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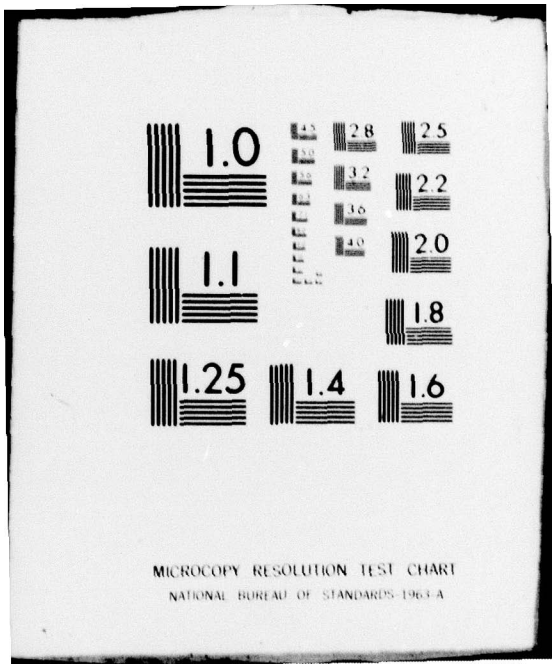
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UNITED STATES ARMY ENVIRONMENTAL HYGIENE AGENCY

ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-36323
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND
STUDY NUMBER 75-51-0832-79
OCTOBER 1975 - JUNE 1979

Approved for public release; distribution unlimited.

Unclassified

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

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3. RECIPIENT'S CATALOG NUMBER

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10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS

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19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Topical Hazard Evaluation
USDA Proprietary Compound
AI3-36323
skin irritation
eye irritation
candidate repellent

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

A hazard evaluation of AI3-36323 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compound caused moderate corneal and conjunctival irritation of the eyes of rabbits, but no primary skin irritation. It did not cause a photochemical sensitization reaction or sensitize guinea pigs, and did not demonstrate an acute ingestion hazard.

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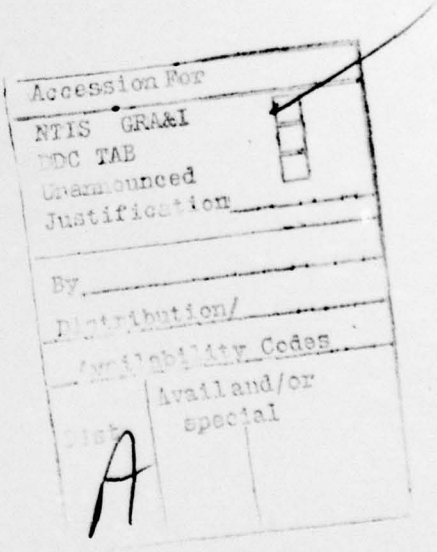
20. it is suggested it be purified through activated charcoal before being resubmitted in its proposed use formulation and/or concentration.



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

CPT Singer/bb/AUTOVON
584-3980

17 AUG 1979

HSE-LT-T/WP

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent AI3-36323, US Department of Agriculture Proprietary Compound, Study No. 75-51-0832-79, October 1975 - 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 AI3-36323 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compound caused moderate corneal and conjunctival irritation of the eyes of rabbits, but no primary skin irritation. It did not cause a photochemical sensitization reaction or sensitize guinea pigs, and did not demonstrate an acute ingestion hazard. Based on the eye irritation reaction, it was recommended that no further testing be peformed on AI3-36323. However, if this compound presents a significant improvement in pest repellent properties over existing compounds, it is suggested it be purified through activated charcoal before being resubmitted in its proposed use formulation and/or concentration.

FOR THE COMMANDER:

1 Incl
as (5 cy)

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

HSE-LT-T/WP

TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT AI3-36323 US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND STUDY NUMBER 75-51-0832-79 OCTOBER 1975 - JUNE 1979

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research Service, Southern Region, Insects Affecting Man Research Laboratory, Gainesville, Florida, 31 October 1975.

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. REFERENCES.

a. Report, HSE-LT, this Agency, 19 March 1975, subject: Primary Irritation Evaluation of Candidate Insect Repellents, Study Numbers 51-060-75 through 51-070-75.

b. Toxicology Division Procedural Guide, USAEHA, 1972, revised 1976.

3. PURPOSE. The purpose of this study is to provide guidance for further entomological testing of the candidate insect repellent AI3-36323.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent AI3-36323, 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 in 1972, and in 1978.

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

Topical Hazard Eval Study No. 75-51-0832 -79, Oct 75-Jun 79

TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
SKIN IRRITATION STUDIES*		
Rabbits		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits.	Compound AI3-36323 produced no primary irritation of the intact skin and the skin surrounding an abrasion.	USAEHA Category I (ref Appendix)
0.5 ml technical grade compound applied to each of six rabbits.		
EYE IRRITATION STUDIES*		
Rabbits		
Single 24-hour application of 0.1 ml technical grade compound to one eye of each of six New Zealand White rabbits.	Compound AI3-36323 produced moderate irritation and injury to the cornea and conjunctiva in all rabbits tested.	USAEHA Category E (ref Appendix)
APPROXIMATE LETHAL DOSE (ALD)		
Oral		
Rats (male) - no diluent	ALD >2200 mg/kg	Presents little lethal hazard from accidental ingestion.

* Data reported in USAEHA report (reference paragraph 2a)

Topical Hazard Eval Study No. 75-51-0832 -79, Oct 75-Jun 79

Test	Results	Interpretation
SENSITIZATION STUDIES		
Guinea Pigs		
Intradermal injections of 0.1 ml of a 0.1 percent suspension (w/v) of AI3-36323, 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 doses over a 3-week period. After 2 weeks' rest, they were challenged with a 0.1 percent solution of AI3-36323.	Challenge dose of test compound (last intradermal injection) did not produce a sensitization reaction.	Compound AI3-36323 did not produce a sensitization reaction under these test conditions and is not expected to produced a sensitization reaction in man.
Ten positive control guinea pigs received ten sensitizing doses of DNCB over a 3-week period. After 2 weeks' rest, they were challenged with a 0.1 percent suspension of DNCB.	Positive control produced a marked sensitization reaction in 10 of 10 guinea pigs.	

* A known skin sensitizer.

Test	Results	Interpretation
PHOTOCHEMICAL SKIN IRRITATION STUDIES		
Rabbits		
A single application (0.05 ml) of a 25 percent (w/v) solution of the compound and of 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 AI3-36323 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 AI3-36323 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 at 24, 48 and 72 hours.	Mild primary irritation was caused by all ethanol solutions of AI3-36323 (both control and test applicatons).	Ethanol solutions may be irritating to some humans.

5. CONCLUSION. The candidate insect repellent AI3-36323 has a potential for causing moderate irritation and damage to corneal and conjunctival tissue and does not qualify as a nonhazardous repellent.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-36323, USDA Proprietary Compound, not be approved for further testing as a candidate insect repellent. However, if this compound presents a significant improvement in pest repellent properties over existing compounds, it is suggested it be purified through activated charcoal before being resubmitted in its proposed use formulation and/or concentration.

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APPROVED:

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Chief, Toxicology Division

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.