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

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: April 30, 2004

MEMORANDUM

Subject: EPA File Symbol: 121-IO CUTTER INSECT REPELLENT 7K
DP Barcode: D301343
Decision No.: 339450
PC Code: 070705 PICARIDIN

From: Byron T. Backus, Ph.D.
Technical Review Branch
Registration Division (7505C)

Byron T. Backus 4/30/2004

To: Joseph Tavano/Linda Arrington, RM 10
Insecticide-Rodenticide Branch
Registration Division (7505C)

Applicant: SPECTRUM - A DIVISION OF UNITED INDUSTRIES CORP.

FORMULATION DECLARATION FROM LABEL:

Active Ingredient(s):	% by wt.
Picaridin (CAS No. 119515-38-7)	7.0%
Other Ingredients:	93.0%
Total:	100.00%

ACTION REQUESTED:

The Product Manager requests:

"Review label and data for new product. MRIDs 46184803 through 08."

BACKGROUND:

This package includes an acute oral LD_{50} study (rat, up-and-down procedure; MRID 46184803); acute dermal LD_{50} study (rat; MRID 46184804); inhalation LC_{50} study (rat; 46184805) primary eye irritation study (rabbit; 46184806); primary dermal irritation study (rabbit; 46184807) and a dermal sensitization study (guinea pig; 46184808). All studies were conducted at Product Safety Labs (Dayton, NJ 08810). With the exception of the primary eye study, all studies were conducted on Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin (not Picardin) and 93% other ingredients. The eye irritation study was conducted on Cutter Insect Repellent-7K - Alternate Formula 2 - Lot #KSC-0903-0211, a pale yellow liquid, pH 7.5, containing 7% Picaridin. According to the cover letter (dated January 26, 2004) from the registrant: "After the acute toxicity studies were conducted on the Original prototype formula, we found the results of the Primary Eye Irritation Study unacceptable. We reformulated the product to contain... [material deleted for reasons of confidentiality] and conducted a new Primary Eye Irritation study, the results of which were acceptable. We feel that if the other Acute Toxicity Studies were conducted on Alternate II, the results would be the same or less toxic than the original formula; therefore we are requesting that these studies be "bridged" to the Alternate II formula, which is the formula we are proposing for registration..."

RECOMMENDATIONS:

1. After an examination of the material received, TRB concludes that the five studies conducted on the original formulation are acceptable as supporting data for the Alternate II formulation.

2. All six acute toxicity studies have been reviewed and classified as acceptable.

3. Based on the results of the acute toxicity studies, the following would be the acute toxicity profile for EPA File Symbol 121-IO Cutter Insect Repellent 7K:

Study Type	Tox. Cat.	Classification & MRID #
Acute Oral LD_{50} (rat)	IV	Acceptable (#46184803)
Acute Dermal LD_{50} (rat)	IV	Acceptable (#46184804)
Acute Inhalation LC_{50} (rat)	IV	Acceptable (#46184805)
Primary Eye Irritation (rabbit)	III	Acceptable (#46184806)
Primary Dermal Irritation (rabbit)	IV	Acceptable (#46184807)
Dermal Sensitization (guinea pig)	No	Acceptable (#46184808)

4. Based on the acute toxicity profile and proposed uses, the following would be the precautionary labeling for this product, as obtained from the Label Review System:

PRODUCT ID #: **000121-00089**

PRODUCT NAME: CUTTER INSECT REPELLENT 7K

PRECAUTIONARY STATEMENTS

SIGNAL WORD: **CAUTION**

Hazards to Humans and Domestic Animals:

Causes moderate eye irritation. Avoid contact with eyes or clothing. Wear protective eyewear. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Wear: Long-sleeved shirt and long pants, Socks, Shoes, and gloves.

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: Byron T. Backus, Ph.D.
Risk Manager (EPA): 10

Date: April 23, 2004

STUDY TYPE: Acute Oral Toxicity - Sprague-Dawley derived albino Rat; OPPTS 870.1100; OECD 425

TEST MATERIAL (% a.i.): Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin (not Picardin) and 93% other ingredients.

