AD-A114 051 ARMY ENVIRONMENTAL HYGIENE AGENCY ABERDEEN PROVING GR--ETC F/G 6/20
TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)
JAN 82 M J TOPPER
UNCLASSIFIED USAEHA-75-51-0281-82 NL

UNITED STATES ARMY ENVIRONMENTAL HYGIENE AGENCY

ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT
AI3-38271a
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICAL
STUDY NUMBER 75-51-0281-82
OCTOBER 1980 - JANUARY 1982

Approved for public release; distribution unlimited.

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE *(When Data Entered)*

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER 75-51-0281-82	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
4. TITLE *(and Subtitle)* Topical Hazard Evaluation Program of Candidate Insect Repellent AI3-38271a, US Department of Agriculture Proprietary Chemical Study No. 75-51-0281-82, Oct 80 - Jan 82		5. TYPE OF REPORT & PERIOD COVERED Final Oct 80 - Jan 82 6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Michael J. Topper, CPT, VC		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS US Army Environmental Hygiene Agency Aberdeen Proving Ground, MD 21010		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 78234		12. REPORT DATE Oct 80 - Jan 82 13. NUMBER OF PAGES
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)*

AI3-38271a
Skin Irritation
Eye Irritation
Photo-Irritation
ALD
Guinea Pig Sensitization
Topical Hazard Evaluation Program
USDA Proprietary Chemical

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

Preliminary hazard evaluations of AI3-38271a was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. AI3-38271a produced mild injury to the cornea of rabbits. The technical grade chemical did not cause skin or photo-irritation. It did not prove to be a skin sensitizer or to be acutely toxic by ingestion. It was recommended that AI3-38271a be approved for further testing as a candidate insect repellent.

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

SECURITY CLASSIFICATION OF THIS PAGE *(When Data Entered)*

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

CPT Topper/mhb/AUTOVON
584-3980

REPLY TO ATTENTION OF

HSHB-LT-T/WP

27 APR 1982

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent AI3-38271a, US Department of Agriculture Proprietary Chemical, Study Number 75-51-0281-82, October 80 - January 82

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

A summary of the pertinent findings and recommendations of the inclosed report follows:

Preliminary hazard evaluations of AI3-38271a was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. AI3-38271a produced mild injury to the cornea of rabbits. The technical grade chemical did not cause skin or photo-irritation. It did not prove to be a skin sensitizer or to be acutely toxic by ingestion. It was recommended that AI3-38271a be approved for further testing as a candidate insect repellent.

FOR THE COMMANDER:

JOHN F. MAZUR
LTC, MSC
Director, Laboratory Services

1 Incl
as (5 cy)

CF:
HQDA (DASG-PSP) wo incl
Cdr, HSC (HSPA-P)
Dir, Advisory Cen on Tox, NRC
Comdt, AHS (HSHA-IPM)
USDA, ARS (Dr. Terrence McGovern)
USDA, ARS-Southern Region

A

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

REPLY TO ATTENTION OF

HSHB-LT/WP

TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT
AI3-38271a
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICAL
STUDY NUMBER 75-51-0281-82
OCTOBER 1980 - JANUARY 1982

1. AUTHORITY.

a. Letter, US Department of Agriculture, Agricultural Research, Southern Region, Insects Affecting Man and Animals, Research Laboratory, Gainesville, Florida, 3 October 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 Administration, titled, Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

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

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent AI3-38271a.

4. SUMMARY OF FINDINGS. Hazard evaluation of the candidate repellent AI3-38271a, US Department of Agriculture Proprietary Chemical, was conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study, and Sprague-Dawley rats for determination of oral toxicity. 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.

