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

TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT A13-36424
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND
STUDY NO. 75-51-0893-79
MAY 1976 - JUNE 1979

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    eye irritation
    skin irritation
    Topical Hazard Evaluation

20. **ABSTRACT (Continue on reverse side if necessary and identify by block number)**
    A preliminary hazard evaluation of AI3-36424 was performed by means of laboratory animal studies using rats, rabbits and guinea pigs. The technical grade compound did not cause any primary or photoirritation in rabbits, or any eye irritation. It did not sensitize guinea pigs or prove to be an acute ingestion hazard.

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SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent
AI3-36424, US Department of Agriculture Proprietary Compound, Study
No. 75-51-0893-79, May 1976 - June 1979

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

A preliminary hazard evaluation of AI3-36424 was performed by means of
laboratory animal studies using rats, rabbits and guinea pigs. The technical
grade compound did not cause any primary or photoirritation in rabbits, or
any eye irritation. It did not sensitize guinea pigs or prove to be an acute
ingestion hazard. It was recommended that AI3-36424, USDA Proprietary
Compound, be approved for further testing as a candidate insect repellent.

FOR THE COMMANDER:

BRENDAN E. JOYCE, Ph.D.
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Director, Laboratory Services

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Cdr, HSC (HSPA-P)
Dir, Advisory Ctr on TOX, NRC
Supt, AHS (HSA-IPM)
USDA, ARS (Dr. Terrence McGovern)
USDA, ARS-Southern Region
TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-36424
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND
STUDY NO. 75-51-0893-79
MAY 1976 - JUNE 1979

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 1, effective August 1974.


3. PURPOSE. The purpose of this study is to provide guidance for further entomological testing of the candidate insect repellent AI3-36424.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent AI3-36424, 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

________________________________________________________________________

* 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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TABULAR PRESENTATION OF DATA

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>SKIN IRRITATION STUDIES</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Rabbits</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single 24-hour application</td>
<td>Compound A13-36424 did</td>
<td>USAEHA Category I</td>
</tr>
<tr>
<td>to intact and abraded skin</td>
<td>not cause irritation</td>
<td>(ref Appendix).</td>
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<tr>
<td>of New Zealand White rabbits</td>
<td>of the intact skin or</td>
<td></td>
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<tr>
<td></td>
<td>to the skin surrounding an abrasion.</td>
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<tr>
<td>0.5 ml technical grade</td>
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<td></td>
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<tr>
<td>compound applied to each</td>
<td></td>
<td></td>
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<tr>
<td>of six rabbits.</td>
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<td></td>
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<tr>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>Single 24-hour application</td>
<td>Compound A13-36424 did</td>
<td>USAEHA Category A</td>
</tr>
<tr>
<td>of 0.1 ml technical grade</td>
<td>not cause irritation</td>
<td>(ref Appendix).</td>
</tr>
<tr>
<td>compound to one eye of</td>
<td>to corneal or conjunctival</td>
<td></td>
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<tr>
<td>each of six New Zealand</td>
<td>tissues.</td>
<td></td>
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<tr>
<td>White rabbits.</td>
<td></td>
<td></td>
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<tr>
<td>APPROXIMATE LETHAL DOSE (ALD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Oral</strong></td>
<td></td>
<td></td>
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<tr>
<td>Rats (male) - no diluent</td>
<td>ALD = 2200 mg/kg</td>
<td>Presents little lethal hazard from</td>
</tr>
<tr>
<td></td>
<td></td>
<td>accidental ingestion.</td>
</tr>
</tbody>
</table>
### PHOTOCHEMICAL SKIN IRRITATION STUDIES

#### Rabbits

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. Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.

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<td>A 25 percent solution of Al3-36424 in ethanol did not cause a photochemical irritation reaction under test conditions.</td>
<td>Compound Al3-36424 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>
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<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>
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</tbody>
</table>
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SENSITIZATION STUDIES

Guinea Pigs (Male)

Intradermal injections of 0.1 ml of a 0.1 percent suspension (w/v) of AI3-36424 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 AI3-36424 did not produce a sensitization reaction.

Compound AI3-36424 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.
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5. CONCLUSION. Technical grade compound AI3-36424 did not cause primary or photoirritation to the skin of rabbits, and caused no eye irritation. It did not sensitize guinea pigs, or prove to be an acute ingestion hazard.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-36424, USDA Proprietary Compound, be approved for further testing as a candidate insect repellent.

ALLEN W. SINGER
CPT, VC
Laboratory Veterinary Officer
Toxicology Division

APPROVED:

ARTHUR A. McCREESEd, Ph.D.
Chief, Toxicology Division
APPENDIX

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.