SYNONYMS: PC Code 070705, 1-Piperidinecarboxylic acid, 2-(2-hydroxyethyl)-, 1-methylpropylester (CAS No. 119515-38-7)

CITATION: Moore, G.E. (2003) Cutter Insect Repellent - 7K: Acute Oral Toxicity Up and Down Procedure in Rats. Product Safety Labs, Dayton, NJ 08810. Lab Study No. 13745. Study Completion Date: 8 September 2003. MRID 46184803. Unpublished,

SPONSOR: SPECTRUM, DIV. OF UNITED INDUSTRIES CORP., St. Louis, MO

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46184803), which was essentially a limit test at 5000 mg/kg, one fasted (overnight) female rat was orally gavaged with 5000 mg/kg Cutter Insect Repellent 7K (a pale yellow liquid with a specific gravity of 0.938 g/mL; active ingredient: 7% Picaridin, CAS No. 119515-38-7). When this female survived, two additional fasted (overnight) female rats were also orally dosed at 5000 mg/kg. The test animals were Sprague-Dawley derived albino rats, 10 weeks old, 175-186 g when dosed, from Ace Animals Inc., Boyertown, PA.

On the day of dosage rats were observed several times for clinical signs of toxicity and mortality and then at least once daily for the remainder of the 14-day observation period. Individual body weights were recorded just prior to dosing (Day 0) and on days 7 and 14.

All rats survived. Symptoms included hypoactivity, piloerection, ano-genital staining and reduced fecal volume. All animals recovered by day 2 (dosing was on day 0). All gained weight in the period from day 0 to day 7 and again from day 7 to day 14.

At post-sacrifice necropsy, there were no observed abnormalities in any of the rats.

Estimated Oral LD_{50} Females > 5000 mg/kg.

Cutter Insect Repellent 7K (a pale yellow liquid with a specific gravity of 0.938 g/mL; active ingredient: 7% Picaridin, CAS No. 119515-38-7) is in EPA Toxicity Category IV based on the observed LD_{50} (>5000 mg/kg) in female rats.

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 (p. 3), Quality Assurance (p. 4), and **[No] Data** Confidentiality (p. 2) statements were provided.

RESULTS and DISCUSSION:

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

Date/Time: Friday, April 23, 2004, 3:58:32 PM
Data file name: cutter7k.dat
Last modified: 4/23/04 3:58:34 PM

Test/Substance: Cutter Insect Repellent 7K
Test type: Main Test
Limit dose (mg/kg): 2000
Assumed LD50 (mg/kg): 5000
Assumed sigma (mg/kg): 0.5

Recommended dose progression: 2000, 500, 158, 50, 15.8, 5, 1.58

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	9354	5000	O	O
2	9387	5000	O	O
3	9388	5000	O	O

(X = Died, O = Survived)

Dose Recommendation: The main test is complete.

WARNING:
Please review the data for accuracy.
At least one dose is much greater than the limit dose.

Stopping criteria met: 3 at Limit Dose.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
5000	3	0	3
All Doses	3	0	3

Statistical Estimate based on long term outcomes:

The LD50 is greater than 5000 mg/kg.

A. Mortality - None, as noted in table.

B. Clinical observations - Symptoms included hypoactivity, piloerection, ano-genital staining and reduced fecal volume. All animals recovered by day 2 (dosing was on day 0). All gained weight in the period from day 0 to day 7 and again from day 7 to day 14.

C. Gross Necropsy - At post-sacrifice necropsy, no observed gross abnormalities were observed in any of the rats.

D. Reviewer's Conclusions: The study is acceptable. The estimated female oral LD_{50} is > 5000 mg/kg, based on the lack of mortality in 3/3 rats orally dosed at that level. The test material is in toxicity category IV in terms of oral toxicity.

E. Deficiencies - None

Reviewer: Byron T. Backus, Ph.D.
Product Manager (EPA): 10

Date: April 27, 2004

STUDY TYPE: Acute Dermal Toxicity - Sprague-Dawley derived albino rats - OPPTS 870.1200; OECD 402

TEST MATERIAL (% a.i.): Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin (not Picardin) and 93% other ingredients.

SYNONYMS: PC Code 070705, 1-Piperidinecarboxylic acid, 2-(2-hydroxyethyl)-, 1-methylpropylester (CAS No. 119515-38-7)

CITATION: Moore, G.E. (2003) Cutter Insect Repellent - 7K: Acute Dermal Toxicity in Rats. Product Safety Labs, Dayton, NJ 08810. Lab Study No. 13746. Study Completion Date: 4 September 2003. MRID 46184804. Unpublished.

