THE PRIMARY DERMAL IRRITATION RESULTING FROM THE ABRASIVE ACTION ETC(U)

UNCLASSIFIED

LETTERMAN ARMY INST OF RESEARCH PRESIDIO OF SAN FRANCISCO

SEP 81 J T FRUIN

LAIR-81-25TN

NL
The Primary Dermal Irritation resulting from the abrasive action when using the M-258A-1 Decontamination Kit (Study 6).

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Fort Detrick
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A modified Draize test was used to determine the level of primary dermal irritation attributable to the physical abrasion resulting from the wiping action needed for decontamination with the Prototype M-258A-1 Decontamination Kit. Scores recorded were below those considered to be caused by a primary irritant.
TECHNICAL NOTE NO. 81–25TN

PRIMARY DERMAL IRRITATION RESULTING FROM THE ABRASIVE ACTION WHEN USING THE M-258A-1 DECONTAMINATION KIT (Study 6)

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TOXICOLOGY GROUP,
DIVISION OF RESEARCH SUPPORT

SEPTEMBER 1981

LETTERMAN ARMY INSTITUTE OF RESEARCH  PRESIDIO OF SAN FRANCISCO  CALIFORNIA 94129
Primary Dermal Irritation GLP Study Report

TESTING FACILITY: Letterman Army Institute of Research
Presidio of San Francisco, CA 94129

SPONSOR: Letterman Army Institute of Research
Presidio of San Francisco, CA 94129

PROJECT: Medical Defense Against Chemical Agents 612772.875.

GLP STUDY NUMBER: 81023

STUDY DIRECTOR AND PRINCIPAL INVESTIGATOR: LTC (P) John T. Fruin, DVM, PhD, VC, Diplomate of American College of Veterinary Preventive Medicine.

RAW DATA: A copy of the final report, study protocol, raw data, and standard operating procedures will be retained in the LAIR Archives.

TEST SUBSTANCES: A. Normal physiological saline on gauze sponges were used to wipe the backs of rabbits for 1 minute.

B. Normal physiological saline on gauze sponges were used to wipe the backs of rabbits for 3 minutes.

C. Normal physiological saline on gauze sponges were used to wipe the back of rabbits for 4 minutes.

D. Control (no treatment)


PURPOSE: The purpose of this study was to determine the primary dermal irritation caused by the abrasive action when using the M-258A-1 Decontamination Kit (occlusive modified Draize).
ACKNOWLEDGMENTS

The authors wish to thank LTC Kenneth Black MD, MC; CPT Martha A. Hanes DVM, VC; SSG Lance White; PFC Evelyn Zimmerman; and Carolyn Lewis, MS; for assistance in performing the research, and for advice in scoring the irritation reactions. The authors also wish to thank E. Houston, PhD, MS; LTC R. Howarth, VMD, VC; M. Mershon, VMD; of the U.S. Army Biomedical Laboratory Edgewood Arsenal, Aberdeen, MD, for providing background information.
Signatures of Principal Scientists Involved In The Study

I, the undersigned, believe the study, GLP number 81023, described in this report to be scientifically sound and the results and interpretation to be valid. The study was conducted to comply, to the best of our ability, with the Good Laboratory Practice Regulations for Nonclinical Laboratory Studies outlined by the Food and Drug Administration.

JOHN T. FRUIN DVM, PhD DATE
LTC (P), VC
Study Director and Principal Investigator
MEMORANDUM FOR RECORD

SUBJECT: Report of GLP Compliance

I hereby certify that in relation to LAIR GLP study 81023 the following inspections were made:

1. July 1981
2. July 1981

Routine inspections with no adverse findings are reported quarterly, thus these inspections are also included in the Oct 81 report to management and the Study Director.

John C. Johnson
CPT, MS
Quality Assurance Officer
PRIMARY DERMAL IRRITATION RESULTING FROM THE ABRASIVE ACTION
WHEN USING THE M-258A-1 DECONTAMINATION KIT (Study 6)

An evaluation of the Prototype M-258A-1 Decontamination Kit for
primary dermal irritation potential by using the modified Draize test
(1) was recently completed (2). That evaluation produced evidence of
severe irritation potential. Further testing was deemed necessary to
determine the kit's irritation potential under conditions of proposed
field usage.

