UNCLASSIFIED

TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT—ETC(U)

OCT 77 M H WEEKS, B J DESENA

USAEHA-51-0859-78
TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-36028
6-DECALACTONE
STUDY NO. 51-0859-78
MARCH 1976 - OCTOBER 1977

Approved for public release; distribution unlimited
A preliminary hazard evaluation of A13-36028 was performed by means of laboratory animal studies using Sprague-Dawley rats, New Zealand White rabbits, and Hartley guinea pigs. The technical grade compound produced some corneal opacity and mild conjunctival eye irritation, but no skin irritation or phototoxic irritation in rabbits; no sensitization reactions in guinea pigs; and did not demonstrate an acute ingestion hazard in rats. It is recommended that A13-36028 be approved for further testing as a candidate insect repellent.
SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent A13-36028, 6-Decalactone, Study No. 51-0859-78, March 1976 - October 1977

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

A preliminary hazard evaluation of A13-36028 was performed by means of laboratory animals studies using Sprague-Dawley rats, New Zealand White rabbits, and Hartley guinea pigs. The technical grade compound produced some corneal opacity and mild conjunctival eye irritation, but no skin irritation or photochemical irritation in rabbits; no sensitization reactions in guinea pigs; and did not demonstrate an acute ingestion hazard in rats. It is recommended that A13-36028, 6-decalactone, be approved for further testing as a candidate insect repellent.

FOR THE COMMANDER:

BRENDAN E. JOYCE, P.H.D.
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HQDA (DASG-HCH)
Cdr, HSC (HSPA-H)
Dir, Advisory Ctr on Tox, NRC
Supt, AHS (HSA-RHE)
USDA (Dr. Terrence McGovern)
TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT A13-36028
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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.


3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent A13-36028.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate insect repellent A13-36028 (6-decalactone) 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.*


† The experiments reported herein were performed in animal facilities fully accredited by the American Association for 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><strong>SKIN IRRITATION STUDIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single 24-hour application to intact and abraded skin of New Zealand White rabbits.</td>
<td>Compound AI3-36028 produced no primary irritation of intact skin or to the skin surrounding an abrasion.</td>
<td>USAEHA Category I (ref Appendix).</td>
</tr>
<tr>
<td>0.5 ml technical grade compound applied to each of six rabbits.</td>
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<tr>
<td><strong>EYE IRRITATION STUDIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single 24-hour application of 0.1 ml technical grade compound to one eye of each of six New Zealand White rabbits.</td>
<td>Compound AI3-36028 produced a mild corneal injury in five of six rabbits, and, in addition, produced mild conjunctival injury in six out 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></td>
<td></td>
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<tr>
<td>Rats (male) - in corn oil</td>
<td>ALD &gt;4300 mg/kg</td>
<td>Presents little lethal hazard from acute accidental ingestion.</td>
</tr>
</tbody>
</table>
**PHOTOCHEMICAL SKIN IRRITATION STUDIES**

### Rabbits

A single application (0.05 ml) of a 25 percent (w/v) solution of the compound (A13-36028) and of 10 percent (w/v) oil of Bergamot (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. A 25 percent solution of A13-36028 in ethanol did not cause a photochemical irritation reaction under test conditions, and is not expected to cause a photochemical irritation in humans.

### Control

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 reactions at 24, 48 and 72 hours. Positive control application and irradiation caused greater irritant effects than on unirradiated areas.

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<tr>
<td>PHOTOCHEMICAL SKIN IRRITATION STUDIES</td>
<td>Rabbits</td>
<td>Compound A13-36028 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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<tr>
<td>Control</td>
<td></td>
<td>Positive control application and irradiation caused greater irritant effects than on unirradiated areas.</td>
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<tr>
<td><strong>SENSITIZATION STUDIES</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Guinea Pigs (Male)</strong></td>
<td></td>
<td></td>
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<tr>
<td>Intradermal injections of 0.1 ml of a 0.1 percent suspension (w/v) of A13-36028 or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.</td>
<td>Challenge dose (last intradermal injection) of test compound did not produce a sensitization reaction.</td>
<td>Compound A13-36028 did not produce a sensitization reaction under these test conditions and is not expected to produce a sensitization reaction in man.</td>
</tr>
<tr>
<td>Ten test guinea pigs received and challenged with a 0.1 percent solution of A13-36028.</td>
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<tr>
<td>Ten positive control guinea pigs received and challenged with 0.1 percent suspension of DNCB.</td>
<td>Positive control (DNCB) produced a marked sensitization reaction in 10 out of 10 guinea pigs.</td>
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</tr>
</tbody>
</table>

* A known skin sensitizer.
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5. CONCLUSION. The candidate insect repellent A13-36028, δ-decalactone, has a potential for causing mild injury to the cornea and conjunctiva, but presented little acute hazard from acute skin contact, photochemical irritation reaction, sensitization reaction, or from acute ingestion.

6. Recommendation. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that A13-36028, δ-decalactone, be approved for further testing as a candidate insect repellent. The compound should be used with caution around the eyes.

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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.
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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.