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

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

15/NOV/2005

MEMORANDUM

Subject:	Name of Pesticide Product:	Cutter Insect Repellent SS
	EPA Reg. No. /File Symbol:	121-OT
	DP Barcode:	D322945
	Decision No.:	361412
	PC Code:	070705
From:	Eugenia Mc Andrew, Biologist	EM
	Technical Review Branch	
	Registration Division (7505C)	
To:	Joseph Tavano, RM Team 10	
	Insecticide Branch	
	Registration Division (7505C)	
Applicant:	Spectrum	
	Division of United Industries Corp.	
	P.O. Box 142642	
	St. Louis, MO 63114-0642	

FORMULATION FROM LABEL:

Active Ingredient(s):		% by wt.
070705	Picaridin	15.0
Inert Ingredient(s):		85.0%
	Total:	100.0%

ACTION REQUESTED: The Risk Manager requests:

"Review data and label for new product. MRIDs 466680-04 thru 09."

BACKGROUND: Spectrum has submitted a six pack of acute toxicity studies to support registration of the proposed product, Cutter Insect Repellent SS, EPA File Symbol 121-OT. The studies were conducted at Product Safety Laboratories, Dayton, New Jersey with assigned MRID numbers 466680-04 to -09.

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

The acute toxicity profile for Cutter Insect Repellent SS, EPA File Symbol 121-OT, is as follows:

Acute oral toxicity	IV	Acceptable	MRID 46668004
Acute dermal toxicity	IV	Acceptable	MRID 46668005
Acute inhalation toxicity	IV	Acceptable	MRID 46668006
Primary eye irritation	III	Acceptable	MRID 46668007
Primary skin irritation	IV	Acceptable	MRID 46668008
Dermal sensitization	Neg.	Acceptable	MRID 46668009

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 #: 000121-00097

PRODUCT NAME: Cutter Insect Repellent SS

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

SIGNAL WORD: CAUTION

Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco.

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.

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 **Date:** November 15, 2005
Risk Manager: 10

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

TEST MATERIAL: Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid)

CITATION: Merkel, D. Cutter Insect Repellent SS. Acute Oral Toxicity Study Up and Down Procedure in Rats. Product Safety Laboratories, Dayton, New Jersey. Laboratory Study Number 17639. August 31, 2005. MRID 46668004 Unpublished.

SPONSOR: Spectrum, Division of United Industries Corp., P.O. Box 142642, St. Louis, MO 63114-0642

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46668004), three female Sprague-Dawley derived young adult albino rats (Age: 11 weeks; Source: Ace Animals, Inc., Boyertown, PA; 204-212 g) were given a single oral dose of Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid) using the Up and Down Procedure. A limit dose of 5000 mg/kg of the test substance was administered to one healthy female rat by oral gavage. This animal survived so two additional females received the same dose level. Animals were then observed for 14 days.

Oral LD_{50} Females > 5000 mg/kg bw

All animals survived and gained weight Hypoactivity and piloerection were noted in two animals during the first three hours after dosing. No gross abnormalities were noted at necropsy.

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

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:

Dosing Sequence	Animal No.	Dose level (mg/kg)	Short Term Outcome	14 Day Outcome
1	3102	5000	S	S
2	3170	5000	S	S
3	3171	5000	S	S

S = survival D = death

A. Mortality - None

B. Clinical observations - All animals survived and gained weight Hypoactivity and piloerection were noted in two animals during the first three hours after dosing.

C. Gross Necropsy - No gross abnormalities were noted.

D. Reviewer's Conclusions: We agree with the study author that the acute oral LD_{50} of Cutter Insect Repellent SS is greater than 5000 mg/kg of body weight in female rats

Reviewer: Eugenia McAndrew
Risk Manager: 10

Date: November 15, 2005

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

TEST MATERIAL: Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid)

CITATION: Merkel, D. Cutter Insect Repellent SS. Acute Dermal Toxicity Study in Rats-Limit Test. Product Safety Laboratories, Dayton, New Jersey. Laboratory Study Number 17640. August 31, 2005. MRID 46668005 Unpublished.

