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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT
REPELLENTS A13-3576. (U) ARMY ENVIRONMENTAL HYGIENE
AGENCY ABERDEEN PROVING GROUND MD R D RUSSELL JAN 86
USAEMA-75-51-0437-86

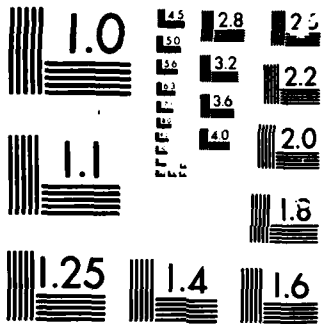
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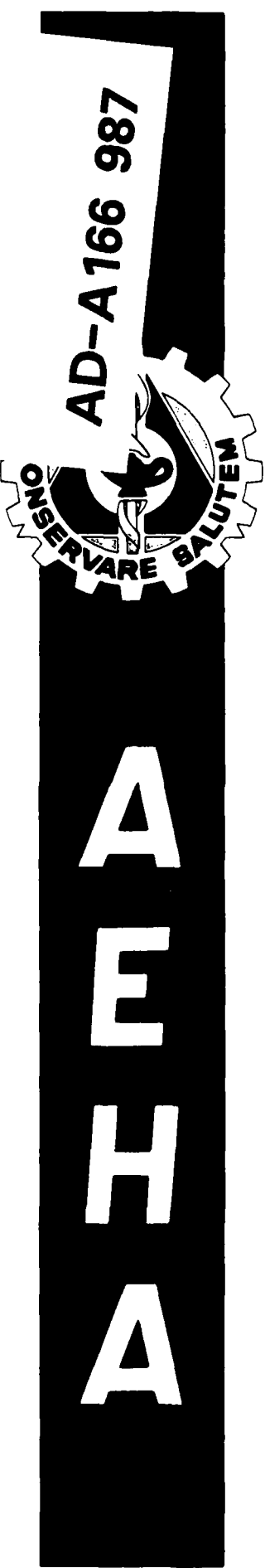




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**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

ABERDEEN PROVING GROUND, MD 21010-5422

TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENTS AI3-35768e&f, AI3-709486a,
AI3-39007a, AI3-38323b, AI3-38324b, AI3-38326b,
AI3-38304b, AI3-38321b, AI3-37487b
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0437-86, 75-51-0466-86, 75-51-0476-86,
75-51-0533-86, 75-51-0534-86, 75-51-0535-86,
75-51-0537-86, 75-51-0538-86, 75-51-0541-86

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SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

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	PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.
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11. TITLE (Include Security Classification) THEP of Candidate Insect Repellents AI3-35768 e and f, AI3-70948Ga, AI3-39007a, AI3-38323b, AI3-38324b, AI3-38326b, AI3-38304b, AI3-38321b, AI3-37487b, US Department of Agriculture Proprietary Chemicals Study Nos. 75-51-0437, 0466, 0476, 0533, 0534, 0535, 0537, 0538, 0541-86			
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FIELD	GROUP	SUB-GROUP	AI3-35768e and f
			AI3-70948Ga
			AI3-39007a
19. ABSTRACT (Continue on reverse if necessary and identify by block number) Lots e and f of AI3-35768 caused severe primary irritation and necrosis (AI3-35768f) of the intact and abraded skin of rabbits. When applied as a diluted ethanol solution AI3-35768e caused mild primary skin irritation. AI3-70948Ga and AI3-39007a caused no primary skin irritation but caused moderate to severe eye irritation. Chemical AI3-70948Ga was only slightly toxic to rats by the oral route (ALD 500mg/Kg) and was not a sensitizer within the limits of our test. AI3-38323b produced moderate primary skin irritation. Chemicals AI3-38324b, AI3-38326b, AI3-38304b, and AI3-38321b produced moderate to severe eye irritation with lesions which persisted at 7 days post application. AI3-38304 and AI3-38321b produced mild primary skin irritation while AI3-37487b produced severe primary skin irritation, necrosis, and eschar formation. These chemicals are not recommended for further entomological testing, however, if efficacy data should warrant, such chemicals could be resubmitted in a further purified form or at the intended use concentration.			
20. DISTRIBUTION / AVAILABILITY OF ABSTRACT <input checked="" type="checkbox"/> UNCLASSIFIED/UNLIMITED <input type="checkbox"/> SAME AS RPT. <input type="checkbox"/> DTIC USERS		21. ABSTRACT SECURITY CLASSIFICATION UNCLASSIFIED	
22a. NAME OF RESPONSIBLE INDIVIDUAL R. DAVID RUSSELL, CPT, VC		22b. TELEPHONE (Include Area Code) (301) 671-3627	22c. OFFICE SYMBOL HSHB-OT