Deviation from GLP standards

Rather than applying liquid test substance on gauze taped to the
skin, the skin was wiped for 1, 3, and 4 minutes with saline
impregnated gauze. Chemical analysis were not conducted except for
measuring pH. Chemical composition was considered to be that printed
on the outer container. Compound stability, the compound was assumed
to be stable under conditions of storage and use. The purity of the
compound was assumed to be that printed on the container.

Chemical Data

Chemical Name: Physiologic Saline
CAS: N/A
Molecular Structure: \(H_2O\) and \(NaCl\)
Molecular Weight: 18.016 and 39.34
pH: 5.0 ± 2
Physical state: clear liquid, colorless, and odorless
Boiling point: 100°C
Compound density: 1.0
Contaminates: unknown
Formulation: 99.1% \(H_2O\) 0.9% \(NaCl\)
Manufacturer: Traverol Laboratories, Deerfield, IL 60015
Manufacturer Lot No: 2C65581
Objective

The objective of this study was to determine the primary dermal irritation caused by the abrasive action when using the Prototype M-258A-1 Decontamination Kit as it is expected to be used in the field. Test sites were covered with a water imperious material for 24 hours (occluded).

METHODS

Historical Listing of Study Events

30 June 1981 Animals were weighed and sites for exposure were randomized. Animals were clipped and exposure sites marked.

1 July 1981 Animals were weighed and dosed.

1-15 July 1981 Animals were observed daily, only significant or abnormal observations were recorded.

2 July 1981 Bandages removed. 24 hr postexposure score.

4 July 1981 72-hr postexposure score.

8 July 1981 7-day postexposure score, weight taken.

15 July 1981 Animals were scored 14-day postexposure and weights taken. Animals were removed from the study.

Animal Data

Animal: New Zealand White Rabbits

Sex: Female and Male

Source: Elkhorn Rabbitry

Pre-test Conditioning:

A. Animals were transferred from the Division of Ocular Hazards and rested for several weeks.
B. Animals were close clipped and test areas marked.

Method of Randomization: Manual, Latin Square, SOP-OP-STX-34

Number of Animals on test: 6 animals - each animal had 4 test sites and received each of the three test treatments and a control with no treatment.

Age of animals at start of study: young adults

Weight Range: 3-4 kg

Condition of animals at start of study: normal

Identification System: ear as per SOP-OP-ARG-1, except the number was applied with an indelible ink felt pen rather than a tattoo.

Environmental Conditions

Caging: Number/cage = 1; Type cage used = stainless steel, wire bottom, battery type, no bedding, automatic flushing.

Diet: Purina Certified Rabbit Chow 5322 (approximately 110 g) was fed per day supplemented with about 45 g of fresh carrots.

Water: Central line to cage battery with automatic lick dispensers.

Temperature: 70 ± 5 F (21 ± 3 C).

Relative Humidity: 50 ± 5%.

Photoperiod: 0530 - 2000 hr/day (14 1/2 hr light).

Dosing Levels

A. Approximately 0.03-0.1 ml wiped for 1 minute
B. Approximately 0.03-0.1 ml wiped for 3 minutes
C. Approximately 0.03-0.1 ml wiped for 4 minutes
D. Control: Nothing was applied.

Dosing Procedures

Method and frequency of administration were dictated by
SOP-OP-STX-34. The backs of the animals were close clipped and divided into quadrants designated I,II,III and IV (SOP-OP-STX-34). Areas I and IV were intact on all animals, and areas II and III were abraded by making two perpendicular scratches in the stratum corneum of the skin about 1 1/2 inch long, using an escarifier. The four application sites were about 10 cm apart. A standard latin square table was used to randomize the test sites (SOP-OP-STX-34).

Test substance impregnated pads were wiped over the test sites for 1,3 and 4 minutes. The rabbits were then wrapped in a water impervious material, which was secured with elastic tape.

