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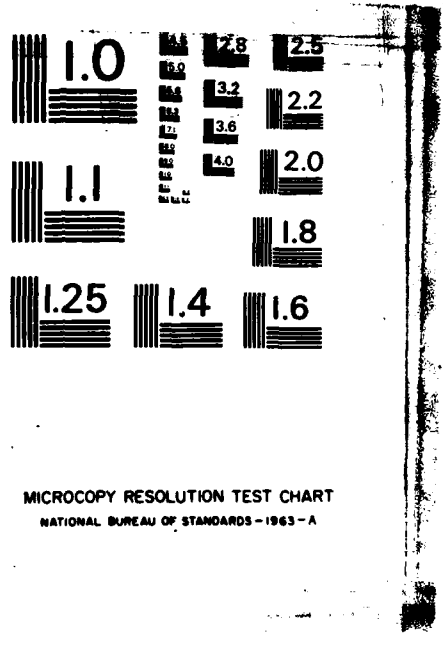
TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT
REPELLENTS AI3-3886. (U) ARMY ENVIRONMENTAL HYGIENE
AGENCY ABERDEEN PROVING GROUND MD J V WADE 10 MAY 84
USAEHA-75-51-0443-84 F/G 6/20

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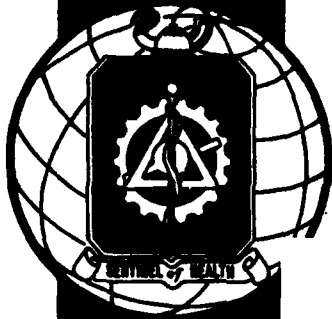
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**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

ABERDEEN PROVING GROUND, MD 21010

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TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENTS AI3-38862a, AI3-38863a,
AI3-39048a, AI3-39049a, AI3-39050a, and AI3-39051a
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0443-84, 75-51-0444-84,
75-51-0467-84, 75-51-0468-84,
75-51-0469-84 and 75-51-0470-84
MAY 1983 - MARCH 1984

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER 75-51-0443-84	2. GOVT ACCESSION NO. AD-7447025	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Topical Hazard Evaluation Program of Candidate Insect Repellents AI3-38862a, AI3-38863a, AI3-39048a, AI3-39049a, AI3-39050a, and AI3-39051a, US Department of Agriculture Proprietary Chemicals, Study No. 75-51-0443-84, 75-51-0444-84, 75-51-0467-84, 75-51-0468-84, 75-51-0469-84, and 75-51-0470-		5. TYPE OF REPORT & PERIOD COVERED Final, May 1983 - March 1984
7. AUTHOR(s) 84, May 1984 - March 1984 John V. Wade, DVM, CPT(P), VC		6. PERFORMING ORG. REPORT NUMBER
9. PERFORMING ORGANIZATION NAME AND ADDRESS Commander US Army Environmental Hygiene Agency Aberdeen Proving Ground, MD 21010		8. CONTRACT OR GRANT NUMBER(s)
11. CONTROLLING OFFICE NAME AND ADDRESS Commander US Army Health Services Command Ft Sam Houston, TX 78234		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)		12. REPORT DATE May 1983 - March 1984
		13. NUMBER OF PAGES 6
		15. SECURITY CLASS. (of this report) Unclassified
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE
16. DISTRIBUTION STATEMENT (of this Report) Approved for public release; distribution unlimited.		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)		
18. SUPPLEMENTARY NOTES		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) USDA Proprietary Chemicals AI3-39050a ALD AI3-38862a AI3-39051a Photochemical Irritation AI3-38863a Topical Hazard Evaluation Program AI3-39048a Skin Irritation AI3-39049a Eye Irritation		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Chemicals AI3-38862a, AI3-39048a, AI3-39049a, AI3-39050a, and AI3-39051a produced moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, produced necrosis and/or eschars. Chemical AI3-38863a produced mild primary irritation of the intact skin and of the skin surrounding an abrasion. The 25% (w/v) solution of chemical AI3-38863a applied during photoirritation testing produced moderate primary irritation of the intact skin, without ultraviolet irradiation. Chemical AI3-38863a produced moderate injury to the cornea and, in addition, some injury to the		

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20. ✓ conjunctiva. All chemicals demonstrated low to slight toxicity upon ingestion.