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83 APR edition may be used until exhausted
All other editions are obsolete.SECURITY CLASSIFICATION OF THIS PAGE
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18. SUBJECT TERMS (Cont)

AI3-38323b

AI3-38324b

AI3-38326b

AI3-38304b

AI3-38321b

AI3-37487

Eye Irritation

Skin Irritation

Approximate Lethal Dose (ALD)

Guinea Pig Sensitivation Test (GPST)

Topical Hazard Evaluation Program

USDA Proprietary Chemicals



DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-8422

REPLY TO
ATTENTION OF

HSNB-OT

25 April 1986

SUBJECT: Topical Hazard Evaluation of Candidate Insect Repellents AI3-35768e&f, AI3-70948Ga, AI3-39007a, AI3-38323b, AI3-38324b, AI3-38326b, AI3-38304b, AI3-38321b, AI3-37487b, US Department of Agriculture Proprietary Chemicals, Study Numbers 75-51-0437-86, 75-51-0466-86, 75-51-0476-86, 75-51-0533-86, 75-51-0534-86, 75-51-0535-86, 75-51-0537-86, 75-51-0538-86, 75-51-0541-86

Executive Director
Armed Forces Pest Management Board
Forest Glenn Section, WRAMC
Washington, DC 20307


EXECUTIVE SUMMARY

The purpose and a summary of the 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 Repellents AI3-35768e&f, AI3-70948Ga, AI3-39007a, AI3-38323b, AI3-38324b, AI3-38326b, AI3-38304b, AI3-38321b, AI3-37487b by means of laboratory animal studies using Sprague-Dawley rats, New Zealand White rabbits, and albino Hartley guinea pigs.

b. Recommendations. Recommend that chemicals AI3-35768e&f, AI3-70948Ga, AI3-39007a, AI3-38323b, AI3-38324b, AI3-38326b, AI3-38304b, AI3-38321b, AI3-37487b be disapproved for further entomological testing. Should any of these chemicals show sufficient repellent activity to warrant further testing the chemical may be resubmitted in a further purified form or at the intended use concentration.

Enc1


N. DOE THOMPSON
Colonel, MC
Director, Occupational and
Environmental Health

CF:
HQDA(DASG-PSP) (w/enc1)
Cdr. HSC (HSCL-P) (w/enc1)
Dir, Advisory Ctr on Tox, NRC (2 cy) (w/enc1)
Comdt, AHS (HSHA-IPM) (w/enc1)
USDA, ARS (Dr. Terrence McGovern) (w/enc1)
USDA, ARS - Southern Region (w/enc1)
USDA, ARS - Southern Region (SGRD-DPM/COL Moussa) (w/enc1)



DEPARTMENT OF THE ARMY
 U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
 ABERDEEN PROVING GROUND, MARYLAND 21010-6422

