AD-A149 721 TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT AI3-30180 (U) ARMY ENVIRONMENTAL HYGIENE AGENCY ABERDEEN PROVING GROUND MD R D RUSSELL

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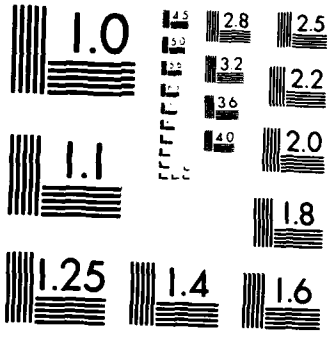

UNITED STATES ARMY ENVIRONMENTAL HYGIENE AGENCY

ABERDEEN PROVING GROUND, MD 21010-5422

AEHA

PHASE 1
TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENT AI3-30180-c
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICAL
STUDY NO. 75-51-0367-85
APRIL 1982 - SEPTEMBER 1984

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE	READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER: 75-51-0367-85	2. GOVT ACCESSION NO.: AD-A149721
	3. RECIPIENT'S CATALOG NUMBER:
4. TITLE (and Subtitle): Topical Hazard Evaluation Program of Candidate Insect Repellent, AI3-30180-c, US Department of Agriculture Proprietary Chemical, Study No. 75-51-0367-85, April 1982 - September 1984 - Phase 1	5. TYPE OF REPORT & PERIOD COVERED: Final, April 1982 - September 1984
	6. PERFORMING ORG. REPORT NUMBER:
7. AUTHOR(s): R. David Russell, DVM, CPT, VC	8. CONTRACT OR GRANT NUMBER(s):
9. PERFORMING ORGANIZATION NAME AND ADDRESS: Commander, US Army Environmental Hygiene Agency, Aberdeen Proving Ground, MD 21010-5422	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS:
11. CONTROLLING OFFICE NAME AND ADDRESS: Commander, US Army Health Services Command, Fort Sam Houston, TX 72834-5000	12. REPORT DATE: April 1982 - September 1984
	13. NUMBER OF PAGES: 6
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office)	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)

AI3-30180c	ALD
Eye Irritation	Topical Hazard Evaluation Program
Skin Irritation	USDA Proprietary Chemicals
Photo Irritation	
GPST	

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Preliminary hazard evaluation of the above candidate repellent was performed by means of laboratory animal studies using New Zealand white rabbits, albino Hartley guinea pigs, and Sprague Dawley rats. Chemical AI3-30180C produced mild to moderate primary skin irritation of the intact skin and the skin surrounding an abrasion. The chemical caused moderate injury to the cornea and conjunctiva. The chemical was not phototoxic or skin sensitizing. The approximate lethal dose (oral) was 2,222 mg/kg.

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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-5422

CPT Russell/slw/AUTOVON
584-3980

REPLY TO
ATTENTION OF

HSHB-OT/WP

10 JAN 1985

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent AI3-30180-c, US Department of Agriculture Proprietary Chemical, Study No. 75-51-0367-85, April 1982 - September 1984

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 enclosed report follow:

a. Purpose. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent AI3-30180-c by means of laboratory animal studies using Sprague-Dawley rats, New Zealand White rabbits, and Albino-Hartley guinea pigs.

b. Essential Findings. Chemical AI3-30180-c produced mild to moderate irritation of intact skin and skin surrounding an abrasion. It produced moderate injury to the cornea and conjunctiva which resolved within 7 days. This chemical was not phototoxic and did not sensitize guinea pig skin. It was moderately toxic orally (reference 2b).

c. Major Recommendations. Recommend subject chemical be approved for further testing under the provisions of the Memorandum of Understanding (reference 1b).

FOR THE COMMANDER:

Encl

JOEL C. GAYDOS
Colonel, MC
Director, Occupational and Environmental Health

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

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-5422

REPLY TO
ATTENTION OF

HSHB-OT/WP

PHASE I
TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENT AI3-30180-c
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICAL
STUDY NO. 75-51-0367-85
APRIL 1982 - SEPTEMBER 1984

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research Service, Northeastern Region, Beltsville Agricultural Research Center, Beltsville, Maryland, 9 April 1982.

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.

a. Toxicology Division Standing Operating Procedures, US Army Environmental Hygiene Agency (USAEHA), 1981.

b. Gleason et. al., Clinical Toxicology of Commercial Products, Williams and Wilkins, Baltimore, Maryland, 1969.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent AI3-30180-c, US Department of Agriculture (USDA).

4. SUMMARY OF FINDINGS. Hazard evaluations of the candidate repellent AI3-30180-c, USDA Proprietary Chemical, 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 skin sensitivity testing. A tabular presentation of animal toxicity data developed in this Agency follows.*†

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* 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.

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 AI3-30180-c produced mild to moderate primary skin irritation of the intact skin and the skin surrounding an abrasion.	Results of two tests: USAEHA Categories I and II (ref Appendix A)
0.5 mL technical grade chemical applied to each of 12 rabbits.		
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.	Chemical AI3-30180-c caused moderate injury to the cornea and conjunctiva of rabbits. Injury resolved within 7 days.	USAEHA Category E (ref Appendix A)
APPROXIMATE LETHAL DOSE (ALD)		
Oral		
Rats (female)-no diluent	ALD for AI3-30180-c: 2,222 mg/kg	This chemical is moderately toxic by ingestion (ref 2b)
PHOTOCHEMICAL SKIN IRRITATION STUDIES		
Rabbits		
A single 0.05 mL application of a 25 percent (w/v) solution of each chemical and 10 percent (w/v) Oil of Bergamot	The 25 percent solution in ethanol did not cause a photochemical irritation reaction under test conditions.	This chemical is not expected to cause photochemical irritation in humans.

Test	Results	Interpretation
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.		
Control		
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 irritations at 24, 48 and 72 hours.	Positive control application and irradiation caused greater irritant effects than 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 chemical 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 2-weeks rest, they were challenged with ID injections of each test compound.	Challenge dose of chemical AI3-30180-c failed to produce a sensitization reaction.	This compound did not produce a sensitization reaction under test conditions and is not expected to cause sensitization reactions in humans.

Test	Results	Interpretation
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 that guinea pigs respond to sensitizing agents.

* A known skin sensitizer.

5. CONCLUSION. Technical grade compound AI3-30180-c produced mild to moderate primary skin irritation in two separate tests. This compound produced moderate corneal and conjunctival irritation which resolved in 7 days and was neither phototoxic or sensitizing. Subject compound is moderately toxic by the oral route. These studies were monitored by the Analytical Quality Assurance Office (see Appendix B).

6. RECOMMENDATION. Recommend that USDA proprietary chemical (AI3-30180-c) be approved for continued testing under the provisions of the Memorandum of Understanding (reference 1b). Further recommend that individuals using this compound be cautioned against using this chemical near the eyes and mucous membranes.

R. DAVID RUSSELL
CPT, 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.

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) 53946-53969, 29 November 1983.

(4) Final Rule, Toxic Substances Control; Good Laboratory Practice Standards; 48 Federal Register (FR) 53922-53944, 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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