received 8-23-05
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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

24/JAN/2005

MEMORANDUM

Acute Tox
Rev.
01-24-05

Subject: Name of Pesticide Product: GF-1004
EPA Reg. No. /File Symbol: 62719-LEU
DP Barcode: D312130
Decision No: 352344
PC Codes: 005209, 030035

From: Eugenia McAndrew, Biologist EM 1/24/05
Technical Review Branch
Registration Division (7505C)

To: Eugene Wilson, RM Team 23
Herbicide Branch
Registration Division (7505C)

Applicant: Dow AgroSciences LLC
9330 Zionsville Road
Indianapolis, IN 46268

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
005209	Triisopropanolammonium salt of aminopyralid	6.54
030035	Triisopropanolammonium salt of 2,4-D	50.75
	Inert Ingredient(s):	42.71
	Total:	100.00

ACTION REQUESTED: RM requests review of acute toxicity data for GF-1004, EPA File Symbol 62719-LEU.

BACKGROUND: Dow AgroSciences LLC has submitted a six pack of acute toxicity studies to support the registration of GF-1004, EPA File Symbol 62719-LEU. The acute oral toxicity, acute dermal toxicity, primary skin irritation and dermal sensitization studies were conducted at Charles River Laboratories, Inc., Discovery and Development Services, Springborn Division, Spencerville, Ohio. The acute inhalation toxicity study was conducted at Toxicology & Environmental Research and Consulting, Midland, Michagan. The primary eye irritation study was conducted at Product Safety Labs, Dayton, New Jersey. The assigned MRID numbers are 464343-03 to -08.

RECOMMENDATIONS: The six studies have been reviewed and are classified as acceptable.

The acute toxicity profile for GF-1004, EPA File Symbol 62719-LEU, is as follows:

acute oral toxicity	III	Acceptable	MRID 46434303
acute dermal toxicity	IV	Acceptable	MRID 46434304
acute inhalation toxicity	IV	Acceptable	MRID 46434305
primary eye irritation	I	Acceptable	MRID 46434306
primary skin irritation	IV	Acceptable	MRID 46434307
dermal sensitization	Negative	Acceptable	MRID 46434308

LABELING: Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System.

PRODUCT ID #: 062719-00524

PRODUCT NAME: GF-1004

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

SIGNAL WORD: DANGER

SPANISH SIGNAL WORD: PELIGRO
Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.
(If you do not understand the label, find someone to explain it to you in detail.)

Restricted Use Pesticide due to toxicity categories. For retail sale to and use only by Certified Applicators or persons under their direct supervision and only for those uses covered by the Certified Applicator's certification.

Corrosive. Causes irreversible eye damage. Harmful if swallowed. Do not get in eyes or on clothing. Wear protective eyewear (goggles, face shield, or safety glasses). Wear: Long-sleeved shirt and long pants, socks, shoes, and chemical-resistant gloves (such as Natural Rubber, Selection Category A).

First Aid:

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

User Safety Recommendations:

Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Remove and wash contaminated clothing before reuse.

NOTE TO PHYSICIAN: Note to RM/Registrant: The proposed label should contain a Note to Physician which addresses the category I Primary Eye Irritant toxicity. The following statements are suggested types of information that may be included, if applicable:

- technical information on symptomatology;
- use of supportive treatments to maintain life functions;
- medicine that will counteract the specific physiological effects of the pesticide;
- company telephone number to specific medical personnel who can provide specialized medical advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

Reviewer: Eugenia McAndrew January 24, 2005
Risk Manager: 23

STUDY TYPE: Acute Oral Toxicity - S-D Rat; OPPTS 870.1100; OECD 425

TEST MATERIAL: GF-1004 (Lot TSN104111; Lot # E0993-44; 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; amber liquid)

CITATION: Smedley, J. GF-1004: An Acute Oral Toxicity Study in Fischer 344 Rats (Up/ Down Design). Charles River Laboratories, Inc., Springborn Division, Spencerville, Ohio. Laboratory Report Number 3504.340. October 7, 2003. MRID 46434303. Unpublished.