REPLY TO
 ATTENTION OF

HSHB-OT

TOPICAL HAZARD EVALUATION PROGRAM
 OF
 CANDIDATE INSECT REPELLENTS AI3-35768e&f, AI3-70948Ga,
 AI3-39007a, AI3-38323b, AI3-38324b, AI3-38326b,
 AI3-38304b, AI3-38321b, AI3-37487b
 US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
 STUDY NOS. 75-51-0437-86, 75-51-0466-86, 75-51-0476-86,
 75-51-0533-86, 75-51-0534-86, 75-51-0535-86,
 75-51-0537-86, 75-51-0538-86, 75-51-0541-86

1. AUTHORITY.

- a. Letter, US Department of Agriculture-Agriculture Research, Northeastern Region, Beltsville Agricultural Research Center, Beltsville, Maryland, 9 May 1983.
- b. Letter, US Department of Agriculture-Agriculture Research Service, Southern Region, Insects Affecting Man and Animals Research Laboratory, Gainesville, Florida, 1 December 1983.
- c. Letter, US Department of Agriculture-Agricultural Research Service, Northeastern Region, Beltsville Agricultural Research Center, Beltsville, Maryland, 6 December 1986.
- d. Letter, US Department of Agriculture-Agricultural Research Service, Northeastern Region, Beltsville Agricultural Research Center, Beltsville, Maryland, 26 November 1984.
- e. 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, Agriculture Research, Science, and Education Administrations; titled Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

2. REFERENCES.

- a. Toxicology Division Standard Operating Procedures, US Army Environmental Hygiene Agency (USAEHA), 1981.
- b. Toxicology Division Topical Hazard Evaluation Program Procedural Guide, USAEHA, October 1985.



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Study Nos. 75-51-0437-86, 75-51-0466-86, 75-51-0476-86, 75-51-0533-86, 75-51-0534-86, 75-51-0535-86, 75-51-0537-86, 75-51-0538-86, 75-51-0541-86

3. PURPOSE. The purpose of this program is to provide guidance for the further testing of the candidate insect repellents AI3-35768e&f, AI3-70948Ga, AI3-39007a, AI3-39013a, AI3-38323b, AI3-38324b, AI3-38326b, AI3-38304b, AI3-38321b, AI3-37487b, US Department of Agriculture (USDA) Proprietary Chemicals.

4. MATERIALS AND METHODS.

a. Testing was conducted using New Zealand White rabbits, Sprague-Dawley rats, and Hartley albino guinea pigs. Rats were obtained from Charles River Laboratories, Wilmington, Massachusetts. Guinea Pigs were obtained from Hazelton-Dutchland Laboratories, Denver, Pennsylvania, and rabbits were obtained either from Hazelton-Dutchland Laboratories, Denver, Pennsylvania, or Buckshire Corporation, Perkasie, Pennsylvania.

b. Samples tested were synthesized by Dr. Terrence P. McGovern, Organic Chemical Synthesis Laboratory, USDA, Beltsville, Maryland or were submitted in confidence through USDA by Agriculture Canada (AI3-70948Ga). The last letter in the chemical designation signifies a specific batch, lot, or purification process. (For example, two lots of AI3-35768 were tested--AI3-35768e and AI3-35768f, however only one lot of AI3-70948Ga was tested.)

c. The Topical Hazard Evaluation Program (THEP) consists of five basic tests, Primary Dermal Irritation, Primary Eye Irritation, Photochemical Irritation, Guinea Pig Sensitization, and Approximate Lethal Dose determination. These tests are described in detail in reference 2b and were conducted as described in that reference. Additionally chemical AI3-35768e was submitted to an extra primary dermal irritancy test as a 25 percent w/v solution in 100 percent ethanol. The application in that case was unoccluded.

5. RESULTS.

a. AI3-35768. Both lots of chemical AI3-35768 (lots e and f) caused severe primary irritation of the intact and abraded skin of rabbits (Category IV, Appendix A). AI3-35768e was retested as a 25 percent w/v solution in 100 percent ethanol and caused only mild primary irritation (Category II, Appendix A) of the intact and abraded skin of rabbits and some scaling at the application sites. AI3-35768e was also subjected to the guinea pig sensitization test and was not a sensitizer within the limits of this test. Chemical AI3-35768f caused not only a severe primary irritation (Category IV, Appendix A) of intact and abraded rabbit skin but caused necrosis of the epidermis.