SPONSOR: SPECTRUM, DIV. OF UNITED INDUSTRIES CORP., St. Louis, MO

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID #46184804), a group (5M & 5F) of Sprague-Dawley derived albino rats (source: Ace Animals, Inc., Boyertown, PA; age: young adults 9-10 weeks old; Males: 317-334 g; Females: 216-235 g) were dermally exposed for 24 hrs to 5000 mg/kg undiluted Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin and 93% other ingredients. Test sites were covered with gauze and tape during the exposure period.

Rats were observed several times following application on day 0 and at least once daily during the 14-day observation period. Individual body weights were recorded just prior to dosing (day 0) and on days 7 and 14.

There was no mortality and there were no signs of systemic toxicity. No dermal irritation was observed. All rats gained weight in the period from day 0 to 7 and again from day 7 to 14.

No gross abnormalities were observed at post-sacrifice necropsy.

Dermal LD_{50} Males > 5000 mg/kg (0/5 died)
Females > 5000 mg/kg (0/5 died)
Combined > 5000 mg/kg (0/10 died)

Based on the LD_{50} > 5000 mg/kg Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin and 93% other ingredients is in EPA Toxicity Category IV in terms of dermal toxicity.

This acute dermal study is classified as 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 Compliance (p. 3), Quality Assurance (p. 4), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS and DISCUSSION:

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

Statistics - Not necessary to compute the dermal LD_{50}.

A. Mortality - None, as noted in the table above.

B. Clinical observations - There were no signs of systemic toxicity. No dermal irritation was observed. All rats gained weight in the period from day 0 to 7 and again from day 7 to 14.

C. Gross Necropsy - No gross abnormalities were observed at post-sacrifice necropsy.

D. Reviewer's Conclusions: The study is acceptable. Based on the LD_{50} > 5000 mg/kg Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin and 93% other ingredients is in EPA Toxicity Category IV in terms of dermal toxicity.

E. Deficiencies - None

Reviewer: Byron T. Backus, Ph.D. **Date:** April 27, 2004
Product Manager (EPA): 10

STUDY TYPE: Acute Inhalation Toxicity - Sprague-Dawley derived albino rats; OPPTS 870.1200; OECD 402

TEST MATERIAL (% a.i.): Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin (not Picardin) and 93% other ingredients.

SYNONYMS: PC Code 070705, 1-Piperidinecarboxylic acid, 2-(2-hydroxyethyl)-, 1-methylpropylester (CAS No. 119515-38-7)

CITATION: Moore, G.E. (2003) Cutter Insect Repellent - 7K: Acute Inhalation Toxicity in Rats. Product Safety Labs, Dayton, NJ 08810. Lab Study No. 13747. Study Completion Date: 8 September 2003. MRID 46184805. Unpublished.

SPONSOR: SPECTRUM, DIV. OF UNITED INDUSTRIES CORP., St. Louis, MO

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 46184805), a group (5/sex) of Sprague-Dawley derived albino rats (source: Ace Animals, Inc., Boyertown, PA; age: young adults 9-10 weeks old; Males: 277-322 g; Females: 182-213 g) were exposed (4 hrs: whole body) to aerosolized Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin and 93% other ingredients. The concentration of test material was measured gravimetrically 6 times during the exposure period. The mean gravimetric concentration was 2.09 mg/L and the nominal concentration was 32.43 mg/L. The MMAD (measured twice during the exposure) was 2.5 µm with a mean GSD of 1.92. Rats were observed for 14 days after exposure.

There was no mortality. Observed effects during the 4-hr exposure period included ocular and nasal discharge, hunched posture and hypoactivity. Following removal from the exposure chamber all rats recovered and were active and healthy during the 14-day observation period. All rats gained weight from day 0 to 7 and again from day 7 to 14. No gross abnormalities were observed at post-sacrifice necropsy.

LC_{50} Males > 2.09 mg/L (0/5M died following exposure to this concentration).
LC_{50} Females > 2.09 mg/L (0/5F died following exposure to this concentration).
LC_{50} Combined > 2.09 mg/L (0/10 died).

