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

TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-36423
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND
STUDY NO. 75-51-0892-79
MAY 1976 - JUNE 1979

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# Topical Hazard Evaluation Program

**Type of Report & Period Covered**
Final, May 76 - Jun 79

**Performing Organization Report Number**

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Unclassified

**Distribution Statement (of this report)**
Approved for public release; distribution unlimited.

**Abstract**
A preliminary hazard evaluation of AI3-36423 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compound caused mild primary skin irritation and mild corneal and conjunctival irritation in rabbits, but no phototoxirritation. It did not sensitize guinea pigs or prove to be an acute ingestion hazard. Ethanol solutions of AI3-36423 also caused mild skin irritation.

**Keywords**
- USDA Proprietary Compound
- Candidate Repellent
- AI3-36423
- Topical Hazard Evaluation
- Eye irritation
- Skin irritation

**Description**

**Topical Hazard Evaluation Program**

**Study No:** 75-51-0892-79, May 1976 - June 1979

**USDA Proprietary Compound**

**Candidate Repellent**

**AI3-36423**

**Topical Hazard Evaluation**

**Eye irritation**

**Skin irritation**

**USDA-75-51-0892-79**

**Final Rept. May 76-Jun 79,**

**Supplementary Notes**

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**All**
SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent
Al3-36423, US Department of Agriculture Proprietary Compound, Study
No. 75-51-0892-79, May 1976 - June 1979

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

A preliminary hazard evaluation of Al3-36423 was performed by means of
laboratory animal studies using rats, rabbits and guinea pigs. The technical
grade compound caused mild primary skin irritation and mild corneal and
conjunctival irritation in rabbits, but no photoirritation. It did not
sensitize guinea pigs or prove to be an acute ingestion hazard. Ethanol
solutions of Al3-36423 also caused mild skin irritation. It was recommended
that Al3-36423, USDA Proprietary Compound, be approved for further testing.
Consideration should be given to the observed irritation caused by both
technical and ethanol solutions when formulating this as a repellent.
Persons experiencing such irritation should wash the compound off as soon as
possible.

FOR THE COMMANDER:

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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 REPELLENT A13-36423
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND
STUDY NO. 75-51-0892-79
MAY 1976 - JUNE 1979

1. AUTHORITY.
   a. Letter, US Department of Agriculture - Agricultural Research Service,
      Southern Region, Insects Affecting Man-Research Laboratory, Gainesville,
      Florida, 5 May 1976.
   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 1, effective
      August 1974.

2. REFERENCE. Toxicology Division Procedural Guide, USAEHA, 1972, revised
   1976.

3. PURPOSE. The purpose of this program is to provide guidance for further
   entomological testing of the candidate insect repellent A13-36423.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent
   A13-36423, USDA Proprietary Compound, 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:*t

* 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,
† 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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**Study No. 75-51-0892-79, May 76 - Jun 79**

**TABULAR PRESENTATION OF DATA**

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SKIN IRRITATION STUDIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbits</td>
<td>Single 24-hour application to intact and abraded skin of New Zealand White Rabbits. Compound A13-36423 caused mild primary irritation of the intact skin and of the skin surrounding an abrasion.</td>
<td>USAEHA Category II (ref Appendix).</td>
</tr>
<tr>
<td></td>
<td>0.5 ml technical grade compound applied to each of six rabbits.</td>
<td></td>
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<tr>
<td><strong>EYE IRRITATION STUDIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbits</td>
<td>Single 24-hour application of 0.1 ml technical grade compound to one eye of each of six New Zealand White rabbits. Compound A13-36423 caused mild corneal and conjunctival irritation to five of six rabbits.</td>
<td>USAEHA Category C (ref Appendix).</td>
</tr>
<tr>
<td><strong>APPROXIMATE LETHAL DOSE (ALD)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>Rats (male) - no diluent ALD&gt;4900 mg/kg</td>
<td>Presents little lethal hazard from accidental ingestion.</td>
</tr>
<tr>
<td>Test</td>
<td>Results</td>
<td>Interpretation</td>
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<tr>
<td>PHOTOCHEMICAL SKIN IRRITATION STUDIES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A single 0.05 ml application of a 25 percent (w/v) solution of the compound 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.</td>
<td>A 25 percent solution of AI3-36423 in ethanol did not cause a photochemical irritation reaction under test conditions.</td>
<td>Compound AI3-36423 did not cause a photochemical irritation reaction under test conditions and is not expected to cause a photochemical irritation in humans.</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
</tr>
<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>Ethanol solutions of AI3-36423 caused mild irritation at both UV and non UV sites.</td>
<td>Ethanol solutions of AI3-36423 may be irritating to human skin.</td>
</tr>
</tbody>
</table>
### SENSITIZATION STUDIES

**Guinea Pigs (Male)**

Intradermal injections of 0.1 ml of a 0.1 percent suspension (w/v) of A13-36423 or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.

Ten test guinea pigs were given ten sensitizing doses over a 3-week period. After 2 weeks' rest, they were challenged with ID injections of test compound. Challenge dose of A13-36423 did not produce a sensitization reaction.

Compound A13-36423 did not produce a sensitization reaction under test conditions and is not expected to produce a sensitization reaction in man.

Ten positive control guinea pigs were sensitized over 3 weeks to 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.
5. CONCLUSION. Technical grade compound AI3-36423 caused mild primary skin irritation and mild corneal and conjunctival irritation, but no photosensitization. It did not sensitize guinea pigs or prove to be an acute ingestion hazard. Ethanol solutions of AI3-36423 also caused mild skin irritation, and may cause a similar irritation on man.

6. RECOMMENDATION. Under the provision of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-36423, USDA Proprietary Compound, be approved for further testing as a candidate insect repellent. Consideration should be given the skin irritation caused by both the technical and ethanol solutions of AI3-36423 when working with or formulating it as a repellent. Persons experiencing irritation should wash the compound off with copious amounts of water.

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Toxicology Division

APPROVED:

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Chief, Toxicology Division
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.