Study No. 75-51-0281-82, Oct 80-Jan 82

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 AI3-38271a did not cause any irritation of the intact skin or of the skin surrounding an abrasion.	USAEHA Category I (ref Appendix A)
0.5 mL technical grade chemical applied to each of six rabbits.		
EYE IRRITATION STUDIES		
Rabbits		
Single 24-hour application of 0.1 mL technical grade chemical to one eye of each of six New Zealand White rabbits.	Chemical AI3-38271a produced mild injury to the cornea of rabbits.	USAEHA Category B (ref Appendix A)
APPROXIMATE LETHAL DOSE (ALD)		
Oral		
Rats (male) - no diluent	1276 mg/Kg	Chemical AI3-38271a is relatively nontoxic from accidental ingestion.

Study No. 75-51-0281-82, Oct 80-Jan 82

Test	Results	Interpretation
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 UV light (365 nm) for 30 minutes at a distance of 10-15 cm.	Chemical AI3-38271a did not produce a photochemical irritation reaction under test conditions.	Chemical AI3-38271a did not cause a photochemical irritation reaction under test conditions and is not expected to cause a photochemical irritation 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.	

Study No. 75-51-0281-82, Oct 80-Jan 82

Test	Results	Interpretation
SENSITIZATION STUDIES		
Guinea Pigs (Male)		
Intradermal injections of 0.1 mL of a 0.1 percent solution (w/v) of AI3-38271a 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 ten sensitizing doses over a 3-week period. After 2 weeks rest, they were challenged with ID injections of each test compound.	Challenge doses of AI3-38271a did not produce a sensitization reaction.	Chemical AI3-38271a did not produce sensitization reactions under test conditions and is not expected to produce sensitization reactions in man.
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 the guinea pigs respond to sensitizing agents.

* A known skin sensitizer.

Study No. 75-51-0281-82, Oct 80-Jan 82

5. CONCLUSION. Technical grade chemical AI3-38271a produced mild injury to the cornea of rabbits but did not cause any skin or photo-irritation, sensitization reaction, nor prove to be an acute ingestion hazard.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-38271a be approved for further testing as a candidate insect repellent.

Michael J. Topper

MICHAEL J. TOPPER, DVM
CPT, VC
Laboratory Animal Veterinary Officer
Toxicology Division

APPROVED:

Arthur H. McCreesh

ARTHUR H. McCREESH, Ph.D.
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 No. 75-51-0281-82, Oct 80-Jan 82

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.

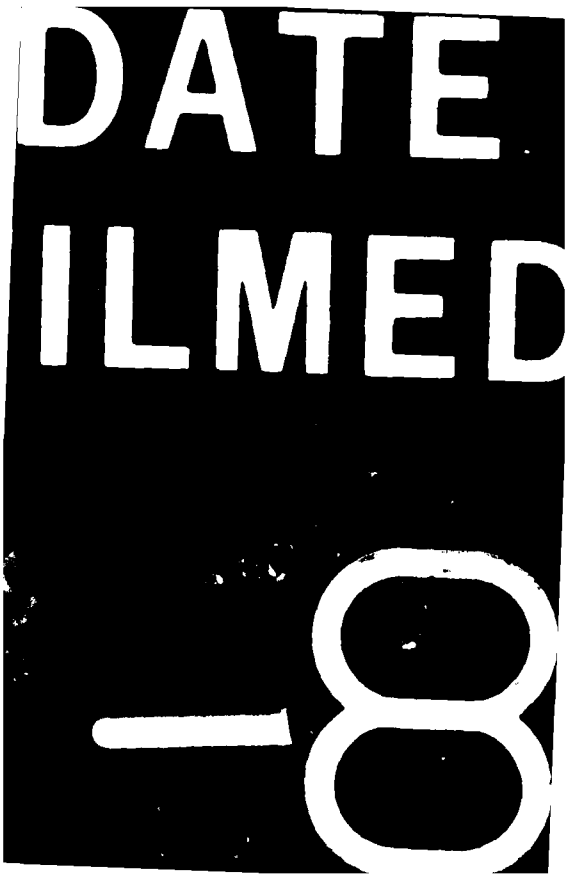
(2) Title 21, Code of Federal Regulations, 1981 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratories Studies.

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

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


DATE
ILMED
-8