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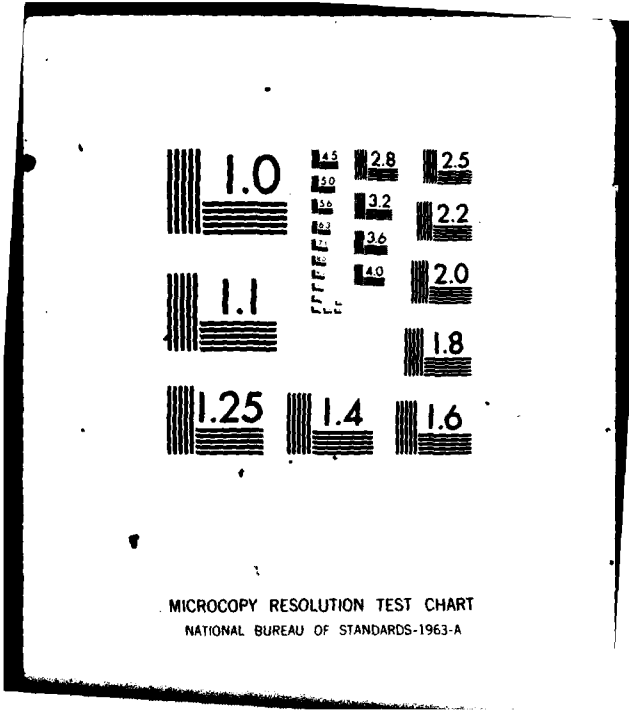
ARMY ENVIRONMENTAL HYGIENE AGENCY ABERDEEN PROVING GR--ETC F/G 6/20
TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)
MAR 81 M J TOPPER, M H WEEKS

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**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT A13-37545
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICAL
STUDY NO. 75-51-0157-81
SEPTEMBER 1978 - DECEMBER 1980

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REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER 75-51-0157-81 (10)	2. GOVT ACCESSION NO. AD-A096	3. RECIPIENT'S CATALOG NUMBER 133
4. TITLE (and Subtitle) Topical Hazard Evaluation Program of Candidate Insect Repellent AI3-37545, US Department of Agriculture Proprietary Chemical, Study No. 75-51-0157-81, September-1978 December 1980		5. TYPE OF REPORT & PERIOD COVERED Final, Sep 78 - Dec 80
7. AUTHOR(S) MICHAEL J. TOPPER, CPT, VC MAURICE H. WEEKS (10)		6. PERFORMING ORG. REPORT NUMBER 75-51-0157-81
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18. SUPPLEMENTARY NOTES		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) USDA Proprietary Chemical Eye irritation AI3-37545 Photochemical irritation Topical Hazard Evaluation ALD Candidate repellent Guinea pig sensitization Skin irritation		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Preliminary hazard evaluation of AI3-37545 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade chemical did not cause skin, eye, or photo irritation. It did not prove to be skin sensitizer or to be acutely toxic by ingestion. However, ethanol solutions may be moderately irritating to sensitive individuals. It was recommended that AI3-37545 be approved for further testing as a candidate insect repellent.		



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 U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
 ABERDEEN PROVING GROUND, MARYLAND 21010

CPT Topper/cf/AUTOVON
 584-3980

REPLY TO
 ATTENTION OF

HSE-LT-T/WP

5 MAR 1981

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent
 AI3-37545, US Department of Agriculture Proprietary Chemical, Study
 No. 75-51-0157-81, September 1978 - December 1980

Executive Secretary
 Armed Forces Pest Management Board
 Forest Glen Section, WRAMC
 Washington, DC 20012

A summary of the pertinent findings and recommendations of the inclosed report follows:

Preliminary hazard evaluation of AI3-37545 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade chemical did not cause skin, eye, or photo irritation. It did not prove to be skin sensitizer or to be acutely toxic by ingestion. However, ethanol solutions may be moderately irritating to sensitive individuals. It was recommended that AI3-37545 be approved for further testing as a candidate insect repellent.