* 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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75-51-0534-86, 75-51-0535-86, 75-51-0537-86, 75-51-0538-86, 75-51-0541-86

b. AI3-70948Ga. Chemical AI3-70948Ga was furnished through the USDA by Agriculture Canada. This substance caused no primary irritation (Category I, Appendix A) of intact or abraded rabbit skin, and was not a sensitizer within the limits of our test. The Approximate Lethal Dose (ALD) by the oral route in rats was >5000 mg/kg. When instilled into rabbit eyes this chemical caused moderate to severe eye irritation (Category E, Appendix A) with lesions persisting at seven days post-application. Washing the eyes after instillation of the substance did not reduce the irritant effect on the eye.

c. AI3-39007a. Chemical AI3-39007a produced no primary irritation (Category I, Appendix A) of the intact and abraded skin of rabbits, but produced moderate to severe primary eye irritation (Category E, Appendix A) when instilled in rabbit eyes. Eye lesions persisted at seven days post-application, and washing did not reduce the irritation to the eye.

d. AI3-38323b. Chemical AI3-38323b produced moderate primary irritation (Category III, Appendix A) of the intact and abraded skin of rabbits. One test animal experienced heavy scurfing with minimal erythema at the application site seven days after application of the test substance.

e. AI3-38324b. Chemical AI3-38324b produced moderate to severe primary eye irritation (Category E, Appendix A) when instilled into rabbit eyes. Corneal scarring and vascularization were evident at seven days post-application and were indicative of probable permanent eye damage. Additionally a mild to moderate iritis developed 48 to 72 hours post-application. Washing after the application reduced the severity of the eye lesions.

f. AI3-38326b. Chemical AI3-38326b produced moderate to severe eye irritation (Category E, Appendix A) when instilled into rabbit eyes. Lesions from this irritation persisted at seven days post-application. Eyes that were washed after application appeared to be more mildly affected but there was insufficient difference to draw firm conclusions based on the small number of washed eyes (3) graded.

g. AI3-38304b. Chemical AI3-38304b produced mild primary irritation (Category II, Appendix A) to the intact and abraded skin of rabbits. This substance did however produce moderate to severe irritation (Category E, Appendix A) to the eyes of rabbits, and lesions persisted in the eyes at seven days post-application. Post-application eye washing made little or no difference in the severity of the eye lesions.


h. AI3-38321b. Chemical AI3-38321b produced mild primary irritation (Category II, Appendix A) of the intact and abraded skin of rabbits. When instilled into the eyes of rabbits this substance produced moderate to severe (Category E, Appendix A) eye irritation which persisted at seven days post-application. Eye washing had no effect on the severity of the eye lesions.

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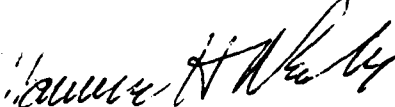
i. AI3-37487b. Chemical AI3-37487b produced severe primary irritation, necrosis, and eschar formation (Category IV, Appendix A) when applied to the intact and abraded skin of rabbits.

6. RECOMMENDATIONS.

a. Recommend that chemicals AI3-35768e and f, AI3-70948Ga, AI3-39007a, AI3-38323b, AI3-38324b, AI3-38326b, AI3-38304b, AI3-38321b, and AI3-37487b be disapproved for further entomological testing. If any of the above chemicals have such entomological efficacy as to warrant further testing, they should be resubmitted in a further purified form or at the intended use concentration.


R. DAVID RUSSELL
CPT, VC
Laboratory Animal Veterinary
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. 75-51-0437-86, 75-51-0466-86, 75-51-0476-86, 75-51-0533-86,
75-51-0534-86, 75-51-0535-86, 75-51-0537-86, 75-51-0538-86, 75-51-0541-86

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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