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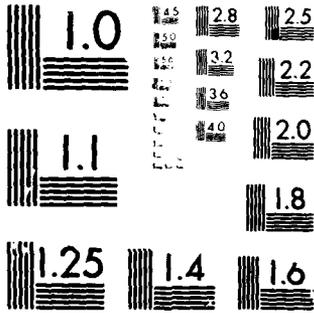
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**UNITED STATES ARMY  
ENVIRONMENTAL HYGIENE  
AGENCY**

**ABERDEEN PROVING GROUND, MD 21010**



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TOPICAL HAZARD EVALUATION PROGRAM  
OF CANDIDATE INSECT REPELLENTS AI3-36568  
AI3-36569, AI3-36583, and AI3-36585.  
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUNDS  
STUDY NUMBERS 75-51-0905-80  
75-51-0906-80, 75-51-0908-80, AND 75-51-0909-80  
MAY 1976-MARCH 1980.

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REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Preliminary hazard evaluations of AI3-36568, AI3-36569, AI3-36583 and AI3-36585 were performed by means of laboratory animal studies using rabbits and guinea pigs. AI3-36583 and AI3-36585 caused mild skin irritation, and all compounds caused moderate corneal injury. In addition, AI3-36568 caused a sensitization reaction in guinea pigs. It was recommended that the above compounds not be approved for further testing as candidate insect repellents.		

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DEPARTMENT OF THE ARMY CPT Singer/lm/AUTOVON  
 U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY 584-3980  
 ABERDEEN PROVING GROUND, MARYLAND 21010

23 MAY 1980

HSE-LT-T/WP

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents  
 AI3-36568, AI3-36569, AI3-36583, and AI3-36585, US Department of  
 Agriculture Proprietary Compounds, Study Numbers 75-51-0905-80,  
 75-51-0906-80, 75-51-0908-80, and 75-51-0909-80, May 1976 to March  
 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 evaluations of AI3-36568, AI3-36569, AI3-36583 and  
 AI3-36585 were performed by means of laboratory animal studies using rabbits  
 and guinea pigs. AI3-36583 and AI3-36585 caused mild skin irritation, and  
 all compounds caused moderate corneal injury. In addition, AI3-36568 caused  
 a sensitization reaction in guinea pigs. It was recommended that the above  
 compounds not be approved for further testing as candidate insect repellents.

FOR THE COMMANDER:

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Director, Laboratory Services

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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 REPELLENTS AI3-36568  
AI3-36569, AI3-36583, and AI3-36585  
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUNDS  
STUDY NUMBERS 75-51-0905-80  
75-51-0906-80, 75-51-0908-80, AND 75-51-0909-80  
MAY 1976-MARCH 1980

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 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 Administrations; 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 repellents AI3-36568, AI3-36569, AI3-36583 and AI3-36585.

4. SUMMARY OF FINDINGS. Hazard evaluations of the above candidate repellents were conducted by this Agency using New Zealand White rabbits for skin and eye studies and Hartley guinea pigs for a skin sensitization study. 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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TABLE. PRESENTATION OF DATA

Test	Results	Interpretation
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SKIN IRRITATION STUDIES

Rabbits

Single 24-hour application to intact and abraded skin of New Zealand White rabbits.	Compounds AI3-36568 and AI3-36569 did not cause any irritation of the intact skin or of the skin surrounding an abrasion.	USAEHA Category I (ref Appendix).
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0.5 mL technical grade compound applied to each of six rabbits.	Compounds AI3-36583 and AI3-36585 produced a mild irritation of intact and abraded skin.	USAEHA Category II (ref Appendix).
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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.	Compounds AI3-36568, AI3-36569, AI3-36583 and AI3-36585 produced moderate injury to all corneal and conjunctival tissues. AI3-36568, AI3-36583 and AI3-36585 produced injuries which lasted longer than 72 hours, but healed by 7 days.	USAEHA Category E (ref Appendix).
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Compound AI3-36569 produced severe ocular injury in two of the six rabbits tested, resulting in permanent destruction of tissues. Four of these six rabbits had detectable corneal injury at 7 days.

Test	Results	Interpretation
<u>SENSITIZATION STUDIES</u>		
<u>Guinea Pigs (Male)</u>		
Intradermal injections of 0.1 mL of a 0.1 percent solution (w/v) of AI3-36568 or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.	Challenge dose of AI3-36568 produced a sensitization reaction in 3 of 10 guinea pigs.	Compound AI3-36568 produced a sensitization reaction under test conditions and has the potential for causing a similar reading in man.
Ten test guinea pigs were given 10 sensitizing doses over a 3-week period. After 2 weeks rest, they were challenged with ID injections of test compound.	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.
Ten positive control guinea pigs were sensitized over 3 weeks with DNCB. After 2 weeks rest, they were challenged with ID injections of DNCB.		

\* A known skin sensitizer

Study No. 75-51-0905-80, 75-51-0906-80, 75-51-0908-80, 75-51-0909-80, May 76 - Mar 80

5. CONCLUSION. The technical grade compounds caused moderate corneal and conjunctival injury and do not qualify as non-hazardous insect repellents. In addition, AI3-36568 has the potential to be a sensitizing chemical.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (reference 1b), it is recommended that AI3-36568, AI3-36569, AI3-36583, and AI3-36585, USDA Proprietary Compounds, not be approved for further testing as candidate insect repellents.

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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.