Toxicity based on male, female & combined LC_{50} (>2.09 mg/L) is 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 Compliance (p. 3), Quality Assurance (p. 4), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS and DISCUSSION:

Nominal Conc. (mg/L)	Actual TWA Mean Conc. (Gravimetric; mg/L)	MMAD µm	GSD	Mortality/Number Tested		
				Males	Females	Combined
32.43	2.09	2.5	1.92	0/5	0/5	0/5

Test Atmosphere / Chamber Description:

Chamber Volume:	**150 L**
Mean Airflow:	**45.7 LPM**
Temperature Range:	**22 - 23°C**
Relative Humidity Range:	**58 - 92%**
Time to 99% Equilibrium:	**15.1 minutes**

Test atmosphere concentration: samples were taken for gravimetric analyses six times during the exposure (from 00:30 to 04:00).

Particle size determination: From p. 9: "An eight-stage Andersen cascade impactor was used to assess the particle size distribution of the test atmosphere. Samples were withdrawn from the breathing zone of the animals at two intervals."

Statistics - It was not necessary to use a statistical method to calculate an LC_{50} value. The MMAD and GSD were determined graphically using two-cycle logarithmic probit axes.

A. **Mortality** - as noted in the table above there was none.

B. **Clinical observations** - Observed effects during the 4-hr exposure period included ocular and nasal discharge, hunched posture and hypoactivity. Following removal from the exposure chamber all rats recovered and were active and healthy during the 14-day observation period. All rats gained weight from day 0 to 7 and again from day 7 to 14.

C. **Gross Necropsy** - No gross abnormalities were observed at post-sacrifice necropsy.

D. **Reviewer's Conclusions:** The results of the study (no mortalities following 4-hr exposure to an analytically determined concentration of 2.09 mg/L, indicating an LC_{50} value greater than this) adequately define an EPA Toxicity Category IV classification for Cutter Insect Repellent-7K, a pale yellow liquid with a specific gravity of 0.938 g/mL containing 7% Picardin as sole active ingredient.

Reviewer: Byron T. Backus, Ph.D.
Product Manager (EPA): 10

Date: April 28, 2004

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

TEST MATERIAL (% a.i.): Cutter Insect Repellent-7K - Alternate Formula 2 - Lot #KSC-0903-0211, a pale yellow liquid, pH 7.5, containing 7% Picaridin (not Picardin) and 93% other ingredients.

SYNONYMS: PC Code 070705, 1-Piperidinecarboxylic acid, 2-(2-hydroxyethyl)-, 1-methylpropylester (CAS No. 119515-38-7)

CITATION: Merkel, D.J. (2003) Cutter Insect Repellent 7K - Alternate Formula 2: Primary Eye Irritation Study in Rabbits. Product Safety Labs, Dayton, NJ 08810. Lab Study No. 14263. Study Completion Date: 15 December 2003. MRID 46184806. Unpublished.

SPONSOR: SPECTRUM, DIV. OF UNITED INDUSTRIES CORP., St. Louis, MO

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 46184806), 0.1 mL of undiluted Cutter Insect Repellent-7K - Alternate Formula 2 - Lot #KSC-0903-0211, a pale yellow liquid, pH 7.5, containing 7% Picaridin (CAS No. 11915-38-7) was instilled into the conjunctival sac of one eye of each of 3 adult (1M & 2F) New Zealand white rabbits (source: Davidson's Mill Farm, South Brunswick, NJ; young adult; weights: not reported). Rabbits were observed for 7 days. Irritation was scored (according to Draize) at 1, 24, 48 and 72 hrs and at 4 and 7 days.

2/3 treated eyes were positive for corneal opacity at 1-4 days, and 1/3 was positive for iritis during the same period. All eyes were positive for redness and chemosis at 1 hr. All 3 eyes were positive for conjunctival irritation (redness, and, for one eye, also chemosis) through 72 hours. One eye was still positive for redness and chemosis on day 4. All eyes had completely cleared (all scores zero) by day 7.

In this study, Cutter Insect Repellent-7K - Alternate Formula 2 - Lot #KSC-0903-0211, a pale yellow liquid, pH 7.5, containing 7% Picaridin is in EPA Toxicity Category III based on the occurrence of irritation in all 3 eyes (with corneal opacity in 2/3 eyes), with clearing by day 7.

