MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS USA
UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY
ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENTS
Ai3-38352a, Ai3-38354a, Ai3-38355a,
Ai3-38357a, Ai3-38360a, AND Ai3-38361a
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0371-84, 75-51-0372-84,
75-51-0373-84, 75-51-0374-84, 75-51-0376-84,
AND 75-51-0377-84
MAY 1982 - NOVEMBER 1983

Approved for public release; distribution unlimited.
## Chemical A13-38352a produced mild irritation of the intact skin and of the skin surrounding an abrasion. Chemicals A13-38354a, A13-38357a, A13-38360a, and A13-38361a produced no primary irritation of the intact skin and no more than mild irritation of the skin surrounding an abrasion. Chemicals A13-38357a and A13-38360a were noninjurious to the eye. Chemical A13-38352a produced mild injury to the cornea. Chemicals A13-38354a, A13-38357a, and A13-38361a produced mild injury to the cornea and, in addition, some injury to the conjunctiva. These chemicals did not elicit a photochemical irritation reaction or produce sensitization. All chemicals were relatively nontoxic by ingestion.
SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents
Study Nos. 75-51-0371-84, 75-51-0372-84, 75-51-0373-84, 75-51-0374-84,
75-51-0376-84, and 75-51-0377-84, May 1982 - November 1983

EXECUTIVE SUMMARY

The purpose, essential findings, and major recommendations of the enclosed
copy of the report follow:

a. Purpose. The purpose of this program is to provide guidance for
further entomological testing of candidate insect repellents A13-38352a,
A13-38354a, A13-38355a, A13-38357a, A13-38360a, and A13-38361a by means of
laboratory studies using New Zealand White rabbits, Sprague-Dawley rats,
and albino Hartley guinea pigs.

b. Essential Findings. Chemical A13-38352a produced mild irritation
of the intact skin and the skin surrounding an abrasion. The other
chemicals produced no primary irritation of the intact skin and no greater
than mild primary irritation of the skin surrounding an abrasion.
Chemicals A13-38357a and A13-38360a were noninjurious to the eye. Chemical
A13-38352a produced mild injury to the cornea. Chemicals A13-38354a,
A13-38355a, and A13-38361a produced mild injury to the cornea. These chemicals did not exhibit
any photochemical irritation reaction or produce sensitization. All six were
relatively nontoxic by ingestion.

c. Major Recommendations. Recommend that chemicals A13-38352a,
A13-38354a, A13-38355a, A13-38357a, A13-38360a, and A13-38361a be approved
for further entomological testing as candidate insect repellents.

FOR THE COMMANDER:

[Signature]
JOEL C. GAVDOSS, M.D.
Colonel, MC
Director, Occupational and Environmental Health

CF:
HQDA (DASG-PSP) wo incl
Cdr, HSC (HSAP-A)
Comdt, AHS (HSHA-P)
Dir, Advisory Commission, NRC (2 cy)
USDA, ARS (Dr. Terrence McGovern)
USDA, ARS-Southern Region
Cdr, USAMRDC, [SGRDP-DWH/LTC(P) Reinert]
TOPOICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENTS
AI3-38352a, AI3-38354a, AI3-38355a,
AI3-38357a, AI3-38360a, AND AI3-38361a
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0371-84, 75-51-0372-84,
75-51-0373-84, 75-51-0374-84, 75-51-0376-84,
AND 75-51-0377-84
MAY 1982 - NOVEMBER 1983

1. AUTHORITY.
   a. Letter, US Department of Agriculture - Agricultural Research,
      Southern Region, Insects Affecting Man and Animals Research Laboratory,
   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

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

3. PURPOSE. The purpose of this program is to provide guidance for
   further entomological testing of candidate insect repellents AI3-38352a,
   AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a, and AI3-38361a, US
   Department of Agriculture (USDA) Proprietary Chemicals.

4. SUMMARY OF FINDINGS. Hazard evaluations of candidate insect repellents
   AI3-38352a, AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a, and AI3-38361a,
   USDA Proprietary Chemicals were conducted by this Agency using New Zealand
   White rabbits, Sprague-Dawley rats, and albino Hartley guinea pigs. A
   tabular presentation of animal toxicity data developed at 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.
TABLE. PRESENTATION OF DATA.

<table>
<thead>
<tr>
<th>TEST</th>
<th>RESULTS</th>
<th>INTERPRETATION</th>
</tr>
</thead>
</table>

**SKIN IRRITATION STUDIES**

Rabbits

- Single 24-hour application to intact and abraded skin of New Zealand White rabbits.
- 0.5 mL technical grade chemical applied to each of six rabbits.
- Chemicals A13-38354a, A13-38355a, A13-38357a, A13-38360a and A13-38361a produced no primary irritation of the intact skin and no greater than mild irritation of the skin surrounding an abrasion.
- Chemical AI3-38352a produced mild primary irritation of the intact skin and of the skin surrounding an abrasion.

**EYE IRRITATION STUDIES**

Rabbits

- Single 24-hour application of 0.1 mL technical grade chemical to one eye of each of nine New Zealand White rabbits. Three of the nine rabbits had the eye flushed with warm water for 1 minute, 25 seconds after application.
- Chemical AI3-38357a and A13-38360a were noninjurious to the eyes of rabbits.
- Chemical AI3-38352a produced mild injury to the cornea.
- Chemicals A13-38354a, A13-38355a, and A13-38361a produced mild injury to the cornea and, in addition, some injury to the conjunctiva.

**APPROXIMATE LETHAL DOSE**

Oral

- Rats (Male) - No Diluent
- A13-38352a >5,000 mg/kg: These chemicals were relatively nontoxic by ingestion.
- A13-38354a ≥3,333 mg/kg
- A13-38355a 3,333 mg/kg
- A13-38357a ≥2,222 mg/kg
- A13-38360a ≥3,333 mg/kg
- A13-38361a ≥3,333 mg/kg
PHOTOCHEMICAL SKIN IRRITATION STUDIES

Rabbits

A single 0.05 mL application of a 25% (w/v) solution of each test chemical and of 10% (w/v) Oil of Bergamot (positive control) in 95% ethyl alcohol was applied to the intact skin of six rabbits. Five minutes after application the rabbits were exposed to ultraviolet (UV) light (365 nm) for 30 minutes at a distance of 10-15 cm.

Control

Following UV exposures of the rabbits, 0.05 mL of the test chemical, positive control (Oil of Bergamot) 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.

SENSITIZATION STUDIES

Guinea Pigs (Male)

Intradermal (ID) injections of 0.1 mL of a minimally irritating concentration of each tested chemical or of dinitrochlorobenzene (DNCB)† in a mixture containing 1 volume of propylene glycol and 29 volumes of saline. Ten guinea pigs were given 10 sensitizing doses over a 3-week period. After a 2-week rest, they were challenged with an ID injection of the test chemical.

Challenge doses of chemicals A13-38352a, A13-38354a, A13-38355a, A13-38357a, A13-38360a, and A13-38361a did not produce sensitizing reactions.

These chemicals did not produce sensitizing reactions under test conditions and are not expected to cause sensitization in humans.

† A known skin sensitizer
Study Nos. 75-51-0371-84, 75-51-0372-84, 75-51-0373-84, 75-51-0374-84, 75-51-0376-84, 75-51-0377-84, May 82 - Nov 83

<table>
<thead>
<tr>
<th>TEST</th>
<th>RESULTS</th>
<th>INTERPRETATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ten positive control guinea pigs were sensitized over a 3-week period. After a 2-week rest, they were challenged with ID injections of DNCB.</td>
<td>Challenge doses 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 that these guinea pigs respond to sensitizing agents.</td>
</tr>
</tbody>
</table>

5. CONCLUSION. Chemical AI3-38352a produced mild irritation of the intact skin and of the skin surrounding an abrasion. Chemicals AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a, and AI3-38361a produced no primary irritation of the intact skin and no more than mild irritation of the skin surrounding an abrasion. Chemicals AI3-38357a and AI3-38360a were noninjurious to the eye. Chemical AI3-38352a produced mild injury to the cornea. Chemicals AI3-38354a, AI3-38355a, and AI3-38361a produced mild injury to the cornea and, in addition, some injury to the conjunctiva. These chemicals did not elicit a photochemical irritation reaction or produce sensitization. All six were relatively nontoxic by ingestion. These studies were monitored by the Analytical Quality Assurance Office (see Appendix B).

6. RECOMMENDATIONS. Recommend USDA Proprietary Chemicals AI3-38352a, AI3-38354a, AI3-38355a, AI3-38357a, AI3-38360a and AI3-38361a be approved for further testing as candidate insect repellents (under the provisions of the Memorandum of Understanding, paragraph 1b, this report).

JOHN V. WADE, DVM  
CPT(P), VC  
Laboratory Animal Veterinary Officer  
Toxicology Division

JOHN G. HARVEY, JR.  
Biological Laboratory Technician  
Toxicology Division

APPROVED:

MAURICE H. WEEKS  
Chief, Toxicology Division
APPENDIX A

TOPOICAL 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.
APPENDIX B

ANALYTICAL QUALITY ASSURANCE

The Analytical Quality Assurance Office certifies the following:

a. These studies were conducted in accordance with:

   (1) Standing Operating Procedures developed by the Toxicology Division, USAEHA.

   (2) Title 21, Code of Federal Regulations (CFR), 1983 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratory Studies.

   (3) Proposed Rule, Pesticide Programs; Good Laboratory Practice Standards; Final Rule, 48 Federal Register (FR) 53946-53969, 29 November 1983.

b. Facilities were inspected during its operational phase to ensure compliance with paragraph a above.

c. The information presented in this report accurately reflects the raw data generated during the course of conducting these studies.

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