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**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENT AI3-38267
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICAL
STUDY NO. 75-51-0292-83
MARCH 1981 - JANUARY 1983

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

CPT Wade/or1/AUTOVON
 584-3980

REPLY TO
 ATTENTION OF

HSMB-OT/WP

28 MAR 1983

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent
 AI3-38267, US Department of Agriculture Proprietary Chemical, Study
 No. 75-51-0292-83, March 1981 - January 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 Repellent AI3-38267 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 chemical was relatively non-toxic by ingestion, did not produce primary skin irritation, and was noninjurious to the eyes of rabbits. This chemical did not cause photoirritation in rabbits nor did it elicit skin sensitization in guinea pigs.

c. Major Recommendations. Recommend that this chemical be approved for further testing as a candidate insect repellent.

FOR THE COMMANDER:

1 Incl
 as (5 cy)

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

CF:
 HQDA (DASG-PSP) w/o incl
 Cdr, HSC (HSPA-P)
 Comdt, AHS (HSHA-IPM)
 Dir, Advisory Cen on TOX, NRC (2 cy)
 USDA, ARS (Dr. Terrence McGovern)
 USDA, ARS-Southern Region (3 cy)
 USDA, ARS-Southern Region (LTC Reinert)



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ABERDEEN PROVING GROUND, MARYLAND 21010

REPLY TO
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TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENT AI3-38267
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICAL
STUDY NO. 75-51-0292-83
MARCH 1981 - JANUARY 1983

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research, Southern Region, Insects Affecting Man and Animals Research Laboratory, Gainesville, Florida, 12 February 1981.

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 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).

3. PURPOSE. The purpose of this program is to provide guidance for further Entomological Testing of Candidate Insect Repellent AI3-38267, US Department of Agriculture (USDA) Proprietary Chemical.

4. SUMMARY OF FINDINGS. Hazard evaluation of the candidate repellent AI3-38267, USDA Proprietary Chemical, was 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 at 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

<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.	Chemical AI3-38267 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.		
<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.	Chemical AI3-38267 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	AI3-38267 >4311 mg/kg	This chemical is relatively nontoxic by ingestion.

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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 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 ultraviolet (UV) light (365 nm) for 30 minutes at a distance of 10-15 cm.

Chemical AI3-38267 did not cause photo-irritation under test conditions.

This chemical did not cause photo-irritation under test conditions and is not expected to cause photoirritation in humans.

Control

Following UV exposures 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.

SENSITIZATION STUDIES

Guinea Pigs (Male)

Intradermal (ID) injections of 0.1 mL of a 0.1 percent solution (w/v) of each tested chemical or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline:

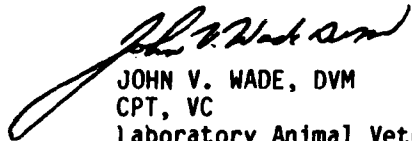
* A known skin sensitizer

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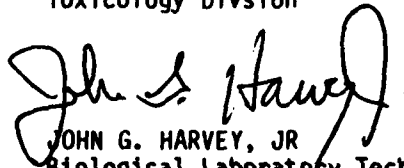
Test	Results	Interpretation
Ten test guinea pigs for each chemical were given 10 sensitizing doses over a 3-week period. After 2-week rest, they were challenged with ID injections of each test compound.	Challenge dose of the tested chemical did not produce a sensitization reaction.	This chemical is not 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.	The DNCB produced a marked reaction, indicating that these guinea pigs do respond to sensitizing agents.

5. CONCLUSION. Chemical AI3-38267 was relatively nontoxic by ingestion, did not produce primary skin irritation, and was noninjurious to the eyes of rabbits. It did not cause photoirritation in rabbits, nor did it elicit skin sensitization in guinea pigs. These studies were monitored by Analytical Quality Assurance Office (see Appendix B).

6. RECOMMENDATION. Recommend that USDA Proprietary Chemical AI3-38267 be approved for further entomological testing (under the provisions of the Memorandum of Understanding, para 1b, this report).



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APPROVED:



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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.

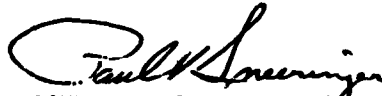
F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.

APPENDIX B

ANALYTICAL QUALITY ASSURANCE

The Analytical Quality Assurance Office certifies the following 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 Laboratory 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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