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 Compliance (p. 3), Quality Assurance (p. 4), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS AND DISCUSSION:

Observations	Number "positive"/number tested					
	1 hr	24 hrs	48 hrs	72 hrs	4 days	7 days
Corneal Opacity	0/3	2/3	2/3	2/3	2/3	0/3
Iritis	0/3	1/3	1/3	1/3	1/3	0/3
Conjunctivae:						
Redness[1]	3/3	3/3	3/3	3/3	1/3	0/3
Chemosis[1]	3/3	1/3	1/3	1/3	1/3	0/3
Discharge[1]	3/3	2/3	1/3	1/3	1/3	0/3

[1]Score of 2 or more considered positive
Fluorescein staining was used at all readings from 24 hrs after installation.

A. **Observations** - No systemic effects were observed. 2/3 treated eyes were positive for corneal opacity at 1-4 days, and 1/3 was positive for iritis during the same period. All eyes were positive for redness and chemosis at 1 hr. All 3 eyes were positive for conjunctival irritation (redness, and, for one eye, also chemosis) through 72 hours. One eye was still positive for redness and chemosis on day 4. All eyes had completely cleared (all scores zero) by day 7.

B. **Reviewer's Conclusions:** The study adequately defines a Toxicity Category III hazard potential in terms of eye exposure for undiluted Cutter Insect Repellent-7K - Alternate Formula 2 - Lot #KSC-0903-0211, a pale yellow liquid, pH 7.5, containing 7% Picaridin (CAS No. 11915-38-7).

C. **Deficiencies** - None

Reviewer: Byron T. Backus, Ph.D. **Date:** April 28, 2004
Product Manager (EPA): 07

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

TEST MATERIAL (% a.i.): Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin (not Picardin) and 93% other ingredients.

SYNONYMS: PC Code 070705, 1-Piperidinecarboxylic acid, 2-(2-hydroxyethyl)-, 1-methylpropylester (CAS No. 119515-38-7)

CITATION: Moore, G.E. (2003) Cutter Insect Repellent 7K: Primary Skin Irritation Study in Rabbits. Product Safety Labs, Dayton, NJ 08810. Lab Study No. 13749. Study Completion Date: 4 September 2003. MRID 46184807. Unpublished.

SPONSOR: SPECTRUM, DIV. OF UNITED INDUSTRIES CORP., St. Louis, MO

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 46184807), 0.5 mL undiluted Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin, was applied to one 6 cm^2 intact dose site on each of 3 young adult (2M & 1F) New Zealand albino rabbits (source: Davidson's Mill Farm, South Brunswick, NJ; weights: not reported). After application, the test site was covered with a 1 inch x 1 inch 4-ply gauze pad; the pad and entire trunk of each rabbit were then wrapped with semi-occlusive Micropore tape, and an Elizabethan collar was applied to each animal.

After 4 hours, the pads and collars were removed and any residual test substance was cleaned from the test site. The test sites were scored (Draize) at 1, 24, 48 and 72 hrs following patch removal.

All 3 sites scored "1" for erythema and "0" for edema at 1 hr; all 3 sites scored "0" for both erythema and edema at 24, 48 and 72 hours. The PII (average of 1, 24, 48 and 72-hour scores) = 0.25.

In this study, Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin, is in EPA Toxicity Category IV for dermal irritation effects, with the only effect slight (grade "1") erythema at 1 hour and all other scores zero.

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 Compliance (p. 3), Quality Assurance (p. 4), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS and DISCUSSION:

A. Observations - All 3 sites scored "1" for erythema and "0" for edema at 1 hr; all 3 sites scored "0" for both erythema and edema at 24, 48 and 72 hours.

B. Results - The PII (average of 1, 24, 48 and 72-hour scores) = 0.25.

C. Reviewer's Conclusions - The study adequately demonstrates a Toxicity Category IV hazard potential in terms of dermal irritation for undiluted Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin.

D. Deficiencies - None

Reviewer: Byron T. Backus, Ph.D. **Date:** April 29, 2004
Product Manager (EPA): 10

STUDY TYPE: Dermal Sensitization - Guinea Pig; OPPTS 870.2600; OECD 406, 429

TEST MATERIAL (% a.i.): Cutter Insect Repellent-7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin (not Picardin) and 93% other ingredients.

