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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

03/DEC/2001

MEMORANDUM

Subject:	Name of Pesticide Product:	Evercide Synergized Permethrin Pour-On 2783
	EPA Reg. No. /File Symbol:	1021-1739
	DP Barcode:	D278754
	Case No:	066277
	PC Code:	209500, 067501
From:	Eugenia McAndrew, Biologist Technical Review Branch Registration Division (7505C)	
To:	Susan Stanton, PM Team 03 Insecticide Branch Registration Division (7505C)	
Applicant:	McLaughlin Gormley King Company 8810 Tenth Avenue North Minneapolis, MN 55427	

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
209500	Permethrin	1.00
067501	Piperonyl Butoxide Technical	1.00
	Inert Ingredient(s):	98.00
	Total:	100.00%

ACTION REQUESTED: PM requests review of acute toxicity data for Evercide Synergized Permethrin Pour-On 2783, EPA Reg. No. 1021-1739.

BACKGROUND: McLaughlin Gormley King Company has submitted a six pack of acute toxicity studies in support of its currently registered product, Evercide Synergized Permethrin Pour-On 2783, EPA Reg. No. 1021-1739. The studies were assigned MRID numbers 455009-01 to -05 and 455163-01. The studies were conducted at Springborn Laboratories, Inc., Spencerville, Ohio. Prior to the submission of this acute toxicity data, this product relied on data from a substantially similar product.

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

The acute toxicity profile for Evercide Synergized Permethrin Pour-On 2783, EPA Reg. No. 1021-1739, is as follows:

acute oral toxicity	IV	Acceptable	MRID 455009-01
acute dermal toxicity	III	Acceptable	MRID 455009-02
acute inhalation toxicity	III	Acceptable	MRID 455163-01
primary eye irritation	IV	Acceptable	MRID 455009-03
primary skin irritation	IV	Acceptable	MRID 455009-04
dermal sensitization	No	Acceptable	MRID 455009-05

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.

Label Review System

PRODUCT ID #: 001021-01739

PRODUCT NAME: EVERCIDE SYNERGIZED PERMETHRIN POUR-ON 2783

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

SIGNAL WORD: CAUTION

Contains Petroleum Distillate.

Harmful if absorbed through skin. Harmful if inhaled. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Remove and wash contaminated clothing before reuse. Avoid breathing spray mist.

First Aid:

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

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.

NOTE TO PHYSICIAN: May pose an aspiration *pneumonia* hazard. Contains petroleum distillate.

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.

DATA EVALUATION RECORD

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

Product Manager: 03 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: Evercide Synergized Permethrin Pour-On 2783; 1.00% Permethrin, 1.02% Piperonyl Butoxide

CITATION: Bonnette, K. (2001) Evercide Synergized Permethrin Pour-On 2783; acute oral toxicity in rats. Springborn Laboratories, Inc., Spencerville, Ohio. Laboratory Report Number 3414.49. February 20, 2001. MRID 45500901. Unpublished.

SPONSOR: McLaughlin Gormley King Company, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In an acute oral toxicity study, five young adult Sprague-Dawley CD rats/sex (Weight: 281-300 g males; 203-241 g females; Source: Harlan Sprague Dawley, Inc.) were given a single oral dose of Evercide Synergized Permethrin Pour-On 2783 (1.00% Permethrin, 1.02% Piperonyl Butoxide; Lot No. GLP-1398; clear colorless liquid) at 5000 mg/kg (limit dose). The test substance was administered as received. Animals were observed for clinical signs of toxicity and mortality for 14 days post dosing.

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

Evercide Synergized Permethrin Pour-On 2783 is classified as Toxicity Category IV based on the calculated LD_{50} value in both sexes.

All animals survived and gained bodyweight during the study. Clinical signs noted were urine stain, rough hair coat and dark material around the facial area. The animals recovered from these symptoms by day 4. At necropsy, a reddened thymic lymph node was observed in one male. No other gross findings were observed.

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.

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 bodyweight during the study. Clinical signs noted were urine stain, rough hair coat and dark material around the facial area. The animals recovered from these symptoms by day 4.

GROSS NECROPSY: A reddened thymic lymph node was observed in one male. No other gross findings were observed.