SPONSOR: Dow AgroSciences LLC, Midland, Michigan

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46434303), eight female young adult Fischer 344 rats (Age: 8-11 weeks; Source: Charles River Laboratories, Inc., Raleigh, NC; 131-163 g) were given a single oral dose of GF-1004 (Lot TSN104111; Lot # E0993-44; 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; amber liquid) using the Up and Down Procedure. The study was initiated as a limit test with one rat at a dose level of 5000 mg/kg. Following death in this first rat, a Main Test was initiated using a starting dose of 175 mg/kg. Following the Up and Down Procedure, six additional female rats were dosed at levels of 550 or 2000 mg/kg. (The 2000 mg/kg dose level was utilized as an alternate level to 1750 mg/kg in consideration of European Regulatory categorization criteria.) Animals were then observed for 14 days.

Oral LD_{50} Females = 1098 mg/kg bw (95% C.L. 550 - 2000 mg/kg)

The four animals dosed at 175 and 550 mg/kg survived and gained weight. Clinical signs noted were soft stools, dark material around the facial area, urine staining and salivation. At 2000 mg/kg, the three animals died within one day of test substance administration. Clinical signs noted included decreased resistance to removal, labored breathing, shallow breathing, cool to the touch, urine staining, activity decrease, decreased pupil size, increased lacrimation, increased salivation, decreased muscle tone, decreased extensor thrust response, decreased reactivity to handling, decreased responsiveness to touch, gait evaluations of poor coordination and inability to walk. At 5000 mg/kg, the one animal died on study day 1. Clinical signs noted were increased lacrimation and salivation. Gross necropsy of the animals dosed at 175 mg/kg and 550 mg/kg revealed no abnormalities. Gross necropsy of the decedents dosed at 2000 mg/kg and 5000 mg/kg revealed abnormal content of the digestive system, dark red areas on the lungs, and reddened thymus, duodenum and jejunum.

Toxicity based on the LD_{50} in females. EPA Toxicity Category III.

This acute oral study is classified as acceptable. It does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 425) in the rat.

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

RESULTS and DISCUSSION:

Individual animals were dosed as follows:

Limit Test

Dosing Sequence	Animal No.	Dose level (mg/kg)	Short Term Outcome	14 Day Outcome
1	1	5000	X	X

Main Test

Dosing Sequence	Animal No.	Dose level (mg/kg)	Short Term Outcome	14 Day Outcome
1	A7809	175	O	O
2	A7805	550	O	O
3	A7780	2000	X	X
4	A7785	550	O	O
5	A7814	2000	X	X
6	A7817	550	O	O
7	A7950	2000	X	X

O= survival X = death

Statistics - The Acute Oral Toxicity (Guideline 425) Statistical Program (Westat, version 1.0, May 2001) was used for all data analyses including: dose progression selections, stopping criteria determinations and/or oral LD_{50} and confidence limit calculations.

A. Mortality - as noted in table.

B. Clinical observations - The four animals dosed at 175 and 550 mg/kg survived and gained weight. Clinical signs noted were soft stools, dark material around the facial area, urine staining and salivation. At 2000 mg/kg, the three animals died within one day of test substance administration. Clinical signs noted included decreased resistance to removal, labored breathing, shallow breathing, cool to the touch, urine staining, activity decrease, decreased pupil size, increased lacrimation, increased salivation, decreased muscle tone, decreased extensor thrust response, decreased reactivity to handling, decreased responsiveness to touch, gait evaluations of poor coordination and inability to walk. At 5000 mg/kg, the one animal died on study day 1. Clinical signs noted were increased lacrimation and salivation.

C. Gross Necropsy - Gross necropsy of the animals dosed at 175 mg/kg and 550 mg/kg revealed no abnormalities. Gross necropsy of the decedents dosed at 2000 mg/kg and 5000 mg/kg revealed abnormal content of the digestive system, dark red areas on the lungs, and reddened thymus, duodenum and jejunum.

