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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

22/MAY/2003

MEMORANDUM

Subject:	Name of Pesticide Product:	GF-443 SC SF
	EPA File Symbol:	62719-LNN
	DP Barcode:	D288073
	Case No:	065247
	PC Codes:	119031
From:	Eugenia McAndrew, Biologist Technical Review Branch Registration Division (7505C)	EM SCR
To:	Philip Errico, PM 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.
119031	Penoxosulam	21.7
	Inert Ingredient(s):	78.3
	Total:	100.0%

ACTION REQUESTED: PM requests review of acute toxicity studies for GF-443 SC SF, EPA File Symbol 62719-LNN.

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BACKGROUND: Dow AgroSciences LLC has submitted a six pack of acute toxicity studies in support of registration of GF-443 SC SF, EPA File Symbol 62719-LNN. Five of the studies were conducted at Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan. The dermal sensitization study was conducted at Springborn Laboratories, Inc., Spencerville, Ohio. MRID numbers are 458308-14, -17, -19, -22, - 25 and -28.

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

The revised acute toxicity profile for GF-443 SC SF, EPA File Symbol 62719-LNN, is as follows:

acute oral toxicity	IV	Acceptable	MRID 45830814
acute dermal toxicity	IV	Acceptable	MRID 45830817
acute inhalation toxicity	III	Acceptable	MRID 45830819
primary eye irritation	IV	Acceptable	MRID 45830822
primary skin irritation	IV	Acceptable	MRID 45830825
dermal sensitization	Negative	Acceptable	MRID 45830828

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 #: 062719-00500

PRODUCT NAME: GF-443 SC SF

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

SIGNAL WORD: CAUTION

Harmful if inhaled. Avoid breathing spray mist. Wear: Long-sleeved shirt and long pants, socks, shoes, and waterproof gloves.

First Aid:

If inhaled:
-Move the person to fresh air.
-If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible.
-Call a poison control center or doctor for further treatment 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.

Use Safety Recommendations:

Remove and wash contaminated clothing before reuse.

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DATA EVALUATION RECORD

STUDY TYPE: ACUTE ORAL TOXICITY TESTING (870.1100 formerly §81-1)

Product Manager: 23 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: GF-443; 21.9% XDE-638

SYNONYM: XDE-638 240 SC Formulation

CITATION: Yano, B.L., Brooks, K.J. and Radtke, B.J. (2002) GF-443: acute oral toxicity in Fischer 344 rats. Toxicology & Environmental Research and Consulting, The Dow Chemcial Company, Midland, Michigan. Laboratory Report Number 011169. January 2, 2002. MRID 454830814. Unpublished.

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

EXECUTIVE SUMMARY: In an acute oral toxicity study, five young adult, Fischer 344 rats/sex (Weight: 156-164 g males; 111-118 g females; Source: Charles River, Inc., Raleigh, NC) were given a single oral dose of GF-443 (Lot # E-828-59/TSN102739; 21.9% XDE-638; white opaque liquid) at 5000 mg/kg (limit dose). The test substance was administered as received. Body weights were obtained pre-study, the day of treatment and on days 2, 8 and 15. Animals were observed for clinical signs of toxicity and mortality for 15 days post dosing. A gross necropsy examination was performed on all animals.

Dermal LD_{50} Males = > 5000 mg/kg (observed)
Dermal LD_{50} Females = > 5000 mg/kg (observed)

GF-443 is classified as Toxicity Category IV based on the LD_{50} values in males and females.

All animals survived and gained weight during the study. One female rat had perineal soiling on day 2. All other animals appeared normal. There were no gross pathologic observations at necropsy.

This study is classified as Acceptable (870.1100) 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.

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RESULTS:

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

OBSERVATIONS: All animals survived and gained weight during the study. One female rat had perineal soiling on day 2. All other animals appeared normal.

GROSS NECROPSY: There were no gross pathologic observations at necropsy.

DATA EVALUATION RECORD

STUDY TYPE: ACUTE DERMAL TOXICITY TESTING (870.1200 formerly §81-2)

Product Manager: 23 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: GF-443; 21.9% XDE-638

SYNONYM: XDE-638 240 SC Formulation

CITATION: Yano, B.L., Brooks, K.J. and Radtke, B.J. (2002) GF-443: acute dermal toxicity in Fischer 344 rats. Toxicology & Environmental Research and Consulting, The Dow Chemcial Company, Midland, Michigan. Laboratory Report Number 011170. January 2, 2002. MRID 454830817. Unpublished.