SPONSOR: Spectrum, Division of United Industries Corp., P.O. Box 142642, St. Louis, MO 63114-0642

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 46668005), 5/sex of Sprague-Dawley derived young adult albino rats (Age: 9-10 weeks; Source: Ace Animals, Inc., Boyertown, PA; 294-316 g males and 194-213 g females) were dermally exposed to Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid). The test substance was applied to a 2 inch x 3 dose area (approximately 10% of the body surface) at a dose of 5000 mg/kg bw. Test sites were covered with a gauze pad and wrapped with tape for a 24 hour period. After 24 hours the pads were removed. 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. "There were no signs of gross toxicity, dermal irritation, adverse pharmacologic effects or abnormal behavior." No gross abnormalities were noted at necropsy.

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:

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

A. Mortality - None

B. Clinical observations - All animals gained weight. "There were no signs of gross toxicity, dermal irritation, adverse pharmacologic effects or abnormal behavior."

C. Gross Necropsy - No gross abnormalities were noted.

D. Reviewer's Conclusions: We agree with the study author that the acute dermal LD_{50} of Cutter Insect Repellent SS is greater than 5000 mg/kg bw in male and female rats.

Reviewer: Eugenia McAndrew **Date:** November 15, 2005
Risk Manager: 10

STUDY TYPE: Acute Inhalation Toxicity - Rat; OPPTS 870.1300; OECD 403

TEST MATERIAL: Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid)

CITATION: Merkel, D. Cutter Insect Repellent SS. Acute Inhalation Toxicity Study in Rats – Limit Test. Product Safety Laboratories, Dayton, New Jersey. Laboratory Study Number 17641. September 1, 2005. MRID 46668006 Unpublished.

SPONSOR: Spectrum, Division of United Industries Corp., P.O. Box 142642, St. Louis, MO 63114-0642

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 46668006), 5/sex of young adult Sprague-Dawley rats (Age: 9-10 weeks; Source: Ace Animals, Inc., Boyertown, PA; 335-361 g males and 195-224 g females) were exposed nose only via the inhalation route to Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid) for 4 hours at a concentration of 2.07 mg/L. Animals were then observed for 14 days.

LC_{50} Males > 2.07 mg/L
LC_{50} Females > 2.07 mg/L
LC_{50} Combined > 2.07 mg/L

All animals survived and gained weight. "There were no signs of gross toxicity, adverse pharmacologic effects or abnormal behavior." No gross abnormalities were noted at necropsy. The gravimetric chamber concentration was 2.07 mg/L and the mass median aerodynamic diameter was estimated to be 2.5 μm with a geometric standard deviation of 1.69.

Toxicity is based on 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 Conc. (mg/L)	Gravimetric Conc. (mg/L)	MMAD μm	GSD μm	Mortality/Number Tested		
				Males	Females	Combined
19.00	2.07	2.5	1.69	0/5	0/5	0/10

Test Atmosphere / Chamber Description:

Chamber Volume:	6.7 L
Airflow:	25.7 LPM
Temperature:	21-23°C
Relative Humidity:	62-68%
Time to Equilibrium:	1.2 min.

Test atmosphere concentration - Gravimetric samples were withdrawn at 6 intervals from the breathing zone of the animals. Filter papers were weighed before and after collection to determine the chamber concentration. This value was divided by the total volume of air sampled to determine the chamber concentration.

Particle size determination - Particle size was determined twice during the exposure. The MMAD and geometric standard deviation were determined graphically using the two-cycle logarithmic probit axes.

A. Mortality - None

B. Clinical observations - All animals gained weight. "There were no signs of gross toxicity, adverse pharmacologic effects or abnormal behavior."

C. Gross Necropsy - No gross abnormalities were noted.

D. Reviewer's Conclusions: We agree with the study author that the acute inhalation LC_{50} of Cutter Insect Repellent SS is greater than 2.07 mg/L in male and female rats.

