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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT
REPELLENTS RI3-3827.. (U) ARMY ENVIRONMENTAL HYGIENE
AGENCY ABERDEEN PROVING GROUND MD J V WADE 03 APR 84

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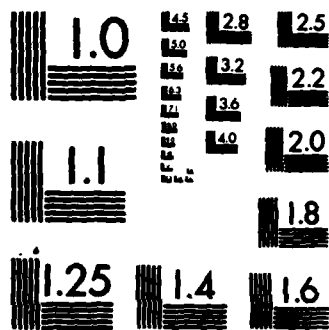
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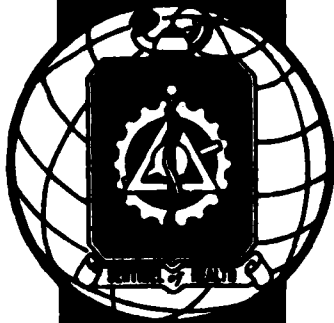
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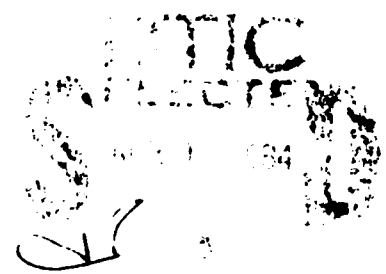
**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

ABERDEEN PROVING GROUND, MD 21010



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TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENTS
AI3-38274, AI3-38276, and AI3-38279
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0417-84, 75-51-0419-84
AND 75-51-0421-84
FEBRUARY - NOVEMBER 1983



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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) The technical grade chemicals produced no greater than mild primary irritation of the intact skin and of the skin surrounding an abrasion. The 24 percent (w/v) solutions of these chemicals in 95 percent ethanol which were applied during photoirritation studies produced mild to moderate primary irritation of the intact skin, without ultraviolet (UV) irradiation. Chemical AI3-38276 produced a photochemical irritant reaction upon irradiation with UV light which was significantly more severe than the primary irritation previously noted. Additionally, although these ethanol solutions were colorless, they produced a		

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20 marked yellow discoloration of the skin upon application. All three chemicals produced moderate injury to the cornea and, in addition, produced some injury to the conjunctiva.

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

CPT(P) WADE/or1/AUTOVON
 584-3627

REPLY TO
 ATTENTION OF

HSHB-OT/WP

3 APR 1984

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents
 AI3-38274, AI3-38276, and AI3-38279, US Department of Agriculture
 Proprietary Chemicals, Study Nos. 75-51-0417-84, 75-51-0419-84, and
 75-51-0421-84, February - November 1983

Executive Secretary
 Armed Forces Pest Management Board
 Forest Glen Section, WRAMC
 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 AI3-38274, AI3-38276, and AI3-38279 by means of laboratory animal studies using New Zealand White rabbits.

b. Essential Findings. The technical grade chemicals produced no greater than mild primary irritation of the intact skin and of the skin surrounding an abrasion. The 25 percent (w/v) solutions of these chemicals in 95 percent ethanol which were applied during photoirritation studies produced mild to moderate primary irritation of the intact skin, without ultraviolet (UV) irradiation. Chemical AI3-38276 produced a photochemical irritant reaction upon irradiation with UV light which was significantly more severe than the primary irritation previously noted. Additionally, although these ethanol solutions were colorless, they produced a marked yellow discoloration of the skin upon application. All three chemicals produced moderate injury to the cornea and, in addition, produced some injury to the conjunctiva.

c. Major Recommendations. Disapprove chemicals AI3-38274, AI3-38276, and AI3-38279 for further testing.

FOR THE COMMANDER:

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 as (5 cy)

for Rodney M. Black
 JOEL C. GAYDOS, M.D.
 Colonel, MC
 Director, Occupational and
 Environmental Health

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 Cdr, HSC (HSCL-P)
 Comdt, AHS (HSHA-P)
 Dir, Advisory Cen on TOX, NRC (2 cy)
 USDA, ARS (Dr. Terrence McGovern)
 USDA, ARS-Southern Region (3 cy)
 Cdr, USAMRDC [SGRD-DPM/LTC(P) Reinert]





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

REPLY TO
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TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENTS
AI3-38274, AI3-38276, and AI3-38279
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0417-84, 75-51-0419-84
AND 75-51-0421-84
FEBRUARY 1983 - NOVEMBER 1983

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research, Southern Region, Insects Affecting Man and Animals Research Laboratory, Gainesville, Florida, 10 February 1983.