SYNONYMS: PC Code 070705, 1-Piperidinecarboxylic acid, 2-(2-hydroxyethyl)-, 1-methylpropylester (CAS No. 119515-38-7)

CITATION: Moore, G.E. (2003) Cutter Insect Repellent 7K: Dermal Sensitization Study in Guinea Pigs (Buehler Method). Product Safety Labs, Dayton, NJ 08810. Lab Study No. 13750. Study Completion Date: 8 September 2003. MRID 46184808. Unpublished.

SPONSOR: SPECTRUM, DIV. OF UNITED INDUSTRIES CORP., St. Louis, MO

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 46184808) with Cutter Insect Repellent-7K (Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin), 20 female (304-359 g at the beginning of the study) Hartley albino guinea pigs (source: Elm Hill Breeding Labs, Chelmsford, MA), were tested using a Buehler design. Based on results from a preliminary dermal range-finding study, each guinea pig was topically treated (left side) with 0.4 mL of undiluted Cutter Insect Repellent-7K once each week for 3 consecutive weeks. Exposures used an occlusive 25 mm Hill Top Chamber, and each was for 6 hours. Application sites were scored at 24 and 48 hours following exposure.

Twenty-seven days after the first induction dose, 0.4 mL of undiluted Cutter Insect Repellent-7K was applied to a naive site on the right side of each guinea pig as a challenge. Also, 10 previously unexposed (negative control) guinea pigs were similarly challenged. Exposure was for 6 hours and the sites were evaluated (scored) for a sensitization response at 24 and 48 hours after the challenge application.

During the induction period the maximum irritation observed at 24 and/or 48 hours was "0.5" and this was also the maximum irritation (seen in 6/20 previously induced and 4/10 negative control guinea pigs at 24 hours, and in 2/20 previously induced and 0/10 negative control guinea pigs at 48 hours) following challenge. All other scores were zero.

In this study **Cutter Insect Repellent-7K (Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin), is not a dermal sensitizer.**

The report includes a positive control study utilizing technical grade (85%)

Hexylcinnamaldehyde (HCA). At challenge, 7/10 induced and 0/5 naive controls showed a positive response (grade 1 erythema at 24 and/or 48 hours). The results are acceptable. This positive control study was completed on March 27, 2003, while the dates of testing for the study on Cutter Insect Repellent-7K were June 9 - July 17, 2003.

This study is classified as acceptable. It does satisfy the guideline requirement for a dermal sensitization study (OPPTS 870.2600; OECD 406, 429) in the Guinea pig.

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 4), and [No] Data Confidentiality (p. 2) statements were provided.

I. PROCEDURE

A. Induction - Following a range-finding study, each guinea pig from a group of 20F Hartley albinos was topically treated (left side) with 0.4 mL of undiluted Cutter Insect Repellent-7K once each week for 3 consecutive weeks. Exposures used an occlusive 25 mm Hill Top Chamber, and each was for 6 hours. Application sites were scored at 24 and 48 hours following exposure.

B. Challenge - Twenty-seven days after the first induction dose, 0.4 mL of undiluted Cutter Insect Repellent-7K was applied to a naive site on the right side of each guinea pig as a challenge. Exposure was for 6 hours and the sites were evaluated (scored) for a sensitization response at 24 and 48 hours after the challenge application.

C. Naive Controls - At the time the 20 previously induced guinea pigs were challenged, 10 previously unexposed (negative control) guinea pigs were similarly challenged.

II. RESULTS and DISCUSSION:

A. Reactions and duration - During the induction period the maximum irritation observed at 24 and/or 48 hours was "0.5" and this was also the maximum irritation (seen in 6/20 previously induced and 4/10 negative control guinea pigs at 24 hours, and in 2/20 previously induced and 0/10 negative control guinea pigs at 48 hours) following challenge. All other scores were zero.

B. Positive control - The report includes a positive control study utilizing technical grade (85%) Hexylcinnamaldehyde (HCA). At challenge, 7/10 induced and 0/5 naive controls showed a positive response (grade 1 erythema at 24 and/or 48 hours). The results are acceptable. This positive control study was completed on March 27, 2003, while the dates of testing for the study on Cutter Insect Repellent-7K were June 9 - July 17, 2003.