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

EXECUTIVE SUMMARY: In an acute dermal toxicity study, five young adult, Fischer 344 rats/sex (Weight: 163-174 g males; 117-126 g females; Source: Charles River Laboratories, Inc., Raleigh, NC) were exposed to a single application of GF-443 (Lot # E-828-59/TSN102739; 21.9% XDE-638; white opaque liquid) at 5000 mg/kg (limit dose) for a 24 hour dermal exposure. The test substance was applied to approximately 10% of the total body surface area of each animal and covered with a gauze patch and elastic tape and wrap. Body weights were obtained pre-study, the day of treatment and on days 2, 8 and 15. A detailed clinical observation was done daily for 15 days. A gross necropsy examination was performed on all animals at the time of scheduled euthanasia.

Dermal LD_{50} Males = > 5000 mg/kg (observed)
Dermal LD_{50} Females = > 5000 mg/kg (observed)

GF-443 is classified as Toxicity Category IV based on the observed LD_{50} value in both sexes.

All animals survived the two week test period. Clinical observations included perioral soiling in one male and all five females, perinasal soiling in one male and perineal soiling in one female. There were ulcerations and reddening of the skin at the test sites of three males and all five females. The animals recovered from these symptoms by day 7. All rats lost weight between days 1 and 2 but gained weight over the duration of the study. At necropsy, there were no treatment-related gross pathologic observations.

This study is classified as Acceptable (870.1200) and satisfies the guideline requirement for an acute dermal study in the rat.

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

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RESULTS:

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

OBSERVATIONS: All animals survived the two week test period. Clinical observations included perioral soiling in one male and all five females, perinasal soiling in one male and perineal soiling in one female. There were ulcerations and reddening of the skin at the test sites of three males and all five females. The animals recovered from these symptoms by day 7. All rats lost weight between days 1 and 2 but gained weight over the duration of the study.

GROSS NECROPSY: At necropsy, there were no treatment-related gross pathologic observations.

DATA EVALUATION RECORD

STUDY TYPE: ACUTE INHALATION TOXICITY TESTING (870.1300 formerly §81-3)

Product Manager: 23 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: GF-443; 21.9% XDE-638

SYNONYM: XDE-638 240 SC Formulation

CITATION: Landry, T.D. and Houtman, C.E. (2001) GF-443: acute liquid aerosol inhalation toxicity in Fischer 344 rats. Toxicology & Environmental Research and Consulting, The Dow Chemcial Company, Midland, Michigan. Laboratory Report Number 011173. December 21, 2001. MRID 45830819. Unpublished.

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

EXECUTIVE SUMMARY: In an acute inhalation toxicity study, five young adult, Fischer 344 rats/sex (Weight: 203-212 g males; 127-133 g females; Source: Charles River, Inc., Raleigh, NC) were exposed by nose-only inhalation to GF-443 (Lot # E-828-59/TSN102739; 21.9% XDE-638; white opaque liquid) at 0.74 mg/L for a 4 hour period. Body weights were obtained prior to exposure and on days 2, 4, 8, 11 and 15. All animals were observed for clinical signs of toxicity and mortality during the exposure and for 14 days post exposure. Gross necropsies were performed on all animals.

Inhalation LC_{50} Males = > 0.74 mg/L (observed)
Inhalation LC_{50} Females = > 0.74 mg/L (observed)

GF-443 is classified as Toxicity Category III based on the observed LC_{50} value in the both sexes.

One female was found dead during the exposure. Its head was tucked between the forelimbs in the restraint tube. The other nine animals survived the exposure and the two-week observation period. Clinical signs noted were soiling of the haircoat during the exposure. Following the exposure, clinical signs included periocular, perineal and general body soiling. The animals appeared normal by day 3. All animals lost weight during the first few days of the study but all animals exceeded initial body weights by the end of the study. At necropsy on day 15, there were no visible lesions attributable to exposure noted in any of the surviving animals. In the animal that died, necropsy observations showed "no significant internal or external findings that would indicate cause of death. The absence of findings is consistent with suffocation as a cause of death." The gravimetric chamber concentration was 0.74 mg/L. The mass median aerodynamic diameter was 3.28 µm with a geometric standard deviation of 1.58.

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This study is classified as Acceptable (870.1300) and satisfies the guideline requirement for an acute inhalation study in the rat.

