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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

14/JUNE/2005

MEMORANDUM

Subject:	Name of Pesticide Product:	Avon Skin-So-Soft SSS Bug Guard Frontier Insect Repellent Spray Outdoor Cool
	EPA Reg. No. /File Symbol:	806-EO
	DP Barcode:	D318054
	Decision No:	352099
	PC Code:	070705
From:	Eugenia McAndrew, Biologist Technical Review Branch Registration Division (7505C)	EM 6/16/05
To:	Richard Gebken, RM Team 10 Insecticide Branch Registration Division (7505C)	
Applicant:	Avon Products, Inc. 1251 Avenue of the Americas New York, NY 10020	

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
070705	Picaridin	10.0
	Other Ingredients:	90.0
	Total:	100.0

ACTION REQUESTED: "Please review the attached acute toxicity studies (MRIDs 46432401-08)."

BACKGROUND: Avon Products, Inc. has submitted a six pack of acute toxicity studies to support the registration of Avon Skin-So-Soft SSS Bug Guard Frontier Insect Repellent Spray Outdoor Cool, EPA File Symbol 806-EO. The studies were conducted at Bayer Healthcare AG, Wuppertal, Germany with assigned MRID numbers 465509-01 to -06.

The sponsor of the studies is LANXESS, Deutschland GmbH, 51639 Leverkusen, Germany. In a letter dated May 6, 2005, LANXESS grants permission to Avon to use the data relating to KBR-3023 Technical to support registration of Avon products.

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

The acute toxicity profile for Avon Skin-So-Soft SSS Bug Guard Frontier Insect Repellent Spray Outdoor Cool, EPA File Symbol 806-EO, is as follows:

acute oral toxicity	III	Acceptable	MRID 46550901
acute dermal toxicity	III	Acceptable	MRID 46550902
acute inhalation toxicity	IV	Acceptable	MRID 46550903
primary eye irritation	III	Acceptable	MRID 46550904
primary skin irritation	IV	Acceptable	MRID 46550905
dermal sensitization	Negative	Acceptable	MRID 46550906

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 #: 000806-00029

PRODUCT NAME: Avon Skin-So-Soft SSS Bug Guard Frontier Insect Repellent Spray Outdoor Cool

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

SIGNAL WORD: CAUTION

Harmful if absorbed through skin. Harmful if swallowed. Causes moderate eye irritation. 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.

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 swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

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 June 14, 2005
Risk Manager: 10

STUDY TYPE: Acute Oral Toxicity - S-D Rat; OPPTS 870.1100; OECD 423

TEST MATERIAL: Formulation AV (KBR-3023 Formulation; Batch No. SDTH; 13.34% picaridin; clear liquid)

CITATION: Schungel, M. Formulation AV. Acute toxicity in the rat after oral administration. Bayer Healthcare AG, Wuppertal, Germany. Laboratory Report Number AT01886. Study No. T4074931. January 10, 2005. MRID 46550901. Unpublished.

SPONSOR: LANXESS Deutschland GmbH, 51369 Leverkusen, Germany

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46550901), two groups of three female Wistar HsdCpb:Wu rats (Age: 10-14 weeks; Source: Harlan/Winkelmann GmbH, Borchen, Germany; 159-171 g) were given a single oral dose of Formulation AV (KBR-3023 Formulation; Batch No. SDTH; 13.34% picaridin; clear liquid). The test substance was formulated in tap water. A fixed dose of 2000 mg/kg of the test substance was administered to the first group of three female rats by oral gavage. Due to the absence of mortality in these animals, a second group of three female rats were tested at the same level according to the rules of the acute toxic class method. Animals were then observed for 14 days.

Oral LD_{50} Females > 2000 mg/kg bw

All animals survived and gained weight. Clinical signs noted included decreased motility and uncoordinated gait. All animals recovered from these symptoms by day 2. Gross necropsy revealed no particular findings.

Toxicity based on the lack of deaths at the fixed dose of 2000 mg/kg. EPA Toxicity Category III.

This acute oral study is classified as acceptable. It does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 423) 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:

Dosage (mg/kg bw)	Number of Deaths/Number Tested		
	Males	Females	Combined
2000 1st group	--	0/3	--
2000 2nd group	--	0/3	--

Statistics - The LD_{50} value was estimated according to OECD Guideline for Testing of Chemicals No. 423 - "Acute Oral Toxicity - Acute Toxic Class Method" adopted December 17, 2001.

A. Mortality - None

B. Clinical observations - All animals survived and gained weight. Clinical signs noted included decreased motility and uncoordinated gait. All animals recovered from these symptoms by day 2.

C. Gross Necropsy - No particular findings were revealed.

D. Reviewer's Conclusions: We agree with the study author's conclusion that the oral LD_{50} for Formulation AV in female rats is greater than 2000 mg/kg.

Reviewer: Eugenia McAndrew
Risk Manager: 10

June 14, 2005

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

TEST MATERIAL: Formulation AV (KBR-3023 Formulation; Batch No. SDTH; 13.34% picaridin; clear liquid)

CITATION: Schungel, M. Formulation AV. Acute toxicity in the rat after dermal administration. Bayer Healthcare AG, Wuppertal, Germany. Laboratory Report Number AT01884. Study No. T5074932. January 10, 2005. MRID 46550902. Unpublished.

SPONSOR: LANXESS Deutschland GmbH, 51369 Leverkusen, Germany

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 46550902), 5/sex of HsdCpb:Wu Wistar rats (Age: 9-13 weeks; Source: Harlan/Winkelmann GmbH, Borchen, Germany; 235-261 g males and 207-215 g females) were dermally exposed to Formulation AV (KBR-3023 Formulation; Batch No. SDTH; 13.34% picaridin; clear liquid). Four thousand mg/kg of the test substance was applied to an area of approximately 10% of body surface of each animal. The test sites were covered with a gauze patch and secured with a "Lomir biomedical Inc rat jacket." After a 24 hour period, the dressings were removed and the test sites were washed. Animals were then observed for 14 days.

Dermal LD_{50} Males > 4000 mg/kg bw
Dermal LD_{50} Females > 4000 mg/kg bw
Dermal LD_{50} Combined > 4000 mg/kg bw

All animals survived and gained weight. No clinical signs were observed. Gross necropsy revealed no particular findings.

Toxicity based on lack of deaths at 4000 mg/kg. EPA Toxicity Category III.

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
4000	0/5	0/5	0/10

A. Mortality - None

B. Clinical observations - All animals gained weight. No clinical signs were observed.

C. Gross Necropsy - Gross necropsy revealed no particular findings

D. Reviewer's Conclusions: We agree with the study author's conclusion that the dermal LD_{50} for Formulation AV in male and female rats is greater than 4000 mg/kg.

Reviewer: Eugenia McAndrew
Risk Manager: 10

June 14, 2005

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

TEST MATERIAL: Formulation AV (KBR-3023 Formulation; Batch No. SDTH; 13.34% picaridin; clear liquid)

CITATION: Pauluhn, J. Formulation AV. Acute Inhalation Toxicity in rats. Bayer Healthcare AG, Wuppertal, Germany. Laboratory Report Number AT01875. Study No. T5073339. February 23, 2005. MRID 46550903. Unpublished.

SPONSOR: LANXESS Deutschland GmbH, 51369 Leverkusen, Germany

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 46550903), 5/sex of HsdCpb:WU (SPF)Wistar young adult rats (Source: Harlan/Winkelmann GmbH, Borchen, Germany; 173-208 g males and 173-186 g females) were exposed nose only via the inhalation route to Formulation AV (KBR-3023 Formulation; Batch No. SDTH; 13.34% picaridin; clear liquid) at a test concentration of 5.943 mg/L for a period of four hours. A control group of ten animals was exposed to conditioned dry air only. Animals were then observed for 14 days.

LC_{50} Males > 5.943 mg/L
LC_{50} Females > 5.943 mg/L
LC_{50} Combined > 5.943 mg/L

All animals survived and gained weight. Clinical signs noted in the test group included piloerection, reduced motility and tachypnea. The animals recovered from these symptoms by day 3. A battery of reflex measurements was made on the first post-exposure day. In comparison to the rats of the control group, none of the rats in the test group exhibited any specific effect. At necropsy, isolated red/gray foci were noted in the lungs of three control animals and two test animals. No other findings were noted. The gravimetric chamber concentration was 5.943 mg/L. The mass median aerodynamic diameter was estimated to be 1.3 with a geometric standard deviation of 1.71.

Toxicity 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)	Actual Conc. (mg/L)	Gravimetric Conc. (mg/L)	MMAD µm	GSD µm	Mortality/Number Tested		
					Males	Females	Combined
15.693	5.943	1.064	1.3	1.71	0/5	0/5	0/10

Test Atmosphere / Chamber Description:

Chamber Volume:	**3.8 L**
Airflow:	**15 LPM**
Temperature:	**21°C**
Relative Humidity:	**24%**

A. Mortality - None

B. Clinical observations - All animals survived and gained weight. Clinical signs noted in the test group included piloerection, reduced motility and tachypnea. The animals recovered from these symptoms by day 3. A battery of reflex measurements was made on the first post-exposure day. In comparison to the rats of the control group, none of the rats in the test group exhibited any specific effect.

C. Gross Necropsy - Isolated red/gray foci were noted in the lungs of three control animals and two test animals. No other findings were noted.

D. Reviewer's Conclusions: We agree with the study author's conclusion that the LC_{50} for Formualtion AV in male and female rats is greater than 5.943 mg/L.

Reviewer: Eugenia McAndrew
Risk Manager: 10

June 14, 2005

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

TEST MATERIAL: Formulation AV (KBR-3023 Formulation; Batch No. SDTH; 13.34% picaridin; clear liquid)

CITATION: Schungel, M. Formulation AV. Acute Eye Irritation on Rabbits. Bayer Healthcare AG, Wuppertal, Germany. Laboratory Report Number AT01883. Study No. T8074421. January 13, 2005. MRID 46550904. Unpublished.

SPONSOR: LANXESS Deutschland GmbH, 51369 Leverkusen, Germany

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 46550904), 0.1 mL of Formulation AV (KBR-3023 Formulation; Batch No. SDTH; 13.34% picaridin; clear liquid) was instilled into the conjunctival sac of one eye of three female young adult albino rabbits (Strain: Crl:KBL(NZW)BR; Source: Charles River, 88353 KiBlegg, Germany). The other eye served as the control. Animals were then observed at 1, 24, 48 and 72 hours and on day 7 post-instillation. Irritation was scored by the method of Draize. The eyes were treated with fluorescein and examined 24 hours after instillation.

Corneal opacity and conjunctivitis were noted in all three eyes from the one hour observation through 72 hours. All eyes were free of irritation by day 7.

In this study, formulation is irritating with reversibility by 7 days. 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	7
Corneal Opacity	3/3	3/3	3/3	3/3	0/3
Iritis	0/3	0/3	0/3	0/3	0/3
Conjunctivae:					
Redness	3/3	3/3	3/3	3/3	0/3
Chemosis	3/3	3/3	3/3	3/3	0/3

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

A. **Observations:** Corneal opacity and conjunctivitis were noted in all three eyes from the one hour observation through 72 hours. All eyes were free of irritation by day 7.

B. **Reviewer's Conclusions:** We agree with study author's conclusion that Formulation AV is irritating to the eye with full reversibility within 7 days.

Reviewer: Eugenia McAndrew
Risk Manager: 10

June 14, 2005

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

TEST MATERIAL: Formulation AV (KBR-3023 Formulation; Batch No. SDTH; 13.34% picaridin; clear liquid)

CITATION: Schungel, M. Formulation AV. Acute Skin/Corrosion Irritation on Rabbits. Bayer Healthcare AG, Wuppertal, Germany. Laboratory Report Number AT01885. Study No. T2074416. January 13, 2005. MRID 46550905. Unpublished.

SPONSOR: LANXESS Deutschland GmbH, 51369 Leverkusen, Germany

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 46550905), three young adult female albino rabbits (Strain: Crl:KBL(NZW)BR; Source: Charles River, 88353 KiBlegg, Germany) were dermally exposed to 0.5 mL of Formulation AV (KBR-3023 Formulation; Batch No. SDTH; 13.34% picaridin; clear 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 patch and wrapped with tape for a period of 4 hours. After the exposure period, the patches were removed and the skin was washed. 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 non irritating to the skin. EPA Toxicity Category IV.

Primary Dermal Irritation Index (PDII) = 0.0 No dermal irritation was noted at any test site.

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 - No dermal irritation was noted at any test site.

B. Results - PDII - 0.0

C. Reviewer's Conclusions - We agree with the study author's conclusion that Formulation AV is not irritating to the skin.

Reviewer: Eugenia McAndrew
Risk Manager: 10

June 14, 2005

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

TEST MATERIAL: Formulation AV (KBR-3023 Formulation; Batch No. SDTH; 13.34% picaridin; clear liquid)

CITATION: Vohr, H.W. Formulation AV. Study for the Skin Sensitization Effect in Guinea Pigs. Bayer Healthcare AG, Wuppertal, Germany. Laboratory Report Number AT01902. Study No. T7074187. January 12, 2005. MRID 46550906. Unpublished.

SPONSOR: LANXESS Deutschland GmbH, 51369 Leverkusen, Germany

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 46550906) with Formulation AV (KBR-3023 Formualtion; Batch No. SDTH; 13.34% picaridin; clear liquid), 30 young adult SPF-bred female guinea pigs (Strain: Crl:HA; Source: Charles River, 88353 KiBlegg, Germany; 322-412 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, a patch loaded with 0.5 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. A control group of 10 animals was treated with a dry patch only. The treatment areas were visually assessed 30 hours after initiation of exposure. Two weeks after the last induction dose, a patch loaded with 0.5 mL of undiluted test substance (the highest non-irritating concentration) was applied to a naive site on each test animal for a 6-hour challenge exposure. The ten naive control guinea pigs were also treated with the undiluted test substance. Readings were made 30 and 54 hours after the challenge application.

In this study, the formulation is not a dermal sensitizer.

One animal died after the first induction. No dermal effects were noted in any of the animals during the induction phase. Following the challenge, no dermal effects were observed in any of the test or naive control animals. 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, a patch loaded with 0.5 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. The treatment areas were visually assessed 30 hours after initiation of exposure. The animals rested for two weeks.

B. Challenge - Two weeks after the last induction dose, a patch loaded with 0.5 mL of undiluted test substance (the highest non-irritating concentration) was applied to a naive site on each test animal for a 6-hour challenge exposure. Readings were made 30 and 54 hours after the challenge application.

C. Naive Controls - A control group of 10 animals was treated with a dry patch only for the induction phase. The ten naive control guinea pigs were treated with the undiluted test substance at challenge.

II. RESULTS and DISCUSSION:

A. Reactions and duration - One animal died after the first induction. No dermal effects were noted in any of the animals during the induction phase. Following the challenge, no dermal effects were observed in any of the test or naive control animals.

B. Positive control - The results of the HCA positive control study were appropriate to validate test procedures.

C. Reviewer's Conclusions: We agree with the study author's conclusion that Formulation AV is not considered to be a dermal sensitizer.

ACUTE TOX ONE-LINERS

1. DP BARCODE: D318054
2. PC CODE: 070709
3. CURRENT DATE: 14/June 14,/2005
4. TEST MATERIAL: Formulation AV (KBR-3023 Formulation; Batch No. SDTH; 13.34% picaridin; clear liquid)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat Bayer Healthcare AG AT01886/1-10-05	46550901	LD_{50} females > 2000 mg/kg	III	A
Acute dermal toxicity/rat Bayer Healthcare AG AT01770/1-10-05	46550902	LD_{50} > 4000 mg/kg (males, females combined)	III	A
Acute inhalation toxicity/rat Bayer Healthcare AG AT01875/2-25-05	46550903	LC_{50} > 5.943 mg/L (males, females combined)	IV	A
Primary eye irritation/rabbit Bayer Healthcare AG AT01883/1-13-05	46550904	Corneal opacity and conjunctivitis in 3/3 eyes resolving by day 7	III	A
Primary dermal irritation/rabbit Bayer Healthcare AG AT01771/1-13-05	46550905	PDII = 0.0 No irritation observed.	IV	A
Dermal sensitization/guinea pig Bayer Healthcare AG AT01772/3-15-05	46550906	Not a sensitizer	–	A

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