FOR THE COMMANDER:

John F. Mazur
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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

REPLY TO
ATTENTION OF

HSE-LT-T/WP

TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-37545
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICAL
STUDY NO. 75-51-0157-81
SEPTEMBER 1978 - DECEMBER 1980

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research Service, Southern Region, Insects Affecting Man Research Laboratory, Gainesville, Florida, 27 September 1978.

b. Memorandum of Understanding between the US Army Environmental Hygiene Agency; the US Army Health Services Command; the Department of the Army, Office of The Surgeon General; the Armed Forces Pest Control Board; and the US Department of Agriculture, Agricultural Research, Science and Education Administration, titled, Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

2. REFERENCE. Toxicology Division Procedural Guide, US Army Environmental Hygiene Agency (USAEHA), 1972, revised 1976.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent AI3-37545.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent AI3-37545 was conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study and Sprague-Dawley rats for determination of oral toxicity. A tabular presentation of animal toxicity data developed in this Agency follows:†*

* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education and Welfare Publication NO. (NIH) 74-23, revised 1978.

† The experiments reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

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Study No. 75-51-0157-81, Sep 78 - Dec 80

TABLE. PRESENTATION OF DATA

Test	Results	Interpretation
<u>SKIN IRRITATION STUDY</u>		
<u>Rabbits</u>		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits.	Chemical AI3-37545 did not cause any irritation of the intact skin or of the skin surrounding an abrasion.	USAEHA Category I (ref Appendix A)
0.5 mL technical grade chemical applied to each of six rabbits.	(See Appendix B for details.)	
<u>EYE IRRITATION STUDY</u>		
<u>Rabbits</u>		
Single 24-hour application of 0.1 mL technical grade chemical to one eye of each six New Zealand White rabbits.	Chemical AI3-37545 did not cause any irritation to the eyes of rabbits. (See Appendix C for details.)	USAEHA Category A (ref Appendix A)
<u>APPROXIMATE LETHAL DOSE (ALD)</u>		
<u>Oral</u>		
Rats (male)-no diluent	ALD = 2900 mg/Kg	Presents little lethal hazard from accidental ingestion.

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Test	Results	Interpretation
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PHOTOCHEMICAL SKIN IRRITATION STUDY

Rabbits

A single 0.05 mL application of a 25-percent (w/v) solution of the chemical and a 10 percent (w/v) Oil of Bergamot solution (positive control) in 95 percent ethyl alcohol were applied to the intact skin of six rabbits. Five minutes after application, the rabbits were exposed to UV light (365 nm) for 30 minutes at a distance of 10-15 cm.

A 25-percent solution of AI3-37545 in ethanol did not cause a photochemical irritation reaction under test conditions. Ethanol solutions of AI3-37545 caused a moderate irritation at both UV- and non-UV skin sites. (See Appendix D for details.)

Chemical AI3-37545 did not cause a photochemical irritation reaction under test conditions and are not expected to cause a photochemical irritation in humans. Ethanol solutions of AI3-37545 may cause skin irritation in some sensitive individuals. Personnel experiencing this reaction should wash off the solution as soon as possible.

Control

Following UV exposures of the rabbits, 0.05 mL of test chemical, positive control, and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for skin irritation at 24, 48 and 72 hours.

Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.

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Test	Results	Interpretation
<u>SENSITIZATION STUDY</u>		
<u>Guinea Pigs (Male)</u>		
<p>Intradermal injections of 0.1 mL of a 0.1-percent solution (w/v) of AI3-37545 in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.</p>		
<p>Ten test guinea pigs for each compound were given 10 sensitizing doses over a 3-week period. After 2 weeks' rest, they were challenged with ID injections of the test chemical.</p>	<p>Challenge doses of AI3-37545 did not produce a sensitization reaction. (See Appendix E for details.)</p>	<p>Chemical AI3-37545 did not produce sensitization reactions under test conditions and are not expected to produce sensitization reactions in man.</p>

Study No. 75-51-0157-81, Sep 78 - Dec 80

5. CONCLUSION. Technical grade chemical AI3-37545 did not cause any skin, eye, or photo irritation, no sensitization reaction, and did not prove to be an acute ingestion hazard. However, it showed some skin irritation from ethanol solutions.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-37545 be approved for further testing as candidate insect repellent. Ethanol solutions of this chemical may cause skin irritation in sensitive individuals and, if experienced, the site should be washed with copious amounts of water.



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APPENDIX A

TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation, and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.