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

RESULTS:

Exposure Concentration mg/L (Gravimetrically Determined)	Number of Deaths/Number Tested		
	Males	Females	Combined
0.74	0/5	1/5	1/10

Chamber Atmosphere		
Gravimetric conc. mg/L	MMAD µm	GSD
0.74	3.28[a]	1.58

[a] 91.3% of the particles were < 6 µm

Chamber Environment	
Chamber Volume	42 L
Airflow	30 LPM
Temperature	20-22 °C
Relative Humidity	72-79%

OBSERVATIONS: One female was found dead during the exposure. Its head was tucked between the forelimbs in the restraint tube. The other nine animals survived the exposure and the two-week observation period. Clinical signs noted were soiling of the haircoat during the exposure. Following the exposure, clinical signs included periocular, perineal and general body soiling. The animals appeared normal by day 3. All animals lost weight during the first few days of the study but all animals exceeded initial body weights by the end of the study.

GROSS NECROPSY: At necropsy on day 15, there were no visible lesions attributable to exposure noted in any of the surviving animals. In the animal that died, necropsy observations showed "no significant internal or external findings that would indicate cause of death. The absence of findings is consistent with suffocation as a cause of death."

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DATA EVALUATION RECORD

STUDY TYPE: PRIMARY EYE IRRITATION TESTING (870.2400 formerly §81-4)

Product Manager: 23 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: GF-443; 21.9% XDE-638

SYNONYM: XDE-638 240 SC Formulation

CITATION: Brooks, K.J. and Radtke, B.J.. (2002) GF-443: acute eye irritation in New Zealand White rabbits. Toxicology & Environmental Research and Consulting, The Dow Chemcial Company, Midland, Michigan. Laboratory Report Number 011171. January 2, 2002. MRID 45830822. Unpublished.

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

EXECUTIVE SUMMARY: In a primary eye irritation study, a 0.1 mL aliquot of GF-443 (Lot # E-828-59/TSN102739; 21.9% XDE-638; white opaque liquid) was placed into the conjunctival sac of the right eye of three young adult New Zealand White rabbits (1 male and 2 female; Source: Covance Research Products, Inc., Kalamazoo, MI). All animals were observed for ocular irritation at 1, 24, 48 and 72 hours post-instillation.

GF-443 is classified as Toxicity Category IV.

There were no positive scores noted at any of the ocular observations.

This study is classified as Acceptable (870.2400) 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.

RESULTS:

Observations	Number "positive"/number tested			
	Hours			
	1	24	48	72
Corneal Opacity	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3
Conjunctivae:				
Redness*	0/3	0/3	0/3	0/3
Chemosis*	0/3	0/3	0/3	0/3
Discharge*	0/3	0/3	0/3	0/3

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

OBSERVATIONS: There were no positive scores noted at any of the ocular observations.

DATA EVALUATION RECORD

STUDY TYPE: PRIMARY DERMAL IRRITATION TESTING (870.2500 formerly §81-5)

Product Manager: 23 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: GF-443; 21.9% XDE-638

SYNONYM: XDE-638 240 SC Formulation

CITATION: Brooks, K.J. and Radtke, B.J.. (2002) GF-317: acute dermal irritation in New Zealand White rabbits. Toxicology & Environmental Research and Consulting, The Dow Chemcial Company, Midland, Michigan. Laboratory Report Number 011172. January 2, 2002. MRID 45830825. Unpublished.

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

EXECUTIVE SUMMARY: In a primary skin irritation study, three adult New Zealand White rabbits (1 male and 2 female; Source: Covance Research Products, Inc., Kalamazoo, MI) were dermally exposed to a 0.5 mL aliquot of GF-443 (Lot # E-828-59/TSN102739; 21.9% XDE-638; white opaque liquid) for a 4 hour period. The test substance was applied to a single 6 cm^2 intact dose site on the back of each animal and covered with a gauze patch and an elastic jacket. The jacket and patch were removed after 4 hours. Animals were observed 1, 24, 48 and 72 hours after patch removal.

GF-443 is classified as Toxicity Category IV.

Primary Dermal Irritation Index (PDII) = 0.0 There were no signs of dermal irritation in any of the three rabbits during the study.

This study is classified as Acceptable (870.2500) and satisfies the guideline requirement for a primary skin irritation study in the rabbit.

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

RESULTS: Primary Dermal Irritation Index (PDII) = 0.0

OBSERVATIONS: There were no signs of dermal irritation in any of the three rabbits during the study.

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DATA EVALUATION RECORD

STUDY TYPE: DERMAL SENSITIZATION TESTING (870.2600 formerly §81-6)

Product Manager: 23 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: GF-443; 21.9% XDE-638

SYNONYM: XDE-638 240 SC Formulation

CITATION: Wilson, C. (2002) GF-443: dermal sensitization in Hartley albino guinea pigs (Modified Buehler Design). Springborn Laboratories, Inc., Spencerville, Ohio. Laboratory Report Number 3504.213. February 22, 2002. MRID 45830828. Unpublished.

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

EXECUTIVE SUMMARY: In a dermal sensitization study conducted with GF-443 (Lot # E-828-59/TSN102739; 21.9% XDE-638; light tan liquid), 30 young adult male and female Hartley albino guinea pigs (Source: Charles River Laboratories, Inc., Raleigh, NC) were tested using the Buehler method. A range finding study was conducted with four animals to determine the correct concentrations for induction and challenge. For the main study, twenty test animals were induced with a total of three applications (six hours/exposure, once per week for three weeks) of 0.3 mL of undiluted test substance. Reactions were scored 24 and 48 hours after each induction. Approximately two weeks after the last induction dose on day 28, 0.3 mL of undiluted test substance (highest non-irritating concentration) was applied to the twenty test guinea pigs and to the ten naive control guinea pigs for a six-hour challenge exposure. Reactions were scored 24 and 48 hours after the challenge. Positive control studies using 1-chloro-2,4-dinitrobenzene (DNCB) and alpha-hexyl-cinnamaldehyde (AHCA) were conducted within six months of the main study to validate the test system.

GF-443 is classified as a non-sensitizer based on the results of this study.

Dermal reactions during the induction were limited to scores of 0. Following the challenge, dermal reactions were limited to scores of 0 in both test animals and naive control animals. Based on these results, the test substance is not considered to be a contact sensitizer. The positive response observed in the AHCA and DNCB studies validate the test system used in this study.

This study is classified as Acceptable (870.2600) and satisfies the guideline requirement for an dermal sensitization study in the guinea pig.

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

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PROCEDURE: In a dermal sensitization study conducted with GF-443 (Lot # E-828-59/TSN102739; 21.9% XDE-638; light tan liquid), 30 young adult male and female Hartley albino guinea pigs (Source: Charles River Laboratories, Inc., Raleigh, NC) were tested using the Buehler method. A range finding study was conducted with four animals to determine the correct concentrations for induction and challenge. For the main study, twenty test animals were induced with a total of three applications (six hours/exposure, once per week for three weeks) of 0.3 mL of undiluted test substance. Reactions were scored 24 and 48 hours after each induction. Approximately two weeks after the last induction dose on day 28, 0.3 mL of undiluted test substance (highest non-irritating concentration) was applied to the twenty test guinea pigs and to the ten naive control guinea pigs for a six-hour challenge exposure. Reactions were scored 24 and 48 hours after the challenge. Positive control studies using 1-chloro-2,4-dinitrobenzene (DNCB) and alpha-hexyl-cinnamaldehyde (AHCA) were conducted within six months of the main study to validate the test system.

RESULTS: Dermal reactions during the induction were limited to scores of 0. Following the challenge, dermal reactions were limited to scores of 0 in both test animals and naive control animals. Based on these results, the test substance is not considered to be a contact sensitizer. The positive response observed in the AHCA and DNCB studies validate the test system used in this study.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D288073
2. **PC CODE:** 065247
3. **CURRENT DATE:** 22/MAY/2003
4. **TEST MATERIAL:** GF-443 (Lot # E-828-59/TSN102739; 21.9% XDE-638; white opaque liquid)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat Toxicology & Environmental Research and Consulting Dow Chemical Company 011169/01-02-02	45830814	LD_{50} > 5000 mg/kg (males females combined)	IV	A
Acute dermal toxicity/rat Toxicology & Environmental Research and Consulting Dow Chemical Company 011170/01-02-02	45830817	LD_{50} > 5000 mg/kg (males females combined)	IV	A
Acute inhalation toxicity/rat Toxicology & Environmental Research and Consulting Dow Chemical Company 011173/12-21-01	45830819	LC_{50} > 0.74 mg/L (males females combined)	III	A
Primary eye irritation/rabbit Toxicology & Environmental Research and Consulting Dow Chemical Company 011171/01-02-02	45830822	No positive observations.	IV	A
Primary dermal irritation/rabbit Toxicology & Environmental Research and Consulting Dow Chemical Company 011172/01-02-02	45830825	PDII = 0.0 Non-irritant	IV	A
Dermal sensitization/guinea pig Springborn Laboratories, Inc. 3504.213/2-22-02	45830828	Not a sensitizer	–	A

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