D. Reviewer's Conclusions: Agree with the study author

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: Thursday, January 13, 2005, 1:59:49 PM
Data file name: GF-1004.dat
Last modified: 1/13/2005 1:59:49 PM

Test/Substance: GF-1004
Test type: **Limit Test**
Limit dose (mg/kg): **5000**
Assumed LD50 (mg/kg): Default
Assumed sigma (mg/kg): 0.5

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	1	5000	X	X

(X = Died, O = Survived)

Dose Recommendation: Stop the limit test and conduct a main test at 175 mg/kg.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
5000	0	1	1
All Doses	0	1	1

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: Thursday, January 13, 2005, 2:03:16 PM
Data file name: GF-1004.dat
Last modified: 1/13/2005 2:03:10 PM

Test/Substance: GF-1004.
Test type: **Main Test**
Limit dose (mg/kg): **2000**
Assumed LD50 (mg/kg): Default
Assumed sigma (mg/kg): 0.5

Recommended dose progression: 2000, 550, 175, 55, 17.5, 5.5, 1.75

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	A7809	175	O	O
2	A7805	550	O	O
3	A7780	2000	X	X
4	A7785	550	O	O
5	A7814	2000	X	X
6	A7817	550	O	O
7	A7950	2000	X	X

(X = Died, O = Survived)

Dose Recommendation: The main test is complete.

Stopping criteria met: 5 reversals in 6 tests.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
175	1	0	1
550	3	0	3
2000	0	3	3
All Doses	4	3	7

Statistical Estimate based on long term outcomes:

Estimated LD50 = 1098 (Based on an assumed sigma of 0.5).
Approximate 95% confidence interval is 550 to 2000.

Reviewer: Eugenia McAndrew January 24, 2005
Risk Manager: 23

STUDY TYPE: Acute Dermal Toxicity - S-D Rat; OPPTS 870.1200; OECD 402

TEST MATERIAL: GF-1004 (Lot TSN104111; Lot # E0993-44; 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; amber liquid)

CITATION: Smedley, J. GF-1004: An Acute Dermal Toxicity Study in Fischer 344 Rats. Charles River Laboratories, Inc., Springborn Division, Spencerville, Ohio. Laboratory Report Number 3504.341. October 2, 2003. MRID 46434304. Unpublished.

SPONSOR: Dow AgroSciences LLC, Midland, Michigan

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 46434304), 5/sex of young adult Fischer 344 rats (Age: 8 weeks; Source: Charles River Laboratories, Inc., Raleigh, NC; 270-310 g males and 198-211 g females) were dermally exposed to GF-1004 (Lot TSN104111; Lot # E0993-44; 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; amber liquid). Five thousand mg/kg of the test substance was applied to approximately 10% of body surface area of each animal. The test sites were covered with a porous gauze dressing backed with a plastic wrap placed over the gauze dressing (occlusive binding) for a period of 24 hours. Animals were then observed for 14 days.

Dermal LD_{50} Males => 5000 mg/kg bw
Dermal LD_{50} Females => 5000 mg/kg bw
Dermal LD_{50} Combined => 5000 mg/kg bw

All animals survived and gained weight. Clinical signs noted were dark material around the facial area, soft stools, urine staining and increased lacrimation. Dermal irritation was noted at all test sites. No gross abnormalities were observed for any of the animals necropsied at the end of the study.

Toxicity based on the lack of deaths at the limit dose. EPA Toxicity Category IV.

This acute dermal study is classified acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402) in the rat.

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

RESULTS and DISCUSSION:

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

A. Mortality - none

B. Clinical observations - All animals survived and gained weight. Clinical signs noted were dark material around the facial area, soft stools, urine staining and increased lacrimation. Dermal irritation was noted at all test sites. No gross abnormalities were observed for any of the animals necropsied at the end of the study.

