group. Body weights of three animals/sex in the 5,000 mg/kg dose group decreased between 0 and 7 days; all animals then gained weight between 7 and 14 days, and exhibited overall (0-14 days) average increases. Necropsy after 14 days revealed no gross

10
abnormalities.

This study is classified **acceptable (§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: Dursban F Insecticidal Chemical
Description: Dark crystalline solid at room temperature
Lot/Batch #: 7299412
Composition: 97.6% Chlorpyrifos
CAS #: 2921-88-2
2. Vehicle: None employed
3. Test animals: Species: Rabbit
Strain: New Zealand White
Age: Young adult
Weight: 2.40-2.74 kg males; 2.26-2.75 kg females
Source: Hazleton Research Products, Inc., Kalamazoo, MI
Acclimation period: At least 2 weeks
Diet: Purina Certified Rabbit Chow (#5322), 4 oz./animal/day
Water: Tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: April 30-May 30, 1996
2. Animal assignment and treatment: Animals were assigned to the test groups noted in Table 1. Fur from the trunk of young adult New Zealand White rabbits/sex was clipped 1 day prior to dermal administration of Dursban F Insecticidal Chemical. The test substance was gently heated to liquefy and applied to a gauze patch (covered by non-absorbent cotton) to an area approximately 10% of the body surface. The gauze patch was held in place by an elastic rabbit jacket. After 24 hours, the coverings were removed, and the application sites were wiped with water-moistened towels and dried. The rabbits were observed for signs of toxicity and/or mortality frequently on the

day of dosing and at least once daily thereafter for the remainder of the 14-day study. Dermal irritation was recorded at 1, 2, 3, 5 (4.5 for 2,000 mg/kg dose group), 6, 7, and 8 hours following patch removal, and on days 1, 2, 3, 6, 7, 8, 9, 10, 13, and 14. In addition, body weights were recorded a day prior to dosing and on days 0, 1, 7, and 14. At 14 days, the surviving animals were sacrificed, necropsied, and examined for gross pathological changes.

Table 1. Doses, mortality/animals treated

Dose, mg/kg	Males	Females	Combined
2,000 ^a	0/5	0/5	0/10
5,000	0/5	0/5	0/10

^a Limit dose

3. Statistics: Not applicable to this study.

II. RESULTS AND DISCUSSION:

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

Dermal LD₅₀ Males = >5,000 mg/kg (observed)

Females = >5,000 mg/kg (observed)

B. Clinical observations: Fecal soiling was observed in 2/10 animals in the 5,000 mg/kg dose group up through day 1. All animals appeared normal in the 2,000 mg/kg dose group throughout the study.

In the 5,000 mg/kg dose group, erythema and edema (not graded) were observed at 9/10 and 6/10 sites, respectively, upon patch removal (day 1); these effects subsided by day 8. Additional dermal effects included scaling at up to 5/10 sites between days 4 and 14, and fissuring of the skin at 1/10 sites between days 4 and 6.

In the 2,000 mg/kg dose group, erythema (not graded) was observed at 4/10 application sites following patch removal, and subsided by day 6. Scaling was also observed at 3/10 sites between days 2 and 3.

C. Body Weight: Body weights of three males and three females in the 5,000 mg/kg dose group decreased between 0 and 7 days following application. All animals then gained weight between 7 and 14 days, and exhibited overall (0-14 days)

12
average increases of 10.2-13.0% for males and 12.2-14.4% for females.

- D. Necropsy: Necropsy after 14 days revealed no gross abnormalities.
- E. Deficiencies: Dermal irritation was not scored during the study, however, this deficiency has no apparent effect on the results of the study and is considered minor.

EPA Reviewer: Masih Hashim, TRB 7505C

114

DATA EVALUATION RECORD

STUDY TYPE: Primary Eye Irritation - Rabbit

OPPTS Number: 870.2400

OPP Guideline Number: §81-4

DP BARCODE: D233219

SUBMISSION CODE: S518298

P.C. CODE: 059101

TOX. CHEM. NO.:

EPA REG. NO.: 62719-15

TEST MATERIAL (PURITY): Dursban F Insecticidal Chemical (97.6% chlorpyrifos)

SYNONYMS: None specified

CITATION: Stebbins, K. (1996) Dursban F Insecticidal Chemical: Primary eye irritation in New Zealand white rabbits. The Toxicology Research Laboratory, The Dow Chemical Company, Midland, MI. Laboratory Study Number K-044793-102C. November 27, 1996. MRID 44209103. Unpublished.