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

CPT(P) Wade/orl/AUTOVON
584-3627

REPLY TO
ATTENTION OF

HSB-OT/HP

10 MAY 1984

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents
AI3-38862a, AI3-38863a, AI3-39048a, AI3-39049a, AI3-39050a, and
AI3-39051a, US Department of Agriculture Proprietary Chemicals,
Study Nos. 75-51-0443-84, 75-51-0444-84, 75-51-0467-84,
75-51-0468-84, 75-51-0469-84, and 75-51-0470-84, May 1983 - March
1984

Executive Secretary
Armed Forces Pest Management Board
Forest Glen Section, HRAMC
Washington, DC 20307

EXECUTIVE SUMMARY

The purpose, essential findings, and major 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 AI3-38862a, AI3-38863a, AI3-39048a, AI3-39049a, AI3-39050a, and AI3-39051a by means of laboratory animal studies using New Zealand White rabbits and Sprague-Dawley rats.

b. Essential Findings. Chemicals AI3-38862a, AI3-39048a, AI3-39049a, AI3-39050a, and AI3-39051a produced moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, produced necrosis and/or eschars. Chemical AI3-38863a produced mild primary irritation of the intact skin and of the skin surrounding an abrasion. The 25 percent (w/v) solution of chemical AI3-38863a applied during photoirritation testing produced moderate primary irritation of the intact skin, without ultraviolet irradiation. Chemical AI3-38863a produced moderate injury to the cornea and, in addition, some injury to the conjunctiva. All chemicals demonstrated low to slight toxicity upon ingestion.

c. Major Recommendations. Recommend that chemicals AI3-38862a, AI3-38863a, AI3-39048a, AI3-39049a, AI3-39050a, and AI3-39051a be disapproved for further testing as candidate insect repellents.

FOR THE COMMANDER:

1 Incl
as (5 cy)

Joel C. Gaydos, M.D.
JOEL C. GAYDOS, M.D.
Colonel, MC
Director, Occupational and
Environmental Health

CF:
HQDA (DASG-PSP) wo Incl
Cdr, HSC (HSCL-P)
Comdt, AHS (HSHA-IPM)
Dir, Advisory Cen on Tox, NRC (2 cy)
USDA, ARS-Southern Region (3 cy)
USDA, ARS (Dr. Terrence McGovern)
Cdr, USAMRDC [SGRD-DPM/LTC(P) Reinert]



REPLY TO
ATTENTION OF
HSHB-07/WP

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

TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENTS AI3-38862a, AI3-38863a,
AI3-39048a, AI3-39049a, AI3-39050a, and AI3-39051a
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0443-84, 75-51-0444-84,
75-51-0467-84, 75-51-0468-84,
75-51-0469-84 and 75-51-0470-84
MAY 1983 - MARCH 1984

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research, Southern Region, Insects Affecting Man and Animals Research Laboratory, Gainesville, Florida, 2 June 1983.

b. Letter, US Department of Agriculture - Agricultural Research, Southern Region, Insects Affecting Man and Animals Research Laboratory, Gainesville, Florida, 17 January 1984.

c. 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 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 (USAEHA), January 1982.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellents AI3-38862a, AI3-38863a, AI3-39048a, AI3-39049a, AI3-39050a, and AI3-39051a, US Department of Agriculture (USDA) Proprietary Chemicals.