Reviewer: Eugenia McAndrew **Date:** November 15, 2005
Risk Manager: 10

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

TEST MATERIAL: Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid)

CITATION: Merkel, D. Cutter Insect Repellent SS. Primary Eye Irritation Study in Rabbits. Product Safety Laboratories, Dayton, New Jersey. Laboratory Study Number 17642. September 1, 2005. MRID 46668007 Unpublished.

SPONSOR: Spectrum, Division of United Industries Corp., P.O. Box 142642, St. Louis, MO 63114-0642

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 46668007), 0.1 mL of Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid) was instilled into the conjunctival sac of the right eye of three young adult New Zealand albino rabbits (1 male and 2 female; Source: Robinson Services, Inc., Clemmons, NC). The left eye served as the control. Animals were then observed at 1, 24, 48, and 72 hours and at 4 and 7 days post-instillation. Irritation was scored by the method of Draize.

By 24 hours, corneal opacity, iritis and conjunctivitis were noted in all three eyes. The irritation decreased with time and all eyes were free of irritation by day 7.

In this study, formulation is moderately irritating to the eye. EPA Toxicity Category III.

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
Corneal Opacity	0/3	3/3	3/3	1/3	1/3	0/3
Iritis	3/3	3/3	3/3	0/3	0/3	0/3
Conjunctivae:						
Redness	3/3	3/3	3/3	1/3	0/3	0/3
Chemosis	3/3	0/3	0/3	0/3	0/3	0/3
Discharge	3/3	3/3	2/3	0/3	0/3	0/3

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

A. Observations - By 24 hours, corneal opacity, iritis and conjunctivitis were noted in all three eyes. The irritation decreased with time and all eyes were free of irritation by day 7.

B. Reviewer's Conclusions: We agree with the study author that Cutter Insect Repellent SS is moderately irritating to the eye.

Reviewer: Eugenia McAndrew **Date:** November 15, 2005
Risk Manager: 10

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

TEST MATERIAL: Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid)

CITATION: Merkel, D. Cutter Insect Repellent SS. Primary Skin Irritation Study in Rabbits. Product Safety Laboratories, Dayton, New Jersey. Laboratory Study Number 17643. September 1, 2005. MRID 46668008 Unpublished.

SPONSOR: Spectrum, Division of United Industries Corp., P.O. Box 142642, St. Louis, MO 63114-0642

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 46668008), three young adult New Zealand albino female rabbits (Source: Robinson Services, Clemmons, NC) were dermally exposed to Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid). Five-tenths of a milliliter of the test substance was applied to one 6 cm^2 intact dose site on each animal for a period of four hours. Test sites were covered with a gauze pad and wrapped with semi-occlusive tape. Animals were then observed at 1, 24, 48 and 72 hours after patch removal. Irritation was scored by the method of Draize.

Primary Dermal Irritation Index (PDII) = 0.5 One hour after patch removal, all sites exhibited very slight erythema. All animals were free of dermal irritation by 48 hours.

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

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:

INDIVIDUAL SKIN IRRITATION

ERYTHEMA/EDEMA

Animal No.	Sex	Hours After Patch Removal			
		1	24	48	72
14691	F	1/0	1/0	0/0	0/0
14692	F	1/0	1/0	0/0	0/0
14693	F	1/0	1/0	0/0	0/0

A. Observations - One hour after patch removal, all sites exhibited very slight erythema. All animals were free of dermal irritation by 48 hours.

B. Results - Primary Dermal Irritation Index (PDII) = 0.5

C. Reviewer's Conclusions - We agree with the study author that Cutter Insect Repellent SS is slightly irritating to the skin.

Reviewer: Eugenia McAndrew **Date:** November 15, 2005
Risk Manager: 10

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

TEST MATERIAL: Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid)

CITATION: Merkel, D. Cutter Insect Repellent SS. Dermal Sensitization Study in Guinea Pigs (Buehler Method). Product Safety Laboratories, Dayton, New Jersey. Laboratory Study Number 17644. September 1, 2005. MRID 46668009 Unpublished.