SPONSOR: DowElanco, 9330 Zionsville Road, Indianapolis, IN.

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 44209103), 0.1 mL of liquefied Dursban F Insecticidal Chemical (97.6% chlorpyrifos) was instilled into the conjunctival sac of the right eye of three young adult New Zealand White rabbits/sex. The animals were observed for up to 72 hours following instillation, and eye irritation was scored using the Draize scheme.

One hour following instillation, slight conjunctival redness, chemosis, and discharge were observed in 6/6, 3/6, and 2/6 eyes, respectively. No corneal or iridial effects were observed, and conjunctival effects subsided from all treated eyes by 24 hours.

In this study, **Dursban F Insecticidal Chemical is not a significant ocular irritant**, and is classified as **TOXICITY CATEGORY IV** for primary eye irritation based on the absence of positive ocular effects.

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

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

14

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Dursban F Insecticidal Chemical
Description: Dark crystalline solid at room temperature
Lot/Batch #: 7299412
Composition: 97.6% Chlorpyrifos
CAS #: 2921-88-2
2. Vehicle and/or positive control: None employed
3. Test animals: Species: Rabbit
Strain: New Zealand White
Age: Young adult
Weight: 2.243-2.634 kg (combined sexes)
Source: Hazleton research Products, Inc., Kalamazoo, MI
Acclimation period: At least 2 week
Diet: Purina Certified Rabbit Chow (#5322), 4 oz/animal/day
Water: Tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: May 7-10, 1994
2. Animal assignment and treatment: A 0.1-mL aliquot of liquefied Dursban F Insecticidal Chemical was instilled into the conjunctival sac of the right eye of three young adult New Zealand White rabbits/sex. The upper and lower lids were held together for approximately 1 second before releasing to prevent loss of the material. The treated eyes were not rinsed and the left eye of each animal served as an untreated control. Ocular irritation was scored (examined by penlight) by the Draize scheme at 1, 24, 48, and 72 hours following instillation.

II. RESULTS AND DISCUSSION:

- A. Clinical observations: One hour following instillation, ocular irritation included slight conjunctival redness, very slight chemosis, and slight discharge (scores of 1; not considered positive) in 6/6, 3/6, and 2/6 eyes, respectively. No corneal or iridial effects were observed during the study, and conjunctival effects subsided from all treated eyes by 24 hours. In this study, Dursban F Insecticidal Chemical is

15
not a significant ocular irritant.

- B. Deficiencies: Aside from ocular irritation, individual observations for the entire day of dosing and individual daily observations thereafter were not provided. These deficiencies, however, have no effect on the results of the study and are considered minor.

16
EPA Reviewer: Masih Hashim, TRB 7505C

MH

DATA EVALUATION
RECORD

STUDY TYPE: Primary Dermal Irritation - Rabbit

OPPTS Number: 870.2500

OPP Guideline Number: §81-5

DP BARCODE: D233219

SUBMISSION CODE: S518298

P.C. CODE: 059101

TOX. CHEM. NO.:

EPA REG. NO.: 62719-15

TEST MATERIAL (PURITY): Dursban F Insecticidal Chemical (97.6% chlorpyrifos)

SYNONYMS: None specified

CITATION: Stebbins, K. (1996) Dursban F Insecticidal Chemical: Primary dermal irritation study in New Zealand White rabbits. The Toxicology Research Laboratory, The Dow Chemical Company, Midland, MI. Laboratory Study Number K-044793-102B. November 27, 1996. MRID 44209104. Unpublished.

SPONSOR: DowElanco, 9330 Zionsville Road, Indianapolis, IN.

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 44209104), three adult New Zealand White rabbits/sex were dermally exposed to 0.5 mL of liquified Dursban F Insecticidal Chemical (97.6% chlorpyrifos) for 4 hours. The test substance was applied to a single intact site/animal using a 25 mm Hill Top Chamber. Animals were observed for dermal irritation for up to 7 days following application, and irritation was scored by the Draize scale.

Irritation was most notable 30 minutes following patch removal and included very slight erythema and edema at 6/6 and 2/6 sites, respectively. At 72 hours, very slight erythema and edema persisted at 2/6 sites. Erythema and edema subsided from all sites by 7 days.