C. Reviewer's Conclusions: In this study there is no indication that Cutter Insect Repellent-7K (Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin) is a dermal sensitizer.

D. Deficiencies - None

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D301343
2. **PC CODES:** 070705 Picaridin
3. **CURRENT DATE:** April 29, 2004
4. **TEST MATERIAL:** EPA File Symbol 121-IO CUTTER INSECT REPELLENT 7K, Lot #KSC-0503-0199, a pale yellow liquid with a specific gravity of 0.938 g/mL, pH 6.0, containing 7% Picaridin (not Picardin) and 93% other ingredients (used for all studies except the eye irritation study in MRID 46184806).
   Cutter Insect Repellent 7K - Alternate Formula 2 - Lot #KSC-0903-0211, a pale yellow liquid, pH 7.5, containing 7% Picaridin (used in the eye irritation study in MRID 46184806).
   Note: the CAS No. for the active ingredient Picaridin is 119515-38-7.

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/Product Safety Labs, Dayton, NJ 08810/ Lab Study No. 13745/8-SEP-2003	46184803	LD_{50}>5000 mg/kg. Essentially a limit test; 3 Sprague-Dawley derived female rats were dosed at 5000 mg/kg. All survived. Symptoms: hypoactivity, piloerection, ano-genital staining and reduced fecal volume. All rats were normal by day 2 (dosing on day 0). All gained weight from day 0 to 7 and again from 7-14. No observed abnormalities at post-sacrifice necropsy.	IV	A
Acute dermal toxicity/rat/Product Safety Labs, Dayton, NJ 08810/ Lab Study No. 13746/4-SEP-2003	46184804	LD_{50} > 5000 mg/kg. 5M & 5F Sprague-Dawley derived albino rats were dermally exposed to 5000 mg/kg for 24 hrs; no mortality & no signs of systemic toxicity. All gained wt day 0-7 and 7-14. No observed abnormalities at post-sacrifice necropsy.	IV	A
Acute inhalation toxicity/rat/ Product Safety Labs, Dayton, NJ 08810/ Lab.Study No. 13747/8-SEP-2003	46184805	LC_{50}>2.09 mg/L.. Whole body exposure. 0/5M & 0/5F died after exposure to gravimetrically determined concentration of 2.09 mg/L; MMAD = 2.5 µm with an average GSD of 1.92. During exposure there was ocular and nasal discharge, hunched posture & hypoactivity. Rats recovered and were healthy after removal from exposure chamber. All gained wt day 0-7 & 7-14. No gross abnormalities observed at post-sacrifice necropsy.	IV	A

Primary eye irritation/rabbit/ Product Safety Labs, Dayton, NJ 08810/ Lab Study No. 14263/15-DEC-2003	46184806	2/3 eyes positive for corneal opacity at 1 to 4 days; 1/3 positive for iritis during the same period. All 3 eyes were positive for conjunctival irritation (redness, and, for one eye, chemosis) from 24 to 72 hrs. One eye still positive for redness & chemosis on day 4. All completely clear (all scores zero) by day 7.	III	A
Primary dermal irritation/rabbit/ Product Safety Labs, Dayton, NJ 08810/ Lab Study No. 13749/4-SEP-2003	46184807	3 rabbits used; 3/3 scored 1 at 1 hr for erythema and 0 for edema. At 24, 48 & 72 hrs all scores were 0 for erythema & edema. PII = 0.25.	IV	A
Dermal sensitization/guinea pig/ Product Safety Labs, Dayton, NJ 08810/ Lab Study No. 13750/4-SEP-2003	46184808	Buehler Test. 3 induction treatments (0.4 mL undiluted Cutter Insect Repellent 7K for six hours) once a week for 3 weeks. At challenge with undiluted Cutter Insect Repellent 7K maximum score was 0.5 seen in 6/20 previously induced and 4/10 negative controls at 24 hrs and in 2/20 previously induced and 0/10 negative controls at 48 hrs. Positive control study with technical (85%) HCA acceptable, and was conducted within 6 months of study on Cutter Insect Repellent 7K.	No	A

Core Grade Key: **A =Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated**