CANDIDATE INSECT REPELLENT AI3-36538-Ga
1-(CYCLOHEXYLCARBONYL)-4-METHYL PIPERIDINE

ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND

1976
TOPICAL HAZARD EVALUATION
OF
CANDIDATE INSECT REPELLENT AI3-36538-Ga
1-(CYCLOHEXYLCARBONYL)-4-METHYL PIPERIDINE
STUDY NUMBER 51-0815-77
OCTOBER 1975 - JULY 1976
Approved for public release; distribution unlimited.
Topical Hazard Evaluation of Candidate Insect Repellent AI3-36538-Ga

Approved for public release; distribution unlimited.

A hazard evaluation of AI3-36538-Ga was conducted using New Zealand White rabbits for skin and eye studies; Hartley guinea pigs for a skin sensitization study; and Sprague-Dawley, Wistar-derived rats for determination of oral toxicity. It was recommended that AI3-36538-Ga be approved for further testing as a candidate insect repellent.
DEPARTMENT OF THE ARMY
U.S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

HSE-LT/WP

27 DEC 1976

TOPICAL HAZARD EVALUATION
OF
CANDIDATE INSECT REPELLENT AI3-36538-Ga
1-(CYCLOHEXYLCARBONYL)-4-METHYL PIPERIDINE
STUDY NUMBER 51-0815-77
OCTOBER 1975 - JULY 1976

1. AUTHORITY.


3. PURPOSE. The purpose of this study is to provide guidance for further entomological testing of the candidate insect repellent AI3-36538-Ga.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent AI3-36538-Ga 1-(Cyclohexylcarbonyl)-4-methyl piperidine 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, Wistar-derived rats for determination of oral toxicity. A tabular presentation of animal toxicity data developed in this Agency follows:*
Study No. 51-0815-77, Oct 75 - Jul 76

**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><strong>Rabbits</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single 24-hour application</td>
<td>AI3-36538-Ga produced no primary irritation of the</td>
<td>USAEHA Category I (ref Appendix)</td>
</tr>
<tr>
<td>to intact and abraded skin of New Zealand White rabbits.</td>
<td>intact skin or the skin surrounding an abrasion.</td>
<td></td>
</tr>
<tr>
<td>0.5 ml technical grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>compound applied to each of six rabbits.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EYE IRRITATION STUDIES</strong></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>AI3-36538-Ga produced moderate injury to the cornea and, in addition, some injury to the conjunctiva in six of six rabbits at 24-hours after application and for 7 days thereafter.</td>
<td>USAEHA Category E (ref Appendix)</td>
</tr>
<tr>
<td>of 0.1 ml of technical grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>compound to one eye of each of six New Zealand White rabbits.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>APPROXIMATE LETHAL DOSE (ALD)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Oral</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rats (males) - corn oil diluent.</td>
<td>ALD &gt;4926 mg/kg</td>
<td>Presents little lethal hazard from acute accidental ingestion.</td>
</tr>
</tbody>
</table>
# TABULAR PRESENTATION OF DATA

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHOTOCHEMICAL SKIN IRRITATION STUDIES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbits</td>
<td>A single application (0.05 ml) of a 25 percent (w/v) solution of the compound (AI3-36538-2a) 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>Compound AI3-36538-Ga did not cause a photochemical irritation reaction under test conditions.</td>
</tr>
<tr>
<td>Control</td>
<td>Following UV exposure of the rabbits 0.05 ml of the test compound, positive control and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for irritation at 24, 48 and 72 hours.</td>
<td>Positive control application and irradiation caused greater irritant effects than in unirradiated areas.</td>
</tr>
</tbody>
</table>


Study No. 51-0815-77, Oct 75 - Jul 76

**TABULAR PRESENTATION OF DATA**

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SENSITIZATION STUDIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guinea Pigs (Male)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intradermal injections of 0.1 ml of a 0.1 percent suspension (w/v) of AI3-36538-Ga or dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.</td>
<td>Challenge dose of test compound (last intradermal injection) did not produce a sensitization reaction.</td>
<td>Compound AI3-36538-Ga did not produce a sensitization reaction under these conditions and is not expected to produce a sensitization reaction in man.</td>
</tr>
<tr>
<td>Ten test guinea pigs received and challenged with an 0.1 percent solution of AI3-36538-Ga.</td>
<td></td>
<td></td>
</tr>
<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 ten out of ten guinea pigs.</td>
<td></td>
</tr>
<tr>
<td>Ten cage control guinea pigs; five receiving challenge dose of test compound without prior sensitizing dose; and five receiving challenge dose of DNCB without prior sensitizing dose.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*A known skin sensitizer.*
5. CONCLUSION. No primary skin irritation was caused by AI3-36538-Ga either as the technical grade compound or as a 25 percent solution in ethyl alcohol. However, this compound caused moderate damage to the cornea and conjunctiva and should not be allowed to get into the eyes.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (reference paragraph 1b), it is recommended that AI3-36538-Ga
l-(cyclohexylcarbonyl)-4-methyl piperidine be approved for further testing as a candidate insect repellent.

Maurice H. Weeks  
Chief, Toxicity Evaluation Branch  
Toxicology Division

Brenda J. DeSena  
PFC  
Veterinarian Specialist  
Toxicology Division

APPROVED:  

Arthur J. McCrystal, Ph.D  
Chief, Toxicology Division

Brendan E. Joyce, Ph.D  
LTC, MSC  
Director, Laboratory Services
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.