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 (USAEHA), January 1982.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of candidate insect repellents AI3-38274, AI3-38276, and AI3-38279, US Department of Agriculture (USDA) Proprietary Chemicals.

4. SUMMARY OF FINDINGS. Hazard evaluation of the candidate insect repellents AI3-38274, AI3-38276, and AI3-38279, USDA Proprietary Chemicals were conducted by this Agency using New Zealand White rabbits for skin, eye, and photochemical irritation studies. 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 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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TABLE. PRESENTATION OF DATA

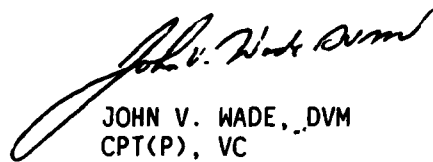
TEST	RESULTS	INTERPRETATION
SKIN IRRITATION STUDIES		
Rabbits		
Single 24-hour application to intact and abraded skin of the New Zealand White rabbits.	Chemical AI3-38279 did not produce irritation of the intact skin and no greater than mild irritation of the skin surrounding an abrasion.	USAEHA Category I (ref Appendix A)
0.5 mL technical grade chemical applied to each of six rabbits.	Chemicals AI3-38274 and AI3-38276 produced mild primary irritation of the intact skin and of the skin surrounding an abrasion.	USAEHA Category II (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 application.	Chemicals AI3-38274, AI3-38276 and AI3-38279 produced moderate injury to the cornea and, in addition, produced some injury to the conjunctiva. Washing with warm water did not significantly decrease the amount of ocular injury noted.	USAEHA Category E (ref Appendix A)

TEST	RESULTS	INTERPRETATION
PHOTOCHEMICAL SKIN IRRITATION STUDIES		
Rabbits		
<p>A single 0.05 mL application of a 25% (w/v) solution of each chemical or a 10% (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 ultraviolet (UV) light (365 nm) for 30 minutes at a distance of 10-15 cm.</p>	<p>Chemical AI3-38276 produced a photochemical irritation reaction under test conditions. Chemicals AI3-38274 and AI3-38279 did not produce a photochemical irritation reaction.</p>	<p>Chemical AI3-38276 could produce a photochemical irritation reaction in humans. Chemicals AI3-38274 and AI3-38279 are not expected to produce photochemical irritation in humans.</p>
Control		
<p>Following UV exposure of the rabbits, 0.05 mL of test chemicals, positive control and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for irritation at 24, 48, and 72 hours</p>	<p>Positive control application and irradiation resulted in greater irritant effects than without irradiation. Ethanol solutions of the test chemicals produced mild to moderate primary irritation of the intact skin at the sites of application, both irradiated and unirradiated. They also produced a yellow discoloration of the skin. Irradiation of chemical AI3-38276 following application significantly increased the irritant response.</p>	

5. CONCLUSION. Technical grade chemicals AI3-38274, AI3-38276 and AI3-38279 produced no greater than mild primary irritation of the intact skin and of the skin surrounding an abrasion. The 25 percent (w/v) solutions of these chemicals in 95 percent ethanol which were applied during photoirritation studies, produced mild to moderate primary irritation of the intact skin, without UV irradiation. Chemical AI3-38276 produced a photochemical irritant reaction upon irradiation with UV light which was significantly more severe

than the primary irritation previously noted. Additionally, although these ethanol solutions were colorless, they produced a marked yellow discoloration of the skin upon application. All three chemicals produced moderate injury to the cornea and, in addition, produced some injury to the conjunctiva. These studies were monitored by the Analytical Quality Assurance Office (see Appendix B).

6. RECOMMENDATION. Recommend that chemicals AI3-38274, AI3-38276, and AI3-38279 be disapproved for further testing as candidate insect repellents (under the provisions of the Memorandum of Understanding, para 1b, this report).



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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.

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

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