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

TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENTS
AI3-38420b, AI3-38421b, AI3-38422b, AND AI3-38423b
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0451-84 THRU 75-51-0454-84
JUNE - OCTOBER 1983

Approved for public release; distribution unlimited.
Candidate Insect Repellents A13-38420b, A13-38421b, A13-38422b, and A13-38423b, US Department of Agriculture Proprietary Chemicals, Study No. 75-51-0451-84 thru 75-51-0454-84, June - October 1983

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Total report number 75-51-0451-84 thru 75-51-0454-84, June - October 1983

A13-38420b, A13-38421b, A13-38422b, and A13-38423b produced moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion. The response was characterized by ulceration, excoriation, acanthosis, and dermal thickening at the sites of application.
SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents AI3-38420b, AI3-38421b, AI3-38422b, and AI3-38423b, US Department of Agriculture Proprietary Chemicals, Study Nos. 75-51-0451-84 thru 75-51-0454-84, June - October 1983

EXECUTIVE SUMMARY

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

a. Purpose. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellents AI3-38420b, AI3-38421b, AI3-38422b, and AI3-38423b by means of laboratory animal studies using New Zealand White rabbits.

b. Essential Findings. Chemicals AI3-38420b, AI3-38421b, AI3-38422b, and AI3-38423b produced moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion. The response was characterized by ulceration, excoriation, acanthosis, and dermal thickening at the sites of application.

c. Major Recommendations. Recommend proprietary chemicals AI3-38420b, AI3-38421b, AI3-38422b, and AI3-38423b be disapproved for further entomological testing.

FOR THE COMMANDER:

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OF
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US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY Nos. 75-51-0451-84 THRU 75-51-0454-84
JUNE - OCTOBER 1983

1. AUTHORITY.

a. Letter, US Department of Agriculture, Agricultural Research
   Service, Northeastern Region, Beltsville Agricultural Research Center,
   Beltsville, Maryland, 10 June 1983.

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 Toxi-

2. REFERENCE. Toxicology Division Topical Hazard Evaluation Program

3. PURPOSE. The purpose of this program is to provide guidance for
   further entomological testing of the candidate insect repellents AI3-38420b,
   AI3-38421b, AI3-38422b, and AI3-38423b, US Department of Agriculture (USDA)
   Proprietary Chemicals.

4. SUMMARY OF FINDINGS. Hazard evaluation of the candidate insect
   repellents AI3-38420b, AI3-38421b, AI3-38422b, and AI3-38423b, USDA
   Proprietary Chemicals, were conducted by this Agency using New Zealand
   White rabbits for primary skin irritation studies. A tabular presentation
   of animal toxicity data developed in this Agency follows:*t

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* 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.

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TABLE. PRESENTATION OF DATA

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
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<tbody>
<tr>
<td>Skin Irritation Studies</td>
<td></td>
<td></td>
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<tr>
<td><strong>Rabbits</strong></td>
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<tr>
<td>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.</td>
<td>Chemicals A13-38420b, A13-38421b, A13-38422b and A13-38423b produced moderate to severe primary irritation of the intact skin surrounding an abrasion. This response was characterized by ulceration, excoriation, acanthosis, and dermal thickening.</td>
<td>USAHA Category IV (reference Appendix A)</td>
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5. CONCLUSION. Chemicals A13-38420b, A13-38421b, A13-38422b, and A13-38423b produced moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion. This damage was apparent both grossly and microscopically at 7 days postapplication. These studies were monitored by the Analytical Quality Assurance Office (see Appendix B).

6. RECOMMENDATION. Recommend proprietary chemicals A13-38420b, A13-38421b, A13-38422b, and A13-38423b be disapproved for further entomological testing (under the provisions of the Memorandum of Understanding, paragraph 1b, this report).

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CPT(P), VC
Laboratory Animal Veterinary Officer
Toxicology Division

APPROVED:

MAURICE H. WEEKS
Chief, Toxicology Division
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 corneal. 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

The US Dept. of Agriculture Proprietary Chemical Study Numbers would not be known by anyone in the public domain who acquired this document. The document should remain for unlimited distribution per Capt. John V. Wade, AEHA