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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)  
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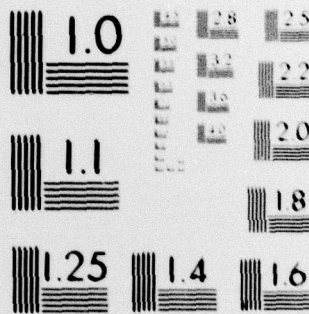
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**UNITED STATES ARMY  
ENVIRONMENTAL HYGIENE  
AGENCY**

**ABERDEEN PROVING GROUND, MD 21010**

TOPICAL HAZARD EVALUATION PROGRAM  
OF CANDIDATE INSECT REPELLENT AI3-36423  
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND  
STUDY NO. 75-51-0892-79  
MAY 1976 - JUNE 1979

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REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER 75-51-0892-79	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
6. TITLE (and Subtitle) Topical Hazard Evaluation Program of Candidate Insect Repellent AI3-36423, US Department of Agriculture Proprietary Compound, Study No. 75-51-0892-79, May 1976 - June 1979	5. TYPE OF REPORT & PERIOD COVERED Final, May 76 - Jun 79	
	8. PERFORMING ORG. REPORT NUMBER	
7. AUTHOR(s) 10. ALLEN W. SINGER	8. CONTRACT OR GRANT NUMBER(s) 11. 7 Sep 79	
9. PERFORMING ORGANIZATION NAME AND ADDRESS US Army Environmental Hygiene Agency Aberdeen Proving Ground, MD 21010	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS	
11. CONTROLLING OFFICE NAME AND ADDRESS Commander US Army Health Services Command Fort Sam Houston, TX 78234	12. REPORT DATE May 76 - Jun 79	
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)	13. NUMBER OF PAGES 6	
	15. SECURITY CLASS. (of this report) Unclassified 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE	
16. DISTRIBUTION STATEMENT (of this Report) Approved for public release; distribution unlimited.		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report) 9. Final rept. May 76-Jun 79, 13. 9		
18. SUPPLEMENTARY NOTES 14. USAEHA-75-51-0892-79		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) USDA Proprietary Compound eye irritation Candidate Repellent AI3-36423 Topical Hazard Evaluation skin irritation		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) A preliminary hazard evaluation of AI3-36423 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compound caused mild primary skin irritation and mild corneal and conjunctival irritation in rabbits, but no photoirritation. It did not sensitize guinea pigs or prove to be an acute ingestion hazard. Ethanol solutions of AI3-36423 also caused mild skin irritation. ↑		

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 ABERDEEN PROVING GROUND, MARYLAND 21010

CPT Singer/lm/AUTOVON  
 584-3980

7 SEP 1979

HSE-LT-T/WP

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent  
 AI3-36423, US Department of Agriculture Proprietary Compound, Study  
 No. 75-51-0892-79, May 1976 - June 1979

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

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

A preliminary hazard evaluation of AI3-36423 was performed by means of laboratory animal studies using rats, rabbits and guinea pigs. The technical grade compound caused mild primary skin irritation and mild corneal and conjunctival irritation in rabbits, but no photoirritation. It did not sensitize guinea pigs or prove to be an acute ingestion hazard. Ethanol solutions of AI3-36423 also caused mild skin irritation. It was recommended that AI3-36423, USDA Proprietary Compound, be approved for further testing. Consideration should be given to the observed irritation caused by both technical and ethanol solutions when formulating this as a repellent. Persons experiencing such irritation should wash the compound off as soon as possible.

FOR THE COMMANDER:

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TOPICAL HAZARD EVALUATION PROGRAM  
OF CANDIDATE INSECT REPELLENT AI3-36423  
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND  
STUDY NO. 75-51-0892-79  
MAY 1976 - JUNE 1979

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research Service, Southern Region, Insects Affecting Man-Research Laboratory, Gainesville, Florida, 5 May 1976.

b. Memorandum of Understanding between the Department of the Army, Office of The Surgeon General; the US Army Health Services Command; the US Army Environmental Hygiene Agency; the Armed Forces Pest Control Board; and the US Department of Agriculture, effective 1970 with Amendment 1, effective August 1974.

2. REFERENCE. Toxicology Division Procedural Guide, USAEHA, 1972, revised 1976.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent AI3-36423.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent AI3-36423, USDA Proprietary Compound, 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:\*†

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\* 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 1972 - second printing 1974.

† 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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TABULAR PRESENTATION OF DATA

<u>Test</u>	<u>Results</u>	<u>Interpretation</u>
<u>SKIN IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hour application to intact and abraded skin of New Zealand White Rabbits.	Compound AI3-36423 caused mild primary irritation of the intact skin and of the skin surrounding an abrasion.	USAEHA Category II (ref Appendix).
0.5 ml technical grade compound applied to each of six rabbits.		
<u>EYE IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hour application of 0.1 ml technical grade compound to one eye of each of six New Zealand White rabbits.	Compound AI3-36423 caused mild corneal and conjunctival irritation to five of six rabbits.	USAEHA Category C (ref Appendix).
<u>APPROXIMATE LETHAL DOSE (ALD)</u>		
<u>Oral</u>		
Rats (male) - no diluent	ALD > 4900 mg/kg	Presents little lethal hazard from accidental ingestion.

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<u>Test</u>	<u>Results</u>	<u>Interpretation</u>
<u>PHOTOCHEMICAL SKIN IRRITATION STUDIES</u>		
<u>Rabbits</u>		
A single 0.05 ml application of a 25 percent (w/v) solution of the compound 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 AI3-36423 in ethanol did not cause a photochemical irritation reaction under test conditions.  Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.	Compound AI3-36423 did not cause a photochemical irritation reaction under test conditions and is not expected to cause a photochemical irritation in humans.
<u>Control</u>		
Following UV exposures of the rabbits, 0.05 ml of test compound, 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.	Ethanol solutions of AI3-36423 caused mild irritation at both UV and non UV sites.	Ethanol solutions of AI3-36423 may be irritating to human skin.

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Test	Results	Interpretation
<u>SENSITIZATION STUDIES</u>		
<u>Guinea Pigs (Male)</u>		
Intradermal injections of 0.1 ml of a 0.1 percent suspension (w/v) of AI3-36423 or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.		
Ten test guinea pigs were given ten sensitizing doses over a 3-week period. After 2 weeks' rest, they were challenged with ID injections of test compound.	Challenge dose of AI3-36423 did not produce a sensitization reaction.	Compound AI3-36423 did not produce a sensitization reaction under test conditions and is not expected to produce a sensitization reaction in man.
Ten positive control guinea pigs were sensitized over 3 weeks to DNCB. After 2 weeks' rest, they were challenged with ID injections of DNCB.	Challenge dose of DNCB in positive control guinea pigs produced a marked sensitization reaction in 10 out of 10 guinea pigs.	DNCB produced a marked reaction, indicating the guinea pigs respond to sensitizing agents.

\* A known skin sensitizer.

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5. CONCLUSION. Technical grade compound AI3-36423 caused mild primary skin irritation and mild corneal and conjunctival irritation, but no photo sensitization. It did not sensitize guinea pigs or prove to be an acute ingestion hazard. Ethanol solutions of AI3-36423 also caused mild skin irritation, and may cause a similar irritation on man.

6. RECOMMENDATION. Under the provision of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-36423, USDA Proprietary Compound, be approved for further testing as a candidate insect repellent. Consideration should be given the skin irritation caused by both the technical and ethanol solutions of AI3-36423 when working with or formulating it as a repellent. Persons experiencing irritation should wash the compound off with copious amounts of water.

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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.