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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT
REPELLENTS A13-3697. (U) ARMY ENVIRONMENTAL HYGIENE
AGENCY ABERDEEN PROVING GROUND MD J V WADE ET AL.

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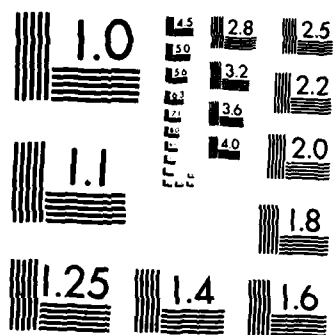
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**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

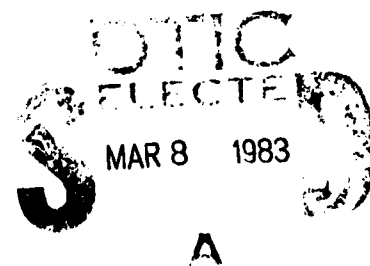
ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM
OF

CANDIDATE INSECT REPELLENTS

AI3-36976a, 36977a, 37013a, 37014a, 37015a
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0263-83 THRU 75-51-0267-83
AUGUST 1980 - AUGUST 1982

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REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER 75-51-0263-83 thru 75-51-0267-83	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
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7. AUTHOR(s) John V. Wade, DVM, CPT, VC John G. Harvey, Jr.		6. PERFORMING ORG. REPORT NUMBER
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AI3-36976a	Skin Irritation	USDA Proprietary Chemicals
AI3-36977a	Eye Irritation	Topical Hazard Evaluation
AI3-37013a	ALD	Program
AI3-37014a	Photo-Irritation	
AI3-37015a	Guinea Pig Sensitization	
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Preliminary hazard evaluations of the above candidate insect repellent chemicals were performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. Chemicals AI3-36976a, 36977a, 37013a, 37014a, and 37015a caused mild primary skin irritation. Chemicals AI3-36976a, 36977a, 37013a, 37014a, and 37015a were noninjurious to the eyes of rabbits. All chemicals were relatively non-toxic by ingestion. Chemicals AI3-36976a, 36977a, 37013a, 37014a, and 37015a caused photo irritation in rabbits. All chemicals did not prove to be skin sensitizers. It is recommended that all chemicals be disapproved for further testing as candidate insect repellents due to their photo-irritation potentiating.		

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

CPT Wade/ldr/AUTOVON
584-3980

REPLY TO
ATTENTION OF

HSHB-OT-T/WP

2 MAR 1983

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents
AI3-36976a, AI3-36977a, AI3-37013a, AI3-37014a, and AI3-37015a, US
Department of Agriculture Proprietary Chemicals, Study Nos.
75-51-0263-83 thru 75-51-0267-83, August 1980 - August 1982

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

EXECUTIVE SUMMARY

The purpose, essential findings and recommendations of the inclosed report follow:

a. Purpose. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellents AI3-36976a, 36977a, 37013a, 37014a, and 37015a by means of laboratory animal studies using New Zealand White rabbits, Sprague-Dawley rats and Albino Hartley guinea pigs.

b. Essential Findings. The technical grade chemicals caused mild primary skin irritation, were relatively nontoxic by ingestion, were noninjurious to the eyes of rabbits and did not prove to be skin sensitizers. They all caused photo irritation in rabbits.

c. Major Recommendations. Based on their photo irritation potentiating properties, it was recommended that these chemicals be disapproved for further testing as candidate insect repellents.

FOR THE COMMANDER:

1 Incl
as (5 cy)


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USDA, ARS-Southern Region

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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
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REPLY TO
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TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENTS
AI3-36976a, 36977a, 37013a, 37014a, 37015a
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0263-83 THRU 75-51-0267-83
AUGUST 1980 - AUGUST 1982

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agriculture Research, Southern Region, Insects Affecting Man and Animals Research Laboratory, Gainesville, Florida, 22 July 1980.

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 Topical Hazard Evaluation Program Procedural Guide, US Army Environmental Hygiene Agency (USAHA), 1982.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellents AI3-36976a, AI3-36977a, AI3-37013a, AI3-37014a, and AI3-37015a, US Department of Agriculture Proprietary Chemicals.