DATA EVALUATION RECORD

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

Product Manager: 03 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: Evercide Synergized Permethrin Pour-On 2783; 1.00% Permethrin, 1.02% Piperonyl Butoxide

CITATION: Bonnette, K. (2001) Evercide Synergized Permethrin Pour-On 2783; acute dermal toxicity in rabbits. Springborn Laboratories, Inc., Spencerville, Ohio. Laboratory Report Number 3414.50. March 12, 2001. MRID 45500902. Unpublished.

SPONSOR: McLaughlin Gormley King Company, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In an acute dermal toxicity study, five adult New Zealand White rabbits/sex (Weight: 2.8-3.2 kg males; 2.7-3.0 kg females; Source: Myrtle's Rabbitry, Thompson Station, TN) were dermally exposed to a single application of Evercide Synergized Permethrin Pour-On 2783 (1.00% Permethrin, 1.02% Piperonyl Butoxide; Lot No. GLP-1398; clear colorless liquid) at 2000 mg/kg (limit dose) for 24 hours. The test substance was applied to approximately 10% of the total body surface area. Animals were observed for clinical signs of toxicity and mortality twice on the day of dosing and once daily for 14 days.

Dermal LD_{50} Males = > 2000 mg/kg (observed); Dermal LD_{50} Females = > 2000 mg/kg (observed)

Evercide Synergized Permethrin Pour-On 2783 is classified as Toxicity Category III based on the observed LD_{50} values in both sexes.

All animals survived and gained weight during the study. No significant adverse clinical signs were noted. Dermal irritation was present at all dose sites. Erythema and edema (grades 1-2) were noted from the day of exposure through the end of the study on day 14. Desquamation was noted in 8/10 animals and eschar in one animal. Necropsy after 14 days revealed cycts on the oviducts of four females and an abscess on the liver of one male.

This study is classified as Acceptable (870.1200) 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.

RESULTS:

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

OBSERVATIONS: All animals survived and gained weight during the study. No significant adverse clinical signs were noted. Dermal irritation was present at all dose sites. Erythema and edema (grades 1-2) were noted from the day of exposure through the end of the study on day 14. Desquamation was noted in 8/10 animals and eschar in one animal.

GROSS NECROPSY: Necropsy after 14 days revealed cycts on the oviducts of four females and an abscess on the liver of one male.

DATA EVALUATION RECORD

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

Product Manager: 03 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: Evercide Synergized Permethrin Pour-On 2783; 1.00% Permethrin, 1.02% Piperonyl Butoxide

CITATION: Bonnette, K. (2001) Evercide Synergized Permethrin Pour-On 2783; acute whole-body inhalation toxicity in rats. Springborn Laboratories, Inc., Spencerville, Ohio. Laboratory Report Number 3414.51. February 20, 2001. MRID 45516301. Unpublished.

SPONSOR: McLaughlin Gormley King Company, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In an acute inhalation toxicity study, five young adult Hsd: Sprague-Dawley SD rats/sex (Weight: 209-232 g males; 169-193 g females; Source: Harlan Sprague Dawley, Inc.) were exposed by whole body inhalation to Evercide Synergized Permethrin Pour-On 2783 (1.00% Permethrin, 1.02% Piperonyl Butoxide; Lot No. GLP-1398; clear colorless liquid) at 0.51 mg/L or 2.35 mg/L for 4 hours. All animals were observed for clinical signs of toxicity and mortality during the exposure and for 14 days post exposure.

Inhalation LC_{50} Males = > 0.51 mg/L (observed); Inhalation LC_{50} Females = > 0.51 mg/L (observed)

Evercide Synergized Permethrin Pour-On 2783 is classified as Toxicity Category III based on the observed LC_{50} values in both sexes.

At 0.51 mg/L, one female was found dead on day 3; all other animals survived. At 2.35 mg/L, all ten animals died on days 1 and 2. Clinical signs observed include decreased activity, wobbly gait, breathing abnormalities, decreased defecation, rough haircoat, unkempt appearance, hunched posture, fecal/urine stain, apparent hypothermia and dark material around the facial area. The mass median aerodynamic diameter was estimated to be 1.2 µm and 1.4 µm with a geometric standard deviation of 2.4. Necropsy at 14 days revealed no gross abnormalities in the surviving animals. The animals that died had red dark lungs and abnormal content in the trachea and digestive tract.