4. SUMMARY OF FINDINGS. Hazard evaluations of the candidate insect repellents AI3-38862a, AI3-38863a, AI3-39048a, AI3-39049a, AI3-39050a, and AI3-39051a, USDA Proprietary Chemicals, were conducted by this Agency using New Zealand White rabbits and Sprague-Dawley rats. A tabular presentation of animal toxicity data developed by 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, Public Health Service, National Institutes of Health (NIH) Publication No. 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. 75-51-0443-84, 75-51-0444-84, 75-51-0467-84, 75-51-0468-84,
75-51-0469-84, and 75-51-0470-84, May 83 - Mar 84

TABLE. PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
SKIN IRRITATION STUDIES		
Rabbits		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits.	Chemical AI3-38863a produced mild primary irritation of the intact skin and of the skin surrounding an abrasion.	USAEHA Category II (ref. Appendix A)
0.5 mL technical grade chemical applied to each of six rabbits.	Chemicals AI3-38862a, AI3-39048a, AI3-39049a, AI3-39050a, and AI3-39051a produced moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, produced necrosis and/or eschars.	USAEHA Category IV (ref. Appendix A)
EYE IRRITATION STUDIES		
Rabbits		
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 applications.	Chemical AI3-38863a produced moderate injury to the cornea and, in addition, some injury to the conjunctiva.	USAEHA Category E (ref. Appendix A)
APPROXIMATE LETHAL DOSE		
Oral		
Rats (female) - no diluent	AI3-38862a 1,480 mg/kg AI3-38863a 3,333 mg/kg AI3-39048a 2,222 mg/kg AI3-39049a ≥5,000 mg/kg AI3-39050a ≥5,000 mg/kg AI3-39051a ≥2,222 mg/kg	These chemicals demonstrate slight to low toxicity.

TEST	RESULTS	INTERPRETATION
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PHOTOCHEMICAL SKIN IRRITATION STUDIES

Rabbits

A single 0.05 mL application of a 25 percent (w/v) solution of each chemical and of a 10 percent (w/v) Oil of Bergamot solution (positive control) in 95 percent ethyl alcohol was 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.

Chemical AI3-38863a did not produce photochemical irritation under test conditions. The ethanol solution produced moderate primary irritation of the intact skin without ultraviolet (UV) irradiation.

This chemical is not expected to produce photochemical irritation in humans. Ethanol solutions should not be used directly on human skin.

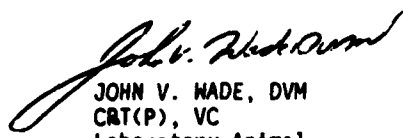
Control

Following UV exposure of the rabbits, 0.05 mL of test chemical, 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.

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

5. **CONCLUSION.** Chemicals AI3-38862a, AI3-39048a, AI3-39049a, AI3-39050a, and AI3-39051a produced moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, produced necrosis and/or eschars. Chemical AI3-38863a produced mild primary irritation of the intact skin and of the skin surrounding an abrasion. The 25 percent (w/v) solution of chemical AI3-38863a applied during photochemical irritation testing produced moderate primary irritation of the intact skin, without UV irradiation. Chemical AI3-38863a produced moderate injury to the cornea and, in addition, some injury to the conjunctiva. All chemicals demonstrated slight to low toxicity upon ingestion. These studies were monitored by the Analytical Quality Assurance Office (see Appendix B).

6. **RECOMMENDATION.** Recommend that chemicals AI3-38862a, AI3-38863a, AI3-39048a, AI3-39049a, AI3-39050a, and AI3-39051a be disapproved for further testing as candidate insect repellents.



JOHN V. WADE, DVM
CRT(P), VC
Laboratory Animal
Veterinary Officer
Toxicology Division

APPROVED:



MAURICE H. WEEKS
Chief, Toxicology Division

APPENDIX A

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.

Study Nos. 75-51-0443-84, 75-51-0444-84, 75-51-0467-84, 75-51-0468-84,
75-51-0469-84, and 75-51-0470-84, May 83 - Mar 84

APPENDIX B

ANALYTICAL QUALITY ASSURANCE

The Analytical Quality Assurance Office certifies the following:

a. These studies were conducted in accordance with:

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

(2) Title 21, Code of Federal Regulations (CFR), 1983 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratory Studies.

(3) Final Rule, Pesticide Programs; Good Laboratory Practice Standards; 48 Federal Register (FR) 53963-539691, 29 November 1983.

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

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



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