C. Gross Necropsy - No gross abnormalities were observed for any of the animals necropsied at the end of the study.

D. Reviewer's Conclusions: Agree with the study author

Reviewer: Eugenia McAndrew January 24, 2005
Risk Manager: 23

STUDY TYPE: Acute Inhalation Toxicity -S-D rat; OPPTS 870.1300; OECD 403

TEST MATERIAL: GF-1004 (Lot TSN104111; Lot # E0993-44; 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; amber liquid)

CITATION: Landry, T.D. and Krieger, S.M.. GF-1004: Acute Liquid Aerosol Inhalation Toxicity Study in Fischer 344 Rats. Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan. Laboratory Report Number 031066. July 23, 2003. MRID 46434305. Unpublished.

SPONSOR: Dow AgroSciences LLC, Midland, Michigan

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 46434305), 5 Fischer 344 rats/sex (Age: 8 weeks; Source: Charles River Laboratories, Inc., Raleigh, NC; 171-189 g males and 121-134 g females) were exposed nose only via the inhalation route to GF-1004 (Lot TSN104111; Lot # E0993-44; 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; amber liquid). The animals were exposed to a test concentration of 5.54 mg/L for a period of four hours. Animals were then observed for 15 days.

LC_{50} Males = > 5.54 mg/L
LC_{50} Females = > 5.54 mg/L
LC_{50} Combined = > 5.54 mg/L

All animals survived the exposure. The only clinical sign noted during the exposure was soiling of the haircoat. Clinical signs noted post-exposure included noisy respiration, ungroomed appearance, perineal, abdominal and/or extensive body soiling. The animals recovered from these symptoms by day 3. Animals lost weight on day 2 but all animals exceeded initial body weights by day 8. No gross abnormalities were noted at necropsy. The mass median aerodynamic diameter was estimated to be 1.17 µm and with a geometric standard deviation of 3.58.

Toxicity based on the lack of deaths at the limit dose. EPA Toxicity Category IV.

This acute inhalation study is classified as acceptable. It does satisfy the guideline requirement for an acute inhalation study (OPPTS 870.1300; OECD 403) in the rat.

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

RESULTS and DISCUSSION:

Nominal Concentration (mg/L)	Gravimetric Concentration (mg/L)	MMAD µm	GSD µm	Mortality/Number Tested		
				Males	Females	Combined
6.13	5.54	1.17	3.58	0/5	0/5	0/10

Test Atmosphere / Chamber Description:

Chamber Volume:	**42 L**
Airflow:	**30 LPM**
Temperature:	**21-22°C**
Relative Humidity:	**29-31%**
Time to Equilibrium:	**13.6min.**

A. Mortality - None

B. Clinical observations - All animals survived the exposure. The only clinical sign noted during the exposure was soiling of the haircoat. Clinical signs noted post-exposure included noisy respiration, ungroomed appearance, perineal, abdominal and/or extensive body soiling. The animals recovered from these symptoms by day 3. Animals lost weight on day 2 but all animals exceeded initial body weights by day 8. No gross abnormalities were noted at necropsy. The mass median aerodynamic diameter was estimated to be 1.17 µm and with a geometric standard deviation of 3.58.

C. Gross Necropsy - No gross abnormalities were noted at necropsy for the 0.52 mg/kg group and for the survivors at 5.54 mg/kg. Gross necropsy of the decedents revealed discoloration of the lungs, liver and intestines.

D. Reviewer's Conclusions: Agree with the study author

Reviewer: Eugenia McAndrew January 24, 2005
Risk Manager: 23

STUDY TYPE: Primary Eye Irritation - NW Rabbit; OPPTS 870.2400; OECD 405

TEST MATERIAL: GF-1004 (Lot # TSN104114 (E0993-44) 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; yelllow liquid)

CITATION: Moore, G. Primary Eye Irritation Study in Rabbits. Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 14299. December 1, 2003. MRID 46434306. Unpublished.

