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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

15/MAR/2005

MEMORANDUM

Subject: Name of Pesticide Product: Cutter Insect Repellent 15KP
EPA Reg. No. /File Symbol: 121-OR
DP Barcode: D313952
Decision No: 353650
PC Code: 070705

From: Eugenia McAndrew, Biologist EM MA
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
	Other Ingredients:	85.0
	Total:	100.00

ACTION REQUESTED: RM requests review of acute toxicity data for Cutter Insect Repellent 15KP, EPA File Symbol 121-OR.

BACKGROUND: Spectrum has submitted a six pack of acute toxicity studies to support the registration of Cutter Insect Repellent 15KP, EPA File Symbol 121-OR. The studies were conducted at Product Safety Labs, Dayton, New Jersey with assigned MRID numbers 464663-03 to -08.

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

The acute toxicity profile for Cutter Insect Repellent 15KP, EPA File Symbol 121-OR, is as follows:

acute oral toxicity	IV	Acceptable	MRID 46466303
acute dermal toxicity	IV	Acceptable	MRID 46466304
acute inhalation toxicity	IV	Acceptable	MRID 46466305
primary eye irritation	II	Acceptable	MRID 46466306
primary skin irritation	IV	Acceptable	MRID 46466307
dermal sensitization	Negative	Acceptable	MRID 46466308

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 #: 000121-00091

PRODUCT NAME: Cutter Insect Repellent 15KP

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

SIGNAL WORD: WARNING

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.

Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Wear protective eyewear (goggles, face shield, or safety glasses). 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
Risk Manager: 10

March 15, 2005

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

TEST MATERIAL: Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale yellow liquid)

CITATION: Merkel, D. Cutter Insect Repellent 20K Concentrate. Acute Oral Toxicity Up and Down Procedure in Rats. Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 15902. October 29, 2004. MRID 46466303. 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 46466303), three female Sprague-Dawley derived young adult albino rats (Age: 10 weeks; Source: Ace Animals, Inc., Boyertown, PA; 173-193 g) were given a single oral dose of Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale 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. Due to the absence of mortality in this animal, two additional female rats were tested at the same level. Animals were then observed for 14 days.

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

All animals survived and gained weight. Clinical signs noted included abnormal posture, hypoactivity, ocular discharge (red), facial staining and reduced fecal volume. All animals recovered from these symptoms by day 3. Gross necropsy revealed no gross abnormalities.

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:

Limit Test

Dosing Sequence	Animal No.	Dose level (mg/kg)	Short Term Outcome	14 Day Outcome
1	6764	5000	S	S
2	6842	5000	S	S
3	6843	5000	S	S

S = survival D = death

A. Mortality - None

B. Clinical observations - All animals survived and gained weight. Clinical signs noted included abnormal posture, hypoactivity, ocular discharge (red), facial staining and reduced fecal volume. All animals recovered from these symptoms by day 3.

C. Gross Necropsy - No gross abnormalities were observed.

D. Reviewer's Conclusions: We agree with the study author's conclusion that the oral LD_{50} for female rats is greater than 5000 mg/kg.

Reviewer: Eugenia McAndrew
Risk Manager: 10

March 15, 2005

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

TEST MATERIAL: Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale yellow liquid)

CITATION: Merkel, D. Cutter Insect Repellent 20K Concentrate. Acute Dermal Toxicity Study in Rats. Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 15903. November 2, 2004. MRID 46466304. 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 46466304), 5/sex of Sprague-Dawley derived young adult albino rats (Age: 8-9 weeks; Source: Ace Animals, Inc., Boyertown, PA; 242-265 g males and 170-189 g females) were dermally exposed to Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale yellow liquid). Five thousand mg/kg of the test substance was applied to a 2 inch by 3 inch dose area (approximately 10% of body surface). The test sites were covered with a gauze pad and wrapped with tape. After a 24 hour period, the wrappings 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 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. "There were no signs of gross toxicity, dermal irritation, adverse pharmacologic effects or abnormal behavior."

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

D. Reviewer's Conclusions: We agree with the study author's conclusion that the dermal LD_{50} for male and female rats is greater than 5000 mg/kg/bw.