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 (Analytically Determined)	Number of Deaths/Number Tested		
	Males	Females	Combined
0.51	0/5	1/5	1/10
2.35	5/5	5/5	10/10

Chamber Atmosphere		
Analytical conc. mg/L	MMAD µm	GSD
0.51	1.2	2.4
2.35	1.4	2.4

Chamber Environment[a]	
Chamber Volume	100 L
Airflow	48-58 LPM
Temperature	67-74 °F
Relative Humidity	19-36%

[a] Whole body

OBSERVATIONS: At 0.51 mg/L, one female was found dead on day 3; all other animals survived. At 2.35 mg/L, all ten animals died on days 1 and 2. Clinical signs observed include decreased activity, wobbly gait, breathing abnormalities, decreased defecation, rough haircoat, unkempt appearance, hunched posture, fecal/urine stain, apparent hypothermia and dark material around the facial area. The mass median aerodynamic diameter was estimated to be 1.2 and 1.4 µm with a geometric standard deviation of 2.4.

GROSS NECROPSY: Necropsy at 14 days revealed no gross abnormalities in the surviving animals. The animals that died had red dark lungs and abnormal content in the trachea and digestive tract.

DATA EVALUATION RECORD

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

Product Manager: 03 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: Evercide Synergized Permethrin Pour-On 2783; 1.00% Permethrin, 1.02% Piperonyl Butoxide

CITATION: Bonnette, K. (2001) Evercide Synergized Permethrin Pour-On 2783; primary eye irritation in rabbits. Springborn Laboratories, Inc., Spencerville, Ohio. Laboratory Report Number 3414.52. March 12, 2001. MRID 45500903. Unpublished.

SPONSOR: McLaughlin Gormley King Company, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In a primary eye irritation study, 0.1 mL of Evercide Synergized Permethrin Pour-On 2783 (1.00% Permethrin, 1.02% Piperonyl Butoxide; Lot No. GLP-1398; clear colorless liquid) was placed into the conjunctival sac of the right eye of six adult New Zealand white rabbits (4 male and 2 female; Source: Myrtle's Rabbitry, Thompson Station, TN). Approximately 30 seconds after the installation of the test article, the eyes of three rabbits were rinsed for approximately 30 seconds with sterile water. The remaining three eyes were not rinsed. All animals were observed for ocular irritation at 1, 24, 48 and 72 hours and up to 7 days post-installation.

Evercide Synergized Permethrin Pour-On 2783 is classified as Toxicity Category IV.

Unrinsed eyes: No corneal opacity or iritis was observed. Conjunctivitis was noted in 3/3 eyes one hour after test substance installation. No positive observations were noted at 24 hours. Rinsed eyes: No positive results were noted during 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				Hours			
	1	24	48	72	1	24	48	72
	Unrinsed eyes				Rinsed eyes			
Corneal Opacity	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Conjunctivae:								
Redness*	3/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Chemosis*	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Discharge*	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3

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

OBSERVATIONS: Unrinsed eyes: No corneal opacity or iritis was observed. Conjunctivitis was noted in 3/3 eyes one hour after test substance installation. No positive observations were noted at 24 hours. Rinsed eyes: No positive results were noted during the ocular observations.

DATA EVALUATION RECORD

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

Product Manager: 03 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: Evercide Synergized Permethrin Pour-On 2783; 1.00% Permethrin, 1.02% Piperonyl Butoxide

CITATION: Bonnette, K. (2001) Evercide Synergized Permethrin Pour-On 2783; primary skin irritation in rabbits. Springborn Laboratories, Inc., Spencerville, Ohio. Laboratory Report Number 3414.53. February 20, 2001. MRID 45500904. Unpublished.

SPONSOR: McLaughlin Gormley King Company, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In a primary skin irritation study, three adult New Zealand White rabbits (2 male and 1 female; Source: Myrtle's Rabbitry, Thompson Station, TN) were dermally exposed to 0.5 mL of Evercide Synergized Permethrin Pour-On 2783 (1.00% Permethrin, 1.02% Piperonyl Butoxide; Lot No. GLP-1398; clear colorless liquid) for 4 hours. The test substance was applied to a single 1 inch x 1 inch intact dose site on each animal. Animals were observed 1, 24, 48 and 72 hours and up to 10 days after patch removal.

