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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)
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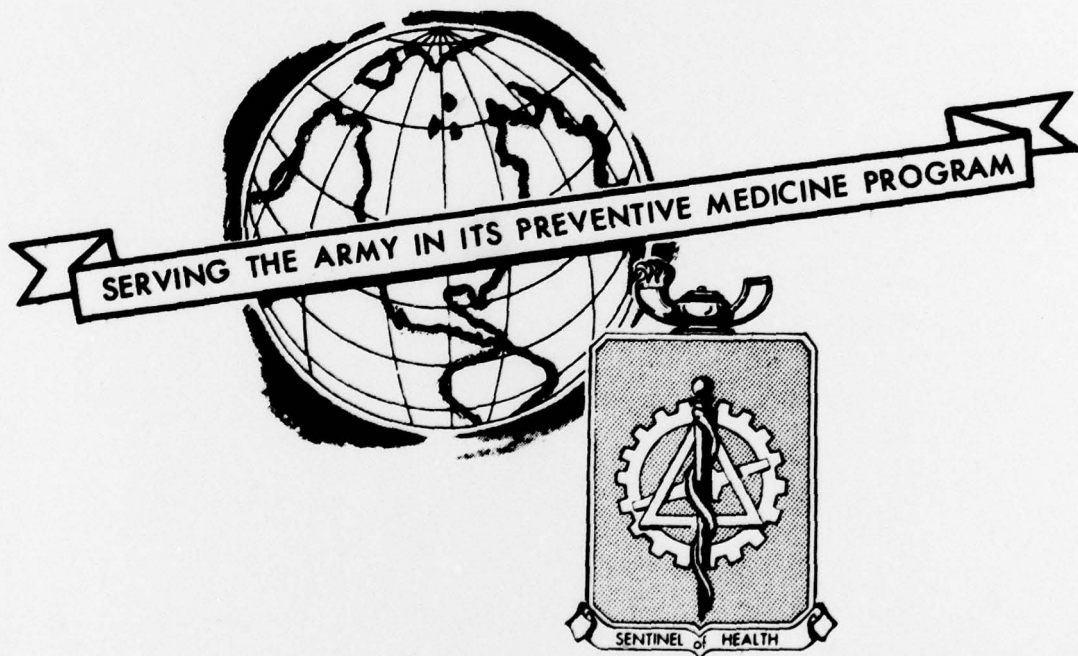
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2 LEVEL II

TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-36388
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND - AMIDE
STUDY NO. 51-0881-78
MAY 1976 - DECEMBER 1977

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) A preliminary hazard evaluation of AI3-36388 was performed by means of labora- tory animal studies using rats, rabbits and guinea pigs. The technical grade compound did not produce eye or skin irritation, or cause a photochemical irritation in rabbits, did not sensitize guinea pigs and did not demonstrate an acute ingestion hazard. It was recommended that AI3-36388 be approved for further testing as a candidate insect repellent.		

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

Mr. Weeks/ag/584-3980

HSE-LT-T/WP

16 JUN 1978

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent
AI3-36388, US Department of Agriculture Proprietary Compound -
AMIDE, Study No. 51-0881-78, May 1976 - December 1977

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 AI3-36388 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compound did not produce eye or skin irritation, or cause a photochemical irritation in rabbits, did not sensitize guinea pigs and did not demonstrate an acute ingestion hazard. It was recommended that AI3-36388 be approved for further testing as a candidate insect repellent.

FOR THE COMMANDER:

BRENDAN E. JOYCE, Ph.D.
LTC, MSC
Director, Laboratory Services

1 Incl
as (4 cy)

CF:
HQDA (DASG-PSP)
Cdr, HSC (HSPA-P)
Dir, Advisory Ctr on Tox, NRC
Supt, AHS (HSA-IHE)
USDA (Dr. Terrence McGovern)

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TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-36388
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND - AMIDE
STUDY NO. 51-0881-78
MAY 1976 - DECEMBER 1977

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, USAEHA, 1972, revised 1976.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent AI3-36388.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent AI3-36388, US Department of Agriculture (USDA) Proprietary Compound - 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 - 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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<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 AI3-36388 produced no primary irritation to the intact skin or to the skin surrounding an abrasion.	USAEHA Category I (ref Appendix).
0.5 ml of 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 AI3-36388 did not produce any injury to the cornea and, in addition, no injury to the conjunctiva in six out of six rabbits.	USAEHA Category A (ref Appendix).
<u>APPROXIMATE LETHAL DOSE (ALD)</u>		
<u>Oral</u>		
Rats (male) - corn oil diluent	ALD >4900 mg/kg	Presents little lethal hazard from acute accidental ingestion.

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Test	Results	Interpretation
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PHOTOCHEMICAL SKIN IRRITATION STUDIES

Rabbits

A single application (0.05 ml) of a 25 percent (w/v) solution of the compound (AI3-36388) 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 AI3-36388 in ethanol did not cause a photochemical skin irritation reaction under test conditions. Ethanol solutions of AI3-36388 applied without irradiation caused a mild erythema reaction.

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

Compound AI3-36388 did not cause a photochemical irritation reaction under test conditions and is not expected to cause a photochemical irritation in humans.

Ethanol solutions of AI3-36388 may cause a mild irritation reaction on sensitive individuals, and if so, should be immediately removed by washing with water.

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.

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Test	Results	Interpretation
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SENSITIZATION STUDIES

Guinea Pigs (Male)

Intradermal injections of 0.1 ml of a 0.1 percent suspension (w/v) of AI3-36388 or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.

Ten test guinea pigs received and challenged with a 0.1 percent solution of AI3-36388.

Ten positive control guinea pigs received and challenged with 0.1 percent suspension of DNCB.

Challenge dose of test compound (last intradermal injection) did not produce a sensitization reaction.

Positive Control (DNCB) produced a marked sensitization reaction in 10 out of 10 guinea pigs.

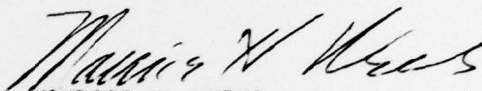
Compound AI3-36388 did not produce a sensitization reaction under these test conditions and is not expected to produce a sensitization reaction in man.

* A known skin sensitizer.

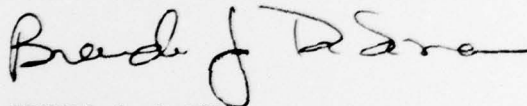
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5. CONCLUSION. Technical grade compound AI3-36388 presents no acute hazard from eye, skin, photochemical or sensitization contact or from acute ingestion.

6. RECOMMENDATION. Under the provision of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-36388, USDA Proprietary Compound, be approved for further testing as a candidate insect repellent.

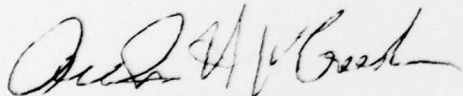


MAURICE H. WEEKS
Chief, Toxicity Evaluation Branch
Toxicology Division



BRENDA J. DeSENA
SP4
Veterinary Specialist
Toxicology Division

APPROVED:



ARTHUR H. McCREESH, Ph.D.
Chief, Toxicology Division

APPENDIX

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.

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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.