UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY
ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-36323
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND
STUDY NUMBER 75-51-0832-79
OCTOBER 1975 - JUNE 1979

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Topical Hazard Evaluation Program of Candidate Insect Repellent AI3-36323, US Department of Agriculture Proprietary Compound No. 75-51-0832-79, October 1975 - June 1979

PERFORMING ORGANIZATION NAME AND ADDRESS
US Army Environmental Hygiene Agency Aberdeen Proving Ground, MD 21010

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SUPPORTING NOTES

KEYWORDS (Continue on reverse side if necessary and identify by block number)
Topical Hazard Evaluation
skin irritation
USDA Proprietary Compound
eye irritation
AI3-36323candidate repellent

ABSTRACT (Continue on reverse side if necessary and identify by block number)
A hazard evaluation of AI3-36323 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compound caused moderate corneal and conjunctival irritation of the eyes of rabbits, but no primary skin irritation. It did not cause a photochemical sensitization reaction or sensitize guinea pigs, and did not demonstrate an acute ingestion hazard.
20. it is suggested it be purified through activated charcoal before being resubmitted in its proposed use formulation and/or concentration.
SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent
A13-36323, US Department of Agriculture Proprietary Compound, Study
No. 75-51-0832-79, October 1975 - June 1979

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

A hazard evaluation of A13-36323 was performed by means of laboratory
animal studies using rats, rabbits, and guinea pigs. The technical grade
compound caused moderate corneal and conjunctival irritation of the eyes of
rabbits, but no primary skin irritation. It did not cause a photochemical
sensitization reaction or sensitize guinea pigs, and did not demonstrate an
acute ingestion hazard. Based on the eye irritation reaction, it was
recommended that no further testing be performed on A13-36323. However, if
this compound presents a significant improvement in pest repellent properties
over existing compounds, it is suggested it be purified through activated
charcoal before being resubmitted in its proposed use formulation and/or
concentration.

FOR THE COMMANDER:

BRENDAN E. JOYCE, PH.D.
LTC(P), MSC
Director, Laboratory Services

1 Incl
as (5 cy)
1. AUTHORITY.


   b. Memorandum of Understanding between the Department of the Army, Office of The Surgeon General; the US Army Health Services Command; the US Army Environmental Hygiene Agency; the Armed Forces Pest Control Board, and the US Department of Agriculture, effective 1970 with Amendment No. 1 effective August 1974.

2. REFERENCES.


3. PURPOSE. The purpose of this study is to provide guidance for further entomological testing of the candidate insect repellent A13-36323.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent A13-36323, USDA Proprietary Compound, was conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for 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) 74-23, revised in 1972, and in 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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### SKIN IRRITATION STUDIES*

**Rabbits**

Single 24-hour application to intact and abraded skin of New Zealand White rabbits.  

0.5 ml technical grade compound applied to each of six rabbits.  

Compound A13-36323 produced no primary irritation of the intact skin and the skin surrounding an abrasion.

**EYE IRRITATION STUDIES**

**Rabbits**

Single 24-hour application of 0.1 ml technical grade compound to one eye of each of six New Zealand White rabbits.

Compound A13-36323 produced moderate irritation and injury to the cornea and conjunctiva in all rabbits tested.

### APPROXIMATE LETHAL DOSE (ALD)

**Oral**

Rats (male) - no diluent  

ALD >2200 mg/kg  

Presents little lethal hazard from accidental ingestion.

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*Data reported in USAEHA report (reference paragraph 2a)
Guinea Pigs

Intradermal injections of 0.1 ml of a 0.1 percent suspension (w/v) of AI3-36323, or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.

Ten test guinea pigs received ten sensitizing doses over a 3-week period. After 2 weeks' rest, they were challenged with a 0.1 percent solution of AI3-36323.

Challenge dose of test compound (last intradermal injection) did not produce a sensitization reaction. Compound AI3-36323 did not produce a sensitization reaction under these test conditions and is not expected to produced a sensitization reaction in man.

Ten positive control guinea pigs received ten sensitizing doses of DNCB over a 3-week period. After 2 weeks' rest, they were challenged with a 0.1 percent suspension of DNCB.

* A known skin sensitizer.
PHOTOCHEMICAL SKIN IRRITATION STUDIES

**Rabbits**

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A single application (0.05 ml) of a 25 percent (w/v) solution of the compound and of 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.</td>
<td>A 25 percent solution of Al3-36323 in ethanol did not cause a photochemical irritation reaction under test conditions.</td>
<td>Compound Al3-36323 did not cause a photochemical irritation reaction under test conditions and is not expected to cause a photochemical irritation in humans.</td>
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</table>

**Control**

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Following UV exposures of the rabbits, 0.05 ml of test compound, 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.</td>
<td>Mild primary irritation was caused by all ethanol solutions of Al3-36323 (both control and test applications).</td>
<td>Ethanol solutions may be irritating to some humans.</td>
</tr>
</tbody>
</table>
5. CONCLUSION. The candidate insect repellent AI3-36323 has a potential for causing moderate irritation and damage to corneal and conjunctival tissue and does not qualify as a nonhazardous repellent.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-36323, USDA Proprietary Compound, not be approved for further testing as a candidate insect repellent. However, if this compound presents a significant improvement in pest repellent properties over existing compounds, it is suggested it be purified through activated charcoal before being resubmitted in its proposed use formulation and/or concentration.

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APPROVED:

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APPENDIX

TOPOCAL 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.