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ARMY ENVIRONMENTAL HYGIENE AGENCY ABERDEEN PROVING GR--ETC F/G 6/20
TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)
MAY 80 A W SINGER

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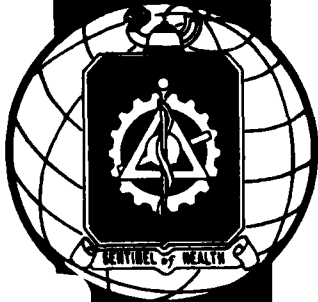
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**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

ABERDEEN PROVING GROUND, MD 21010

11 May 80 *4258*

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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENTS
AI3-16734-(T,11,78)-Ga, AI3-37519, AI3-37521, AI3-37529a,
AI3-37531a, AND AI3-37532a

US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUNDS,
STUDY NOS. 75-51-0109-80, 75-51-0111-80, 75-51-0113-80
75-51-0151-80, 75-51-0152-80 AND 75-51-0153-80
JUNE 1978 - MAY 1980

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Allen W. Singer

Final report, June 11 - May 1980

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REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Insect repellent compound AI3-16734-(1,11,78)-Ga was tested for primary irritation by application to clipped dorsal skin and to the eyes of New Zealand White rabbits. Although it was only mildly irritating to the skin, eye applications resulted in rapid systemic absorption and sudden generalized convulsions in both rabbits used, with one of the rabbits dying overnight. This response was also seen with a chemically related candidate repellent AI3-37528a (rejected September 1979). Five additional homologs of AI3-16734-(1,11,78)-Ga currently await testing. With the concurrence of the originator, the Organic Synthesis Labora-		

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20. tory, Beltsville Research Center, Department of Agriculture, all six related compounds are recommended for withdrawal from future consideration as candidate insect repellents. These are:

- (1) AI3-16734(1,11,78)-Ga,
- (2) AI3-37519,
- (3) AI3-37521,

- (4) AI3-37529a,
- (5) AI3-37531a, AND
- (6) AI3-37532a,

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DEPARTMENT OF THE ARMY CPT Singer/cf/AUTOVON
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY 584-3980
ABERDEEN PROVING GROUND, MARYLAND 21010

8 JUL 1980

HSE-LT-T/WP

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents
AI3-16734-(1,11,78)-Ga, AI3-37519, AI3-37521, AI3-37529a,
AI3-37531a, and AI3-37532a, US Department of Agriculture
Proprietary Compounds, Study Nos. 75-51-0109-80, 75-51-0111-80,
75-51-0113-80, 75-51-0151-80, 75-51-0152-80 and 75-51-0153-80, June
1978 - May 1980

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

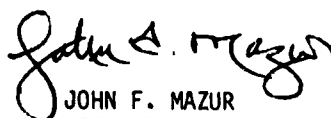
A summary of the pertinent findings and recommendations of the inclosed
report follows:

Insect repellent compound AI3-16734-(1,11,78)-Ga was tested for primary
irritation by application to clipped dorsal skin and to the eyes of New
Zealand White rabbits. Although it was only mildly irritating to the skin,
eye applications resulted in rapid systemic absorption and sudden generalized
convulsions in both rabbits used, with one of the rabbits dying overnight.
This response was also seen with a chemically related candidate repellent
AI3-37528a (rejected September 1979). Five additional homologs of
AI3-16734-(1,11,78)-Ga currently await testing. With the concurrence of the
originator, the Organic Synthesis Laboratory, Beltsville Research Center,
Department of Agriculture, all six related compounds are recommended for
withdrawal from future consideration as candidate insect repellents. These
are:

AI3-16734(1,11,78)-Ga
AI3-37519
AI3-37521

AI3-37529a
AI3-37531a
AI3-37532a

FOR THE COMMANDER:


JOHN F. MAZUR

MAJ, MSC
Director, Laboratory Services

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USDA, ARS-Southern Region

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

HSE-LT-T/WP

TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENTS
AI3-16734-(1,11,78)-Ga, AI3-37519, AI3-37521, AI3-37529a,
AI3-37531a, AND AI3-37532a
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUNDS
STUDY NOS. 75-51-0109-80, 75-51-0111-80, 75-51-0113-80
75-51-0151-80, 75-51-0152-80 AND 75-51-0153-80
JUNE 1978 - MAY 1980

1. AUTHORITY.

a. Letters, US Department of Agriculture - Agricultural Research Service, Southern Region, Insects Affecting Man Research Laboratory, Gainesville, Florida, 30 June 1978 [AI3-16734-(1,11,78)-Ga, AI3-37519, and AI3-37521]; and 13 September 1978 (AI3-37529a, AI3-37531a, and AI3-37532a).

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. REFERENCES.

a. Toxicology Division Procedural Guide, US Army Environmental Hygiene Agency (USAEHA), 1972, revised 1976.

b. Letter, USDA-Agricultural Research Service, Northeastern Region, Beltsville Agricultural Research Center, Beltsville, Maryland, 15 May 1979, subject: Chemicals Structurally Related to AI3-37528.

c. Letter, this Agency, HSE-LT-T/WP, subject: Topical Hazard Evaluation Program of Candidate Insect Repellent AI3-37528a, 12 September 1979.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellents AI3-16734-(1,11,78)-Ga, AI3-37519, AI3-37521, AI3-37529a, AI3-37531a, and AI3-37532a.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent AI3-16734-(1,11,78)-Ga, conducted by this Agency using New Zealand White rabbits for skin and eye studies. 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) 74-23, revised 1978.

† The experiments 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
<u>SKIN IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hour application to intact and abraded skin of New Zealand rabbits.	Compound AI3-16734-(1,11,78)-Ga caused mild primary irritation to intact and abraded skin.	USAEHA Category II (ref Appendix).
0.5 mL technical grade compound applied to each of six rabbits.		
<u>EYE IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hour application of 0.1 mL technical grade compound to one eye of each of six New Zealand White rabbits.	Compound AI3-1734-(1,11,78)-Ga caused generalized convulsions in two of two rabbits within 1 minute of application. After 2 minutes, both rabbits became stiff and prostrate for 35 minutes; rabbits were very depressed throughout the rest of the day; one rabbit eventually fully recovered; the other rabbit died 20 hours after application.	Compound AI3-16734-(1,11,78)-Ga is extremely toxic to rabbits and rapidly absorbed through mucous membranes. The possibility of a similar toxicity to man requires extreme caution when handling this compound.

Study Nos. 75-51-0109-80, 75-51-0111-80, 75-51-0113-80, 75-51-0151-80,
75-51-0152-80 and 75-51-0153-80, Jun 78 - May 80

5. DISCUSSION. The generalized convulsions caused by 0.1 mL technical grade AI3-16734-(1,11,78)-Ga were similar to those caused by administration of a structurally related compound, AI3-37528a (paragraph 2c). In a letter dated 15 May 1979 (paragraph 2b) from the Beltsville Agricultural Research Center various USDA proprietary compounds structurally related to AI3-37528 were named. It was also stated that if one or two gave unsatisfactory preliminary hazard evaluations it would be best to withdraw the entire lot. The six subject repellents of this report are all named as related to the highly toxic AI3-37528a.

6. CONCLUSION. The technical grade compound AI3-16734-(1,11,78)-Ga is extremely toxic to rabbits and rapidly absorbed through mucous membranes.

7. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-16734-(1,11,78)-Ga, AI3-37519, AI3-37521, AI3-37529a, AI3-37531a, and AI3-37532a, and any other compounds structurally similar to AI3-37528, be withdrawn from further consideration as candidate repellents. In addition, extreme care should be used when handling any of these compounds.

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Study Nos. 75-51-0109-80, 75-51-0111-80, 75-51-0113-80, 75-51-0151-80,
75-51-0152-80 and 75-51-0153-80, Jun 78 - May 80

APPENDIX

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.