**Title:** Topical Hazard Evaluation Program of Candidate Insect Repellent AI3-20351 (10.9.80)

**US Department of Agriculture Proprietary Chemical**

**Performing Organization Name and Address:**
US Army Environmental Hygiene Agency
Aberdeen Proving Ground, MD 21010

**Author(s):**
Michael J. Topper, CPT, VC
John G. Harvey, Jr.

**Abstract:**

Preliminary hazard evaluations of AI3-20351 (10.9.80) was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade chemical produced mild injury to the cornea of rabbits. It did not cause skin irritation or prove to be acutely toxic by ingestion. Chemical AI3-20351 (10.9.80) produced a moderate sensitization reaction in 6 out of 10 guinea pigs. Based on the skin sensitization, it is recommended that this chemical not be approved for further testing as a candidate.
SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent A13-20351 (10.9.80), US Department of Agriculture Proprietary Chemical, Study No. 75-51-0286-82, Feb 81 - Jan 82

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

Preliminary hazard evaluations of A13-20351 (10.9.80) was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade chemical produced mild injury to the cornea of rabbits. It did not cause skin irritation or prove to be acutely toxic by ingestion.

Chemical A13-20351 (10.9.80) produced a moderate sensitization reaction in 6 out of 10 guinea pigs. Based on the skin sensitization, it is recommended that this chemical not be approved for further testing as a candidate insect repellent.

FOR THE COMMANDER:

[Signature]

JOHN F. MAZUR
LTC, MSC
Director, Laboratory Sciences

CF:
HQDA (DASG-PSP) wo incl
Cdr, HSC (HSPA-P)
Dir, Advisory Cen on Tox, NRC
Comdt, AHS (HSHA-IPM)
USDA, ARS (Dr. Terrence McGovern)
USDA, ARS-Southern Region

[Distribution and Availability Codes]

[Code: A]
TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT
A13-20351 (10.9.80)
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICAL
STUDY NO. 75-51-0286-82
FEBRUARY 1981 - JANUARY 1982

1. AUTHORITY.


b. Memorandum of Understanding between the US Army Environmental Hygiene Agency; the US Army Health Services Command; the Department of The Army, Office of The Surgeon General; the Armed Forces Pest Control Board; and the US Department of Agriculture, Agricultural Research, Science and Education Administrations, titled, Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

2. REFERENCE. Toxicology Division Standing Operating Procedures, US Army Environmental Hygiene Agency (USAHEA), 1981.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent A13-20351 (10.9.80).

4. SUMMARY OF FINDINGS. Hazard evaluations of the candidate repellent A13-20351 (10.9.80), US Department of Agriculture (USDA) Proprietary Chemical 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:*

* 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) 80-23, revised 1978.
† The studies reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

Approved for public release, distribution unlimited.
Study No. 75-51-0286-82, Feb 81 - Jan 82

TABLE. 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>Rabbits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single 24-hour application</td>
<td>Chemical AI3-20351 (10.9.80) did not</td>
<td>USAEHA Category I</td>
</tr>
<tr>
<td>to intact and abraded skin</td>
<td>cause any irritation of the intact skin or</td>
<td>(ref Appendix A)</td>
</tr>
<tr>
<td>of New Zealand White rabbits.</td>
<td>of the skin surrounding an abrasion.</td>
<td></td>
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<tr>
<td>0.5 mL technical grade</td>
<td></td>
<td></td>
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<tr>
<td>chemical applied to each</td>
<td></td>
<td></td>
</tr>
<tr>
<td>of six rabbits.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EYE IRRITATION STUDIES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single 24-hour application</td>
<td>Chemical AI3-20351 (10.9.80) produced mild</td>
<td>USAEHA Category B</td>
</tr>
<tr>
<td>of 0.1 mL technical grade</td>
<td>injury to the cornea.</td>
<td>(ref Appendix A)</td>
</tr>
<tr>
<td>chemical to one eye of each</td>
<td>Application followed by washing did not</td>
<td></td>
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<tr>
<td>of nine New Zealand</td>
<td>cause any irritation to the eyes of rabbits.</td>
<td></td>
</tr>
<tr>
<td>White Rabbits. Three of the</td>
<td></td>
<td></td>
</tr>
<tr>
<td>nine rabbits had the eye</td>
<td></td>
<td></td>
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<tr>
<td>flushed with warm water for</td>
<td></td>
<td></td>
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<tr>
<td>1 minute 25 seconds after</td>
<td></td>
<td></td>
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<tr>
<td>application.</td>
<td></td>
<td></td>
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<tr>
<td>APPROXIMATE LETHAL DOSE (ALD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rats (male)-no diluent</td>
<td>4311 mg/kg</td>
<td>AI3-20351 (10.9.80) should</td>
</tr>
<tr>
<td></td>
<td></td>
<td>not be acutely toxic by</td>
</tr>
<tr>
<td></td>
<td></td>
<td>accidental ingestion.</td>
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</tbody>
</table>
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<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
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</tr>
</thead>
<tbody>
<tr>
<td>SENSITIZATION STUDIES</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 solution (w/v) of A13-20351 (10.9.80) or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.</td>
<td>Challenge doses of A13-20351 (10.9.80) produced a sensitization reaction in 6 out of 10 guinea pigs.</td>
<td>Chemical A13-20351 (10.9.80) produced a moderate sensitization reaction under test conditions and may produce sensitization reaction in man.</td>
</tr>
<tr>
<td>Ten test guinea pigs for each chemical were given ten sensitizing doses over a 3-week period. After 2 weeks rest, they were challenged with ID injections of test chemical.</td>
<td>Challenge dose of DNCB in positive control guinea pigs produced a marked sensitization reaction in 10 out of 10 guinea pigs.</td>
<td>DNCB produced a marked reaction, indicating the guinea pigs respond to sensitizing agents.</td>
</tr>
<tr>
<td>Ten positive control guinea pigs were sensitized over 3 weeks with DNCB. After 2 weeks rest, they were challenged with ID injections of DNCB.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* A known skin sensitizer.

5. CONCLUSION. Technical grade chemical A13-20351 (10.9.80) produced mild injury to the cornea of rabbits. It did not cause skin irritation or prove to be acutely toxic by ingestion. Chemical A13-20351 (10.9.80) produced a moderate sensitization reaction in guinea pigs and may be expected to cause such a reaction in humans. The Analytical Quality Assurance review is listed in Appendix B.
6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b); it is recommended that A13-20351 (10.9.80) not be approved for further testing as a candidate insect repellent.

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APPROVED:

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APPENDIX A

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.

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APPENDIX B

ANALYTICAL QUALITY ASSURANCE

The Quality Assurance Office certifies the following with regard to this study:

This study was conducted in accordance with:

1) Standing Operating Procedures developed by the Toxicology USAEHA.


Facilities were inspected during its operational phase to insure that the information presented in this report accurately reflects the raw data recorded during the course of conducting the study.

PAUL V. SNEERINGER, Ph.D.
Chief, Analytical Quality Assurance Office
DATE
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