In this study, **Dursban F Insecticidal Chemical is a very slight dermal irritant** and is classified as **Toxicity Category IV** for primary dermal irritation.

This study is classified **acceptable (§81-5)** and satisfies the guideline requirement for a primary dermal irritation 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: Dursban F Insecticidal Chemical
Description: Dark crystalline solid at room temperature
Lot/Batch #: 7299412
Purity: 97.6% Chlorpyrifos
CAS #: 2921-88-2
2. Vehicle: None employed
3. Test animals: Species: Rabbit
Strain: New Zealand White
Age: Adult
Weight: 2.044-2.598 kg (combined sexes)
Source: Hazleton Research Products, Inc., Kalamazoo, MI
Acclimation period: ≥ 2 weeks
Diet: Purina Certified Rabbit Chow (#5322), 4 oz/animal/day
Water: Tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: April 16-22, 1996
2. Animal assignment and treatment: Prior to use, the test material was gently heated to achieve a liquid state.

Fur from the dorsal trunk areas (10 x 10 cm) of three adult animals/sex was clipped 1 day prior to dermal administration with 0.5 mL of Dursban F Insecticidal Chemical. The test substance was applied using a 25 mm Hill Top Chamber to a single intact site/animal and held in place with an elastic rabbit jacket. The chambers were removed 4 hours following application, and the sites were gently wiped with water-moistened towels. The rabbits were observed for dermal irritation at 30 minutes, 24, 48, and 72 hours, and 7 days following patch removal. Erythema and edema were scored separately using the Draize scale.

II. RESULTS AND DISCUSSION:

- A. Clinical observations: Irritation was most notable 30 minutes following patch removal and included very slight erythema and edema (scores of 1) at 6/6 and 2/6 sites, respectively. At 72 hours, very slight erythema and edema persisted at 2/6 sites. Erythema and edema subsided from all sites by 7 days. In this study, Dursban F Insecticidal Chemical is a very slight dermal irritant.
- B. Deficiencies: Aside from dermal irritation, individual observations for the entire day of dosing and individual daily observations thereafter were not provided. These deficiencies, however, have no effect on the results of the study and are considered minor.

19
EPA Reviewer: Masih Hashim, TRB 7505C

o/h

DATA EVALUATION
RECORD

STUDY TYPE: Dermal Sensitization - Guinea pig

OPPTS Number: 870.2600

OPP Guideline Number: §81-6

DP BARCODE: D233219

SUBMISSION CODE: S518298

P.C. CODE: 059101

TOX. CHEM. NO.:

EPA REG. NO.: 62719-15

TEST MATERIAL (PURITY): Dursban F Insecticidal Chemical (97.6% chlorpyrifos)

SYNONYMS: None specified

CITATION: Stebbins, K. (1996) Dursban F Insecticidal Chemical: Dermal sensitization potential in Hartley Albino guinea pigs. The Toxicology Research Laboratory, The Dow Chemical Company, Midland, MI. Laboratory Study Number K-044793-102E, GPIGS02/27/96, GPIGS01/10/96. November 27, 1996. MRID 44209105. Unpublished.

SPONSOR: DowElanco, 9330 Zionsville Road, Indianapolis, IN.

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 44209105) conducted with Dursban F Insecticidal Chemical (97.6% chlorpyrifos), ten young adult male Hartley Albino guinea pigs were tested using the Buehler method. An additional five animals served as naive controls. Data were provided from two previously-conducted positive control studies using DER 331 epoxy resin and dinitrochlorobenzene.

Twenty-four or 48 hours following the single challenge treatment with 100% Dursban F Insecticidal Chemical to previously-induced animals, slight erythema was observed at 0/10 and 1/10 sites, respectively. In comparison, slight erythema was observed at 1/5 and 0/5 sites 24 and 48 hours, respectively, following challenge to naive controls. Acceptable positive control data were provided to validate the test methodology. Based on the results of this study, Dursban F Insecticidal Chemical is not a dermal sensitizer.

This study is classified as **acceptable (§81-6)** and satisfies the guideline requirement for a dermal sensitization study 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: Dursban F Insecticidal Chemical
 Description: Dark crystalline solid at room temperature
 Lot/Batch #: 7299412
 Purity: 97.6% Chlorpyrifos
 CAS #: 2921-88-2

- 2. Vehicle and positive control: None employed.