APPENDIX B

COMPOUND: AI3-37545, USDA Proprietary Chemical		USAEHA STUDY NO. 75-51-0157-81				
PRIMARY SKIN EFFECTS NEW ZEALAND WHITE RABBITS		USAEHA TOXICITY CATEGORY I				
CONDITIONS - Single 24-hour application to intact and abraded skin of New Zealand White rabbits.		Score				
Time of Observation	Hours	Response				Comments
		961	962	963	964	
Erythema & Eschar						
Intact Skin	24	0	0	0	2	2
Intact Skin	48	0	0	0	0	0
Abraded Skin	24	0	0	0	0	0
Abraded Skin	48	0	0	0	0	0
					Subtotal	2
Edema Formation						
Intact Skin	24	0	0	0	1	1
Intact Skin	48	0	0	0	0	0
Abraded Skin	24	0	0	0	0	0
Abraded Skin	48	0	0	0	0	0
					Subtotal	1
					Total	3
					Mean	0.25

APPENDIX C

COMPOUND: A13-37545, USDA Proprietary Chemical		USAEHA TOXICITY CATEGORY		USAEHA STUDY NO. 75-51-0157-81					
ACUTE EYE EFFECTS NEW ZEALAND WHITE RABBITS		A		CONDITIONS - Single 24-hour applica- tion of 0.1 mL of technical grade chemical to one eye of each of six New Zealand White Rabbits.					
Time of Reading	Structure	Scores						Mean Score	Comments
		Rabbit No.							
Hrs-Days		767	768	769	770	771	772		
24	Cornea	0	0	0	0	0	0	0	
	Iris	0	0	0	0	0	0	0	
	Conjunctivae	0	0	0	0	0	0	0	
48	Cornea	0	0	0	0	0	0	0	
	Iris	0	0	0	0	0	0	0	
	Conjunctivae	0	0	0	0	0	0	0	
72	Cornea	0	0	0	0	0	0	0	
	Iris	0	0	0	0	0	0	0	
	Conjunctivae	0	0	0	0	0	0	0	
7-Days	Cornea	0	0	0	0	0	0	0	
	Iris	0	0	0	0	0	0	0	
	Conjunctivae	0	0	0	0	0	0	0	

APPENDIX D
PHOTOCHEMICAL IRRITATION-NEW ZEALAND WHITE RABBITS

COMPOUND: AI3-37545, USDA Proprietary Chemical		USAEHA STUDY NO. 75-51-0157-81						
COMMENTS: Ethanol solutions caused moderate irritation of both UV and non-UV skin sites.								
PROCEDURE: A single application (0.05 mL) of a 25% (w/v) solution of the chemical and of a 10% (w/v) oil of Bergamot solution (positive control) in 95% ethanol, was applied to the intact skin of six rabbits. The rabbits were exposed to UV light for 30 minutes.								
MEAN SKIN IRRITATION SCORE								
Observation Time	Test Chemical UV Exposure		Test Chemical Non-UV Exposure		Positive Control UV Exposure		Positive Control Non-UV Exposure	
	Erythema	Edema	Erythema	Edema	Erythema	Edema	Erythema	Edema
24 Hours	12	10	9	8	12	6	9	4
48 Hours	9	4	8	3	9	5	0	0
72 Hours	10	4	9	3	8	4	0	0
TOTAL	31	18	25	14	29	15	9	4
Mean Irritant Responses	1.72	1.0	1.55	0.78	1.61	0.93	0.50	0.22
Net Score								

APPENDIX E

COMPOUND: AI3-37545		STUDY NO.: 75-51-0157-81	
GUINEA PIG SENSITIZATION MALE HARTLEY STRAIN		Substance: AI3-37545 Identify: USDA Proprietary Chemical	
Scoring Time 24 hours	Mean Body Wt (G) Initial	Mean Irritation Scores	
		Diluent	Test Compound
Test Compound	609	Initial	Final
		0	0
		Initial	Final
		Initial	Final
Scoring Time 48 hours	Mean Body Wt (G) Initial	Mean Irritation Scores	
		Diluent	Test Compound
Test Compound	-	Initial	Final
		0	0
		Initial	Final
		Initial	Final
Final Scores >100 - Strong Sensitizing 25-100 - Mild Sensitizing <25 - No Sensitizing			