SPONSOR: Spectrum, Division of United Industries Corp., P.O. Box 142642, St. Louis, MO 63114-0642

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 46668009) with Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid) 30 Hartley albino male guinea pigs (Source: Elm Hill Breeding Labs, Chelmsford, MA; 336-411 g) were tested using the Buehler method. The procedures were validated using alpha-Hexylcinnamaldehyde (HCA) as the positive control substance.

Once each week for three weeks, 0.4 mL of undiluted test substance was applied to the left side of 20 test animals for a 6-hour exposure period for a total of three exposures. Readings were made 24 and 48 hours after each induction application. The animals were left untreated for two weeks. For the challenge 27 days after the first induction, 0.4 mL of a 50% w/w mixture of the test substance in acetone (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 treated with the 50% w/w mixture of the test substance in acetone at challenge only. Readings were made at 24 and 48 hours after the exposure period.

In this study, formulation is not a dermal sensitizer.

Very faint to faint erythema (0.5-1) was noted at all test animal sites during the induction phase. Following the challenge, very faint erythema (0.5) was observed at 5/20 test animal sites at 24 hours and at 2/20 sites at 48 hours. In the naive control group, very faint erythema (0.5) was noted at 3/10 sites at 24 hours and at one site at 48 hours. No positive responses were noted in either the test or naïve control animals.

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, 0.4 mL of undiluted test substance was applied to the left side of 20 test animals for a 6-hour exposure period for a total of three exposures. Readings were made 24 and 48 hours after each induction application. The animals were left untreated for two weeks. Ten naive control guinea pigs were treated with the 50% w/w mixture of the test substance in acetone at challenge only. Readings were made at 24 and 48 hours after the exposure period.

B. Challenge - Twenty-seven days after the first induction dose, 0.4 mL of a 50% w/w mixture of the test substance in acetone (the highest non-irritating concentration) was applied to a naive site on each test animal for a 6-hour challenge exposure. Readings were made at 24 and 48 hours after the exposure period.

C. Naive Controls - Ten naive control guinea pigs were treated with the 50% w/w mixture of the test substance in acetone at challenge only.

II. RESULTS and DISCUSSION:

A. Reactions and duration - Very faint to faint erythema (0.5-1) was noted at all test animal sites during the induction phase. Following the challenge, very faint erythema (0.5) was observed at 5/20 test animal sites at 24 hours and at 2/20 sites at 48 hours. In the naive control group, very faint erythema (0.5) was noted at 3/10 sites at 24 hours and at one site at 48 hours. No positive responses were noted in either the test or naïve control animals.

B. Positive control - The positive results of the HCA study validate the test system used in this study.

C. Reviewer's Conclusions: We agree with the study author that based on the findings and evaluation system used, Cutter Insect Repellent SS is not considered to be a contact sensitizer.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D322945
2. **PC CODE:** 070705
3. **CURRENT DATE:** 15/NOV/2005
4. **TEST MATERIAL:** Cutter Insect Repellent SS (Lot # KSC-0605-0511; 15 % Picaridin (KBR 3023); yellow liquid)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity / rat Product Safety Lab 17639/8-31-05	46668004	LD_{50} > 5000 mg/kg (males and females)	IV	A
Acute dermal toxicity / rat Product Safety Lab 17640/8-31-05	46668005	LD_{50} > 5000 mg/kg (males and females)	IV	A
Acute inhalation toxicity / rat Product Safety Lab 17641/9-1-05	46668006	LC_{50} > 2.07 mg/L (males and females)	IV	A
Primary eye irritation / rabbit Product Safety Lab 17642/9-1-05	46668007	Corneal opacity, iritis and conjunctivitis in 3/3 eyes at 24 hours resolving by day 7.	III	A
Primary dermal irritation / rabbit Product Safety Lab 17643/9-1-05	46668008	PDII = 0.5 Very slight erythema at 3/3 sites at one hour. No irritation at 48 hours.	IV	A
Dermal sensitization / guinea pig Product Safety Lab 17644/9-1-05	46668009	Not a sensitizer	--	A

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