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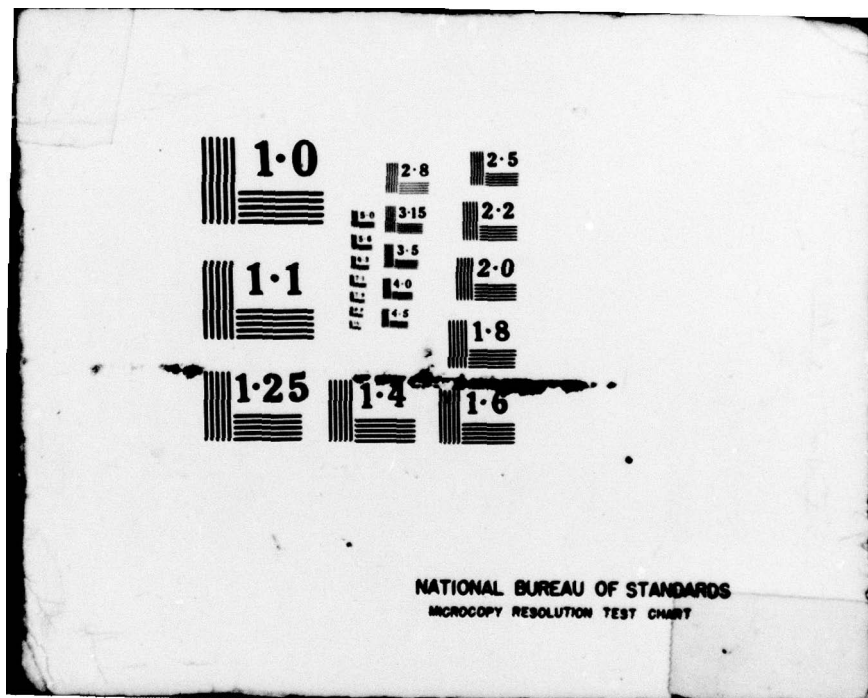
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**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-33019a
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICAL-AMIDE
STUDY NO. 75-51-0870-79
MAY 1976 - JUNE 1979

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) A hazard evaluation of candidate insect repellent AI3-33019a was performed by means of laboratory studies using rats, rabbits, and guinea pigs. The technical grade compound caused moderate irritation to corneal and conjunctival tissue of rabbits, but no skin irritation or photoirritation. It did not sensitize guinea pigs or prove to be an acute ingestion hazard.		

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

CPT Singer/jg/AUTOVON
 584-3980

17 AUG 1979

HSE-LT-T/WP

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent
 AI3-33019a, US Department of Agriculture Proprietary Chemical-
 Amide, Study No. 75-51-0870-79, 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 hazard evaluation of candidate insect repellent AI3-33019a was performed by means of laboratory studies using rats, rabbits, and guinea pigs. The technical grade compound caused moderate irritation to corneal and conjunctival tissue of rabbits, but no skin irritation or photoirritation. It did not sensitize guinea pigs or prove to be an acute ingestion hazard. Based on the eye irritation, it was recommended that AI3-33019a not be approved for further testing as a candidate repellent. If, however, this compound proves to be superior in pest repellent properties over existing compounds, it is suggested that it be resubmitted in its proposed use formulation and/or concentration.

FOR THE COMMANDER:

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TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-33019a
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICAL-AMIDE
STUDY NO. 75-51-0870-79
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 No. 1, effective August 1974.

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 AI3-33019a.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate insect repellent AI3-33019a, USDA Proprietary Chemical-Amide, 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 1972.

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

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Study No. 75-51-0870-79, May 76 - Jun 79

<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 AI3-33019a did not produce any irritation of the intact skin or of skin surrounding an abrasion.	USAEHA Category I (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 AI3-33019a caused moderate corneal irritation in 5 of 6 rabbits and moderate conjunctival irritation in all 6 rabbits. No corneal effects visible at day 7.	USAEHA Category E (ref Appendix)
<u>APPROXIMATE LETHAL DOSE (ALD)</u>		
<u>Oral</u>		
Rats (male) - no diluent	ALD = 1460 mg/kg	Presents little lethal hazard from acute accidental ingestion.

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Test	Results	Interpretation
<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 of a 10 percent (w/v) oil of Bergamot solution* 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 AI3-33019a in ethanol did not cause a photochemical skin irritation reaction under test conditions. Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.	Compound AI3-33019a did not cause a photochemical irritation reaction under test conditions and is not expected to cause a photochemical irritation in humans.

Control

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 reactions at 24, 48 and 72 hours.

* Positive control.

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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 AI3-33019a or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.		
Ten test guinea pigs received ten sensitizing injections of AI3-33019a over 3 weeks. After resting 2 weeks, they were challenged with a 0.1 percent solution of AI3-33019a.	Challenge dose of test compound did not produce a sensitization reaction.	Compound AI3-33019a did not produce a sensitization reaction under these test conditions and is not expected to produce a sensitization reaction in man.
Ten positive control guinea pigs received ten sensitizing injections of DNCB over 3 weeks. After 2 weeks' rest, they were challenged with a 0.1 percent suspension of DNCB.*	Positive Control (DNCB) produced a marked sensitization reaction in 9 out of 10 guinea pigs.	

* A known skin sensitizer.

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5. CONCLUSION. Technical grade compound A13-33019a caused moderate corneal and conjunctival irritation and damage and does not qualify as a nonhazardous insect repellent.

6. RECOMMENDATIONS. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that A13-33019a, USDA Proprietary Compound, not be approved for further testing as a candidate insect repellent. If, however, this compound should show a significant improvement in pest repellent properties over existing compounds, it is suggested that it be resubmitted in its proposed use formulation and/or concentration for reevaluation.

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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.