SPONSOR: Dow AgroSciences LLC, 9330 Zionsville Road, Indianapolis, IN 46268

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 46434306), 0.1 mL of GF-1004 (Lot # TSN104114 (E0993-44) 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; yelllow liquid) was instilled into the conjunctival sac of the right eye of one female young adult New Zealand albino rabbit (Source: Robinson Services, Inc., Clemmons, NC). The left eye served as the control. Immediately following the one-hour evaluation, 1-2 drops of ocular anesthetic were placed into both the treated and control eye of the animal. At the end of day 0 through the beginning of day 7, the animal also received twice daily 0.1mL of Buprenex SQ (Buprenorphine) via intramuscular injection. Animals were then observed at 1, 24, 48, 72 hours and at 4,7,10, 14, 17 and 21 days post-instillation. Irritation was scored by the method of Draize.

By 24 hours, corneal opacity, iritis and conjunctivitis were present. Pannus was noted on days 14-21. The iritis and conjunctivitis resolved by day 7. The corneal opacity persisted through day 21.

In this study, formulation is severely irritating. EPA Toxicity Category I.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

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

RESULTS AND DISCUSSION:

	Number "positive"/number tested									
	Hours				Days					
Observations	1	24	48	72	4	7	10	14	17	21
Corneal Opacity	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1
Iritis	0/1	1/1	1/1	1/1	1/1	0/1	0/1	0/1	0/1	0/1
Conjunctivae:										
Redness	1/1	1/1	1/1	1/1	1/1	0/1	0/1	0/1	0/1	0/1
Chemosis	1/1	1/1	1/1	1/1	1/1	0/1	0/1	0/1	0/1	0/1
Discharge	1/1	1/1	1/1	0/1	0/1	0/1	0/1	1/1	0/1	0/1

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

A. Observations - By 24 hours, corneal opacity, iritis and conjunctivitis were present. Pannus was noted on days 14-21. The iritis and conjunctivitis resolved by day 7. The corneal opacity persisted through day 21.

B. Reviewer's Conclusions: Agree with study author

Reviewer: Eugenia McAndrew January 24, 2005
Risk Manager: 23

STUDY TYPE: Primary Dermal Irritation - NW Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL: GF-1004 (Lot TSN104111; Lot # E0993-44; 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; amber liquid)

CITATION: Smedley, J. GF-1004: A Primary Skin Irritation Study in New Zealand White Rabbits. Charles River Laboratories, Inc., Springborn Division, Spencerville, Ohio. Laboratory Report Number 3504.342. August 26, 2003. MRID 46434307. Unpublished.

SPONSOR: Dow AgroSciences LLC, Midland, Michigan

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 46434307), three adult male New Zealand White rabbits (Source: Myrtle's Rabbitry, Thompson Station, TN) were dermally exposed to 0.5 mL of GF-1004 (Lot TSN104111; Lot # E0993-44; 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; amber liquid). The test substance was applied to a 1 inch by 1 inch area of intact skin on the dorsal area of each animal. Test sites were covered with a gauze patch and held in place with semi-occlusive elastic wrap for a 4 hour period. Animals were then observed at 1, 24, 48 and 72 hours after patch removal. Irritation was scored by the method of Draize.

In this study, formulation is slightly irritating. EPA Toxicity Category IV.

Primary Dermal Irritation Index (PDII) = 0.25 One hour after patch removal, very slight erythema was noted at all three test sites. All sites were free of irritation by 24 hours.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary dermal irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

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

RESULTS and DISCUSSION:

A. **Observations** - One hour after patch removal, very slight erythema was noted at all three test sites. All sites were free of irritation by 24 hours.

B. **Results** - PDII - 0.25

C. **Reviewer's Conclusions** - Agree with study author

Reviewer: Eugenia McAndrew January 24, 2005
Risk Manager: 23

STUDY TYPE: Dermal Sensitization - Guinea Pig; OPPTS 870.2600; OECD 406

TEST MATERIAL: GF-1004 (Lot TSN104111; Lot # E0993-44; 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; amber liquid)

CITATION: Smedley, J. GF-1004: A Dermal Sensitization Study in Hartley Albino Guinea Pigs. Modified Buehler Design. Charles River Laboratories, Inc., Springborn Division, Spencerville, Ohio. Laboratory Report Number 3504.322. Ocotber 22, 2003. MRID 46434308. Unpublished.