Reviewer: Eugenia McAndrew
Risk Manager: 10

March 15, 2005

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

TEST MATERIAL: Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale yellow liquid)

CITATION: Merkel, D. Cutter Insect Repellent 20K Concentrate. Acute Inhalation Toxicity Study in Rats- Limit Test. Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 15904. October 29, 2004. MRID 46466305. 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 46466305), 5/sex Sprague-Dawley derived young adult albino rats (Age: 9-10 weeks; Source: Ace Animals, Inc., Boyertown, PA; 254-352 g males and 200-218 g females) were exposed nose only via the inhalation route to Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale yellow liquid) at a test concentration of 2.09 mg/L for a period of four hours. Animals were then observed for 14 days.

LC_{50} Males > 2.09 mg/L
LC_{50} Females > 2.09 mg/L
LC_{50} Combined > 2.09 mg/L

All animals survived and gained weight. The only clinical sign noted was hypoactivity in one animal. No gross abnormalities were noted at necropsy. The gravimetric chamber concentration was 2.09 mg/L. The mass median aerodynamic diameter was estimated to be 2.5 µm with a geometric standard deviation of 2.02.

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
26.19	2.09	2.5	2.02	0/5	0/5	0/10

Test Atmosphere / Chamber Description:

Chamber Volume:	**6.7 L**
Airflow:	**25.7 LPM**
Temperature:	**20-22°C**
Relative Humidity:	**60-700%**
Time to Equilibrium:	**1.2 min.**

A. **Mortality** - None

B. **Clinical observations** - All animals gained weight. The only clinical sign noted was hypoactivity in one animal.

C. **Gross Necropsy** - No gross abnormalities were noted at necropsy.

D. **Reviewer's Conclusions:** We agree with the study author's conclusion that the LC_{50} for male and female rats is greater than 2.09 mg/L.

Reviewer: Eugenia McAndrew
Risk Manager: 10

March 15, 2005

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

TEST MATERIAL: Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale yellow liquid)

CITATION: Merkel, D. Cutter Insect Repellent 20K Concentrate. Primary Eye Irritation Study in Rabbits. Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 15906. October 29, 2004. MRID 46466306. 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 46466306), 0.1 mL of Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale yellow liquid) was instilled into the conjunctival sac of the right eye of three female young adult New Zealand albino rabbits (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 on 4,7,10, 14 and 17 days post-instillation. Irritation was scored by the method of Draize. A fluorescein dye evaluation procedure was used at 24 hours to evaluate the extent of corneal damage or to verify reversal of effects.

Corneal opacity, iritis and conjunctivitis were noted in all three eyes at the one hour observation. The irritation decreased gradually with time. All eyes were free of irritation by day 17.

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

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:

Observations	Number "positive"/number tested								
	Hours				Days				
	1	24	48	72	4	7	10	14	17
Corneal Opacity	3/3	3/3	3/3	3/3	3/3	3/3	2/3	2/3	0/3
Iritis	3/3	2/3	3/3	3/3	3/3	2/3	2/3	0/3	0/3
Conjunctivae:									
Redness	3/3	3/3	3/3	3/3	3/3	2/3	1/3	0/3	0/3
Chemosis	3/3	3/3	2/3	2/3	2/3	0/3	0/3	0/3	0/3
Discharge	3/3	3/3	1/3	1/3	1/3	0/3	0/3	0/3	0/3

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

A. Observations: Corneal opacity, iritis and conjunctivitis were noted in all three eyes at the one hour observation. The irritation decreased gradually with time. All eyes were free of irritation by day 17.

B. Reviewer's Conclusions: We agree with study author's conclusion that the test substance is severely irritating to the eye.