4. SUMMARY OF FINDINGS. Hazard evaluations of the candidate repellents AI3-36976a, 36977a, 37013a, 37014a, and 37015a, US Department of Agriculture (USDA) Proprietary Chemicals were conducted by this Agency using New Zealand White rabbits for skin and eye studies, Sprague-Dawley rats for determination of oral toxicity, and Albino Hartley guinea pigs for sensitization studies. 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) 80-23, revised 1978.

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

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Study Nos. 75-51-0263-83 thru 75-51-0267-83, Aug 80 - Aug 82

TABLE. PRESENTATION OF DATA

Test	Results	Interpretation
<u>SKIN IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits.	Chemicals AI3-36976a, 36977a, 37013a, 37014a, and 37015a produced mild primary irritation of the intact skin and the skin surrounding an abrasion.	USAEHA Category II (ref Appendix A)
0.5 mL technical grade chemical applied to each of six rabbits.		
<u>EYE IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hour application of 0.1 mL technical grade chemical to one eye of each of nine New Zealand White rabbits. Three of the nine rabbits had the eye flushed with warm water for 1 minute 25 seconds after application.	Chemicals AI3-36976a, 36977a, 37013a, 37014a and 37015a did not cause any irritation to the eyes of rabbits.	USAEHA Category A (ref Appendix A)
<u>APPROXIMATE LETHAL DOSE (ALD)</u>		
<u>Oral</u>		
Rats (male)-no diluent	AI3-36976a 4300 mg/kg AI3-36977a > 9688 mg/kg AI3-37013a > 9688 mg/kg AI3-37014a > 9688 mg/kg AI3-37015a > 9688 mg/kg	These chemicals are relatively nontoxic by ingestion.

Study Nos. 75-51-0263-83 thru 75-51-0267-83, Aug 80 - Aug 82

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 each chemical 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.	All tested chemicals caused a severe photochemical irritation under test conditions.	All tested chemicals are classified as photochemical irritants and are expected to cause a photochemical irritation in humans.
<u>Control.</u>		
Following UV exposures of the rabbits, 0.05 mL of test chemical, positive control (oil of Bergamot), 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.	Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.	

Study Nos. 75-51-0263-83 thru 75-51-0267-83, Aug 80 - Aug 82

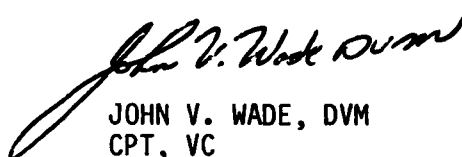
Test	Results	Interpretation
<u>SENSITIZATION STUDIES</u>		
<u>Guinea Pigs (Male)</u>		
Intradermal injections of 0.1 mL of a 0.1 percent solution (w/v) of AI3-38017 or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.		
Ten test guinea pigs for each chemical were given 10 sensitizing doses over a 3-week period. After a 2-week rest, they were challenged with intradermal (ID) injections of each test compound.	Challenge doses of the tested chemicals did not produce a sensitization reaction.	The tested chemicals did not produce sensitization reactions under test conditions and are not expected to produce a sensitization reaction in humans.
Ten positive control guinea pigs were sensitized over 3 weeks with 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 these guinea pigs respond to sensitizing agents.

* A known skin sensitizer.

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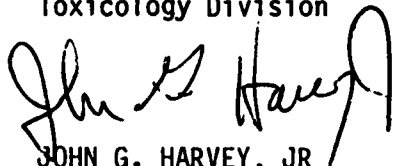
5. CONCLUSION. Chemicals AI3-36976a, 36977a, 37013a, 37014a, and 37015a are mild primary skin irritants. All chemicals were noninjurious to the eye, were relatively nontoxic by ingestion, and did not elicit skin sensitization reactions. Chemicals AI3-36976a, 36977a, 37013a, 37014a, and 37015a are severe photo irritants.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1c), it is recommended that the above USDA proprietary chemicals be disapproved for further testing as candidate insect repellents, due to their severe photoirritation potentiating properties.



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APPENDIX

ANALYTICAL QUALITY ASSURANCE

The Analytical Quality Assurance Office certifies the following with regard to this study:

a. This study was conducted in accordance with:

(1) Standing Operating Procedures developed by the Toxicology Division, USAEHA.

(2) Title 21, Code of Federal Regulations, 1981 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratories Studies.

b. Facilities were inspected during its operational phase to insure compliance with paragraph a above.

c. The information presented in this report accurately reflects the raw data generated during the course of conducting the study.



PAUL V. SNEERINGER, Ph.D.
Chief, Analytical Quality
Assurance Office

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