Data from two previously-conducted positive control studies were provided (Study No. GPIGS01/10/96) using neat DER 331 epoxy resin (CAS # 1675-54-3) or 0.5% solution of dinitrochlorobenzene (DNCB; CAS # 97-00-7) in dipropylene glycol monomethyl ether (DPGME) solvent.

- 3. Test animals: Species: Guinea pig
 Strain: Hartley Albino
 Age: Young adult
 Weight: 360-390 g males (test and control groups)
 Source: Charles River Breeding Laboratories, Portage, MI
 Acclimation period: ≥ 1 Week
 Diet: Purina Certified Guinea Pig Chow (#5026), ad libitum
 Water: Tap water, ad libitum
 Housing: Five/cage

B. STUDY DESIGN and METHODS:

- 1. In-life dates: March 8-April 4, 1996
- 2. Animal assignment and treatment: The study was conducted using the Buehler method [Buehler, E.V. Arch. Dermat. 91:171-175 (1965)]. Prior to use, the test material was gently heated to achieve a liquid state. Preliminary testing was conducted using two animals/concentration group and 0.4 mL of neat Dursban F Insecticidal Chemical (100%) or 0.5, 1, 3.75, 5, 10, 20, 40, or 80% dilutions in DPGME. Based on the results of these experiments, the test substance was administered at 100% for both phases of the definitive experiment.

For the induction phase, fur from the left sides of ten animals was clipped 1

21

day prior to dermal administration with 0.4 mL of Dursban F Insecticidal Chemical using a 25-mm Hilltop Chamber. Each chamber was secured with Vetrap and held in place with Elastikon. Following a 6-hour exposure period, the coverings were removed. Application of the test substance was repeated once weekly at 7-day intervals for 2 consecutive weeks (three total applications).

For the challenge phase, 14 days following the final induction application, 0.4 mL of Dursban F Insecticidal Chemical was applied in the same manner as described to the previously-untreated right sides of each animal. An additional five animals were treated in the same manner and served as naive controls.

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

- 0 - No reaction
- 0.5 - Very slight erythema
- 1 - Slight erythema
- 2 - Moderate erythema
- 3 - Marked erythema

Prior to the 24-hour observation interval following the challenge treatment, each site was depilated. Body weights were recorded on the day prior to the first induction treatment (day 1) and at termination (day 29).

The positive control studies were conducted according to the same Buehler method as for the definitive study.

II. RESULTS AND DISCUSSION:

- A. Induction reactions and duration: Slight erythema (score of 1) was observed in 1/10 sites following the first induction treatment. No dermal irritation was observed 24 hours following the second and third induction treatments.
- B. Challenge reactions and duration: Twenty-four or 48 hours following the single challenge treatment with 100% Dursban F Insecticidal Chemical to previously-induced animals, slight erythema (score of 1) was observed at 0/10 and 1/10 sites, respectively. In comparison, slight erythema (score of 1) was observed at 1/5 and

72
0/5 sites 24 and 48 hours, respectively, following challenge to naive controls. Based on the results of this study, Dursban F Insecticidal Chemical is not a dermal sensitizer.

No significant effect on overall (1 to 29 days) body weight was observed between the treatment and control groups.

- C. Positive control: For the DER 331 study: No dermal irritation was observed 24 hours following the first two induction treatments, and slight erythema (score of 1) was observed at 6/10 sites 24 hours following the third induction treatment. Twenty-four and 48 hours following challenge to previously-induced animals, slight to moderate erythema (scores of 1 to 2) was observed at 4/10 and 8/10 sites, respectively. Slight edema (score of 1) was also observed at 1/10 sites at 48 hours following challenge treatment. In contrast, no dermal irritation was observed 24 and 48 hours following challenge to naive controls. These data confirm the adequacy of the test methods and species employed in the definitive study.

For the DNCB study: No dermal irritation was observed 24 hours following the first two induction treatments, and slight erythema (score of 1) was observed at 9/10 sites 24 hours following the third induction treatment. Twenty-four and 48 hours following the challenge treatment to previously-induced animals, slight to moderate erythema (scores of 1 to 2) was observed at 9/10 and 10/10 sites, respectively. In contrast, no dermal irritation was observed 24 and 48 hours following challenge to naive controls. These data further confirm the adequacy of the test methods and species employed in the definitive study.

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