Reviewer: Eugenia McAndrew
Risk Manager: 10

March 15, 2005

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

TEST MATERIAL: Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale yellow liquid)

CITATION: Merkel, D. Cutter Insect Repellent 20K Concentrate. Primary Skin Irritation Study in Rabbits. Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 15906. October 29, 2004. MRID 46466307. 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 46466307), three young adult New Zealand albino rabbits (1 male and 2 female; Source: Robinson Services, Inc., Clemmons, NC) were dermally exposed to 0.5 mL of Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale yellow liquid). The test substance was applied to one 6 cm^2 dose site on the dorsal area of each animal. Test sites were covered with a gauze pad and wrapped with semi-occlusive tape for a period of 4 hours. 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 a slight irritant. EPA Toxicity Category IV.

Primary Dermal Irritation Index (PDII) = 1.5 One hour after patch removal, well defined erythema and very slight edema were noted at all test sites. The irritation decreased with time. All sites were free of dermal irritation by 72 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, well defined erythema and very slight edema were noted at all test sites. The irritation decreased with time. All sites were free of dermal irritation by 72 hours.

B. Results - PDII - 1.5

C. **Reviewer's Conclusions** - We agree with the study author's conclusion that the test substance is slightly irritating to the skin.

Reviewer: Eugenia McAndrew
Risk Manager: 10

March 15, 2005

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

TEST MATERIAL: Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale yellow liquid)

CITATION: Merkel, D. Cutter Insect Repellent 20K Concentrate. Dermal Sensitization Study in Guinea Pigs (Buehler Method). Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 15907. October 29, 2004. MRID 46466308. 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 46466308) with Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale yellow liquid), 30 young adult male Hartley albino guinea pigs (Source: Elm Hill Breeding Labs, Chelmsford, MA; 302-380 g) were tested using the Buehler method. The procedures were validated using alpha-Hexylcinnamaldehyde, technical grade (85% 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 each animal for a 6-hour exposure period for a total of three exposures. 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. Ten naive control guinea pigs were also treated with the 50% w/w mixture of the test substance in acetone 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.

Very faint erythema (0.5) was noted at 16/20 test animal sites during the induction phase. Following the challenge, very faint erythema was noted at 10/20 test animal sites at 24 hours and at 3/20 sites at 48 hours. Very faint erythema was noted at 3/10 naive control animal sites at 24 hours only. No positive scores were observed in any of the animals at the challenge. The results of the HCA positive control study were appropriate to validate test procedures.

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 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. The animals rested for two weeks.

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.

C. Naive Controls - Ten guinea pigs were treated with 0.4 mL of a 50% w/w mixture of the test substance in acetone at challenge only.

II. RESULTS and DISCUSSION:

A. Reactions and duration - Very faint erythema (0.5) was noted at 16/20 test animal sites during the induction phase. Following the challenge, very faint erythema was noted at 10/20 test animal sites at 24 hours and at 3/20 sites at 48 hours. Very faint erythema was noted at 3/10 naive control animal sites at 24 hours only. No positive scores were observed in any of the animals at the challenge.

B. Positive control - Results were appropriate to validate test procedures.

C. Reviewer's Conclusions: We agree with the study author's conclusion that the test substance is not a dermal sensitizer.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D313952
2. **PC CODE:** 070705
3. **CURRENT DATE:** 15/MAR/2005
4. **TEST MATERIAL:** Cutter Insect Repellent 20K Concentrate (Lot # KSC-0804-0415; 22% picaridin; pale yellow liquid)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat Product Safety Labs 15902/10-29-04	46466303	LD_{50} females > 5000 mg/kg	IV	A
Acute dermal toxicity/rat Product Safety Labs 15903/11-2-04	46466304	LD_{50} > 5000 mg/kg (males, females combined)	IV	A
Acute inhalation toxicity/rat Product Safety Labs 15904/10-29-04	46466305	LC_{50} > 2.09 mg/L (males, females combined)	IV	A
Primary eye irritation/rabbit Product Safety Labs 15905/10-29-04	46466306	Corneal opacity, iritis and conjunctivitis in 3/3 eyes resolving by day 17.	II	A
Primary dermal irritation/rabbit Product Safety Labs 15906/10-29-04	46466307	PDII = 1.5 No irritation at 72 hours	IV	A
Dermal sensitization/guinea pig Product Safety Labs 15907/10-29-04	46466308	Not a sensitizer	–	A

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