SPONSOR: Dow AgroSciences LLC, Midland, Michigan

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 46434308) with GF-1004 (Lot TSN104111; Lot # E0993-44; 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; amber liquid), 20 young adult Hartley-derived albino guinea pigs (Source: Hilltop Lab Animals, Scottdale, PA; 371-395 g males and 300-327 g females) were tested using a modified Buehler design. The procedures were validated using alpha-Hexylcinnamaldehyde, (HCA) and 1-Chloro-2,4-dinitrobenzene (DNCB)as the positive control substances.

Once each week for three weeks, 0.3 mL of undiluted test substance was applied to the left side of each animal for a 6-hour exposure period for a total of three exposures. Twenty-seven days after the first induction, 0.3 mL of undiluted test substance (the highest non-irritating concentration) was applied to a naive site on each test animal for a 6-hour challenge exposure. Ten naive control guinea pigs were also treated with the test substance at challenge only. Readings were made 24 and 48 hours after each induction application and after the challenge application.

In this study, the formulation is not a dermal sensitizer.

No dermal irritation was noted at any test animal or naive control animal site during the induction phase or following the challenge.

This study is classified as acceptable. It does satisfy the guideline requirement for a dermal sensitization study (OPPTS 870.2600; OECD 406) in the Guinea pig.

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

I. PROCEDURE

A. **Induction** - Once each week for three weeks, 0.3 mL of undiluted test substance was applied to the left side of each animal for a 6-hour exposure period for a total of three exposures. Readings were made 24 and 48 hours after each induction application.

B. **Challenge** - Twenty-seven days after the first induction, 0.3 mL of undiluted test substance (the highest non-irritating concentration) was applied to a naive site on each test animal for a 6-hour challenge exposure. Readings were made 24 and 48 hours after the challenge application.

C. **Naive Controls** - Ten naive control guinea pigs were also treated with the test substance at challenge only.

II. RESULTS and DISCUSSION:

A. **Reactions and duration** - No dermal irritation was noted at any test animal or naive control animal site during the induction phase or following the challenge.

B. **Positive control** - The results of the HCA and DNCB positive control studies were appropriate to validate test procedures.

C. **Reviewer's Conclusions**: Agree with study author

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D312130
2. **PC CODES:** 005209, 030035
3. **CURRENT DATE:** 24/JAN/2004
4. **TEST MATERIAL:** GF-1004 (Lot TSN104111; Lot # E0993-44; 6.54% XDE-750 TIPA and 50.7% 2,4-dichlorophenoxyacetic acid; amber liquid)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat Charles River Laboratories, Inc. Springborn Division 3504.340/10-7-03	46434303	LD_{50} females = 1098 mg/kg	III	A
Acute dermal toxicity/rat Charles River Laboratories, Inc. Springborn Division 3504.341/10-2-03	46434304	LD_{50} > 5000 mg/kg (males, females combined)	IV	A
Acute inhalation toxicity/rat Toxicology & Environmental Research and Consulting 031066/7-23-03	46434305	LC_{50} > 5.54 mg/L (males, females combined)	IV	A
Primary eye irritation/rabbit Product Safety Labs 14299/12-1-03	46434306	Corneal opacity, iritis and conjunctivitis with corneal opacity persisting through day 21.	I	A
Primary dermal irritation/rabbit Charles River Laboratories, Inc. Springborn Division 3504.342/8-26-03	46434307	PDII = 0.25 No irritation at 24 hours	IV	A
Dermal sensitization/guinea pig Charles River Laboratories, Inc. Springborn Division 3504.322/10-22-03	46434308	Not a sensitizer	–	A

Core Grade Key: **A =Acceptable, S = Supplementary, U = Unacceptable, W = Waived**