Evercide Synergized Permethrin Pour-On 2783 is classified as Toxicity Category IV.

Primary Dermal Irritation Index (PDII) = 0.8 Very slight to well defined erythema was present at al three dose sites one hour after patch removal. The irritation subsided with time. At 72 hours, two sites were free of dermal irritation and one site had very slight erythema. Desquamation was noted at one site.

This study is classified as Acceptable (870.2500) and satisfies the guideline requirement for an 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) = 0.8

OBSERVATIONS: Very slight to well defined erythema was present at al three dose sites one hour after patch removal. The irritation subsided with time. At 72 hours, two sites were free of dermal irritation and one site had very slight erythema. Desquamation was noted at one site.

DATA EVALUATION RECORD

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

Product Manager: 03 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: Evercide Synergized Permethrin Pour-On 2783; 1.00% Permethrin, 1.02% Piperonyl Butoxide

CITATION: Bonnette, K. (2001) Evercide Synergized Permethrin Pour-On 2783; dermal sensitization in guinea pigs. Springborn Laboratories, Inc., Spencerville. Ohio. Laboratory Report Number 3414.54. March 12, 2001. MRID 45500905. Unpublished.

SPONSOR: McLaughlin Gormley King Company, 8810 Tenth Avenue North, Minneapolis, MN 55427

EXECUTIVE SUMMARY: In a dermal sensitization study conducted with Evercide Synergized Permethrin Pour-On 2783 (1.00% Permethrin, 1.02% Piperonyl Butoxide; Lot No. GLP-1398; clear colorless liquid), 30 young adult male and female Hartley-derived albino guinea pigs (Source: Hilltop Lab Animals. Inc., Scottdale, PA) were tested using methods based on those derived by Buehler. Preliminary testing was conducted to determine the correct concentrations for induction and challenge. Twenty test animals were induced with three applications (six hours/exposure, once per week for three weeks) of 0.4 mL of 75% w/v test substance in mineral oil. Twenty-seven days after the first induction dose, 0.4 mL of 50% w/v test substance in mineral oil (highest non-irritating concentration) was applied to the twenty test guinea pigs and to ten naive control guinea pigs for a six-hour challenge exposure. Reactions were scored 24 and 48 hours after each induction and after the challenge. A positive control study using α-Hexylcinnamaldehyde (HCA) was conducted within six months of the main study to validate the test system.

Evercide Synergized Permethrin Pour-On 2783 is classified as a non-sensitizer based on the results of this study.

Erythema grades 0.5-1 was observed at all test animal sites during the induction phase. Following the challenge, erythema grade 0.5 was observed at 6/20 test animal sites and at 5/10 naive control animal sites. No positive responses (scores > 0.5) were observed. Based on these results, the test substance is not considered to be a contact sensitizer. The positive response observed in the HCA study validates 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.

PROCEDURE: In a dermal sensitization study conducted with Evercide Synergized Permethrin Pour-On 2783 (1.00% Permethrin, 1.02% Piperonyl Butoxide; Lot No. GLP-1398; clear colorless liquid), 30 young adult male and female Hartley-derived albino guinea pigs (Source: Hilltop Lab Animals, Inc., Scottdale. PA) were tested using methods based on those derived by Buehler. Preliminary testing was conducted to determine the correct concentrations for induction and challenge. Twenty test animals were induced with three applications (sixhours/exposure. once per week for three weeks) of 0.4 mL of 75% w/v test substance in mineral oil. Twenty-seven days after the first induction dose, 0.4 mL of 50% w/v test substance in mineral oil (highest non-irritating concentration) was applied to the twenty test guinea pigs and to ten naive control guinea pigs for a six-hour challenge exposure. Reactions were scored 24 and 48 hours after each induction and after the challenge. A positive control study using α-Hexylcinnamaldehyde (HCA) was conducted within six months of the main study to validate the test system.

RESULTS: Erythema grades 0.5-1 was observed at all test animal sites during the induction phase. Following the challenge, erythema grade 0.5 was observed at 6/20 test animal sites and at 5/10 naive control animal sites. No positive responses (scores > 0 5) were observed. Based on these results. the test substance is not considered to be a contact sensitizer. The positive response observed in the HCA study validates the test system used in this study.