RESULTS

Scoring

Six animals were exposed to the chemicals. Animals were scored at 24 and 72 hr, 7 and 14 days for edema/erythema (Table 1). Tabular data appear in Appendix A. Abraded areas (sites II and III) and intact areas (sites I and IV) were graded separately as well as together. The scores obtained were used for a basis for categorization. Primary irritation potential values were calculated from the 24 and 72-hr scores.
TABLE 1
EVALUATION OF SKIN REACTIONS (3)

<table>
<thead>
<tr>
<th>Erythema and Eschar Formation</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No erythema</td>
<td>0</td>
</tr>
<tr>
<td>Very slight erythema (barely perceptible)</td>
<td>1</td>
</tr>
<tr>
<td>Well-defined erythema</td>
<td>2</td>
</tr>
<tr>
<td>Moderate-to-severe erythema</td>
<td>3</td>
</tr>
<tr>
<td>Severe erythema (beet redness) to slight eschar formation (injurious in depth)</td>
<td>4</td>
</tr>
<tr>
<td>Possible total erythema score</td>
<td>4*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Edema Formation</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No edema</td>
<td>0</td>
</tr>
<tr>
<td>Very slight edema (barely perceptible)</td>
<td>1</td>
</tr>
<tr>
<td>Slight edema (edges of area well defined by definite raising)</td>
<td>2</td>
</tr>
<tr>
<td>Moderate edema (edges raised approximately 1 mm)</td>
<td>3</td>
</tr>
<tr>
<td>Severe edema (raised more than 1 mm and extending beyond area of exposure)</td>
<td>4</td>
</tr>
<tr>
<td>Possible total edema score</td>
<td>4*</td>
</tr>
<tr>
<td>Possible total score for primary irritation</td>
<td>8</td>
</tr>
</tbody>
</table>

* Any skin reaction more serious than severe erythema, severe edema, vesiculation, ulceration, or necrosis places the chemical in Category IV.
Compounds producing combined averages (intact and abraded scores) of 0.0-2.0 are considered nonirritating (Category I), if the intact score is 0.5 or less. (Category assignment and interpretation, A. H. McCreesh, personnel communication 1980.)

Table 2 demonstrates the primary irritation indexes for the exposed areas.

**Table 2**

**PRIMARY DERMAL IRRITATION INDEX**

**ABRASIVE POTENTIAL OF THE M-258A-1 DECONTAMINATION KIT.**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Intact Score*</th>
<th>Abraded Score</th>
<th>Combined Score</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wipe 1 minute</td>
<td>0.25</td>
<td>0.25</td>
<td>0.25</td>
<td>I</td>
</tr>
<tr>
<td>Wipe 3 minutes</td>
<td>0.33</td>
<td>0.83</td>
<td>0.58</td>
<td>I</td>
</tr>
<tr>
<td>Wipe 4 minutes</td>
<td>0.50</td>
<td>0.86</td>
<td>0.75</td>
<td>I</td>
</tr>
<tr>
<td>Control</td>
<td>0.50</td>
<td>0.00</td>
<td>0.25</td>
<td>I</td>
</tr>
</tbody>
</table>

* If intact score is less than 0.5, compounds are considered non-irritating (Category I).

**DISCUSSION AND CONCLUSIONS**

The abrasive action caused by wiping the skin of rabbit for 1, 3, and 4 minutes did not produce scores high enough to be considered irritating.

**RECOMMENDATIONS**

Recommendations will be made after the current series of studies are completed.
REFERENCES

1. DRAIZE, J., H.Z. WOODARD, and H.O. CALVERY. Method for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J Pharmacol Exp Ther 83:377-390, 1944


Summary of Primary Skin Irritation Test Data

Page

APPENDIX A-1 Saline 1 min 10
APPENDIX A-2 Saline 3 min 11
APPENDIX A-3 Saline 4 min 12
APPENDIX A-4 Control 13

APPENDIX A

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TABLE A-1
Summary of Primary Skin Irritation Test Data

GLP Study No. B1023  Chemical Name  Conc  Solvent  Amt Applied  Code
Date of Application 1 July 1981  Saline 1 min  NA  NA  0.03-0.1 ml  A
Principal Investigator LTC FRUIN

Irritation Scores

<table>
<thead>
<tr>
<th>Rabbit No.</th>
<th>Site</th>
<th>Erythema 24 hr</th>
<th>Edema 24 hr</th>
<th>Site</th>
<th>Erythema 24 hr</th>
<th>Edema 24 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>F8100086</td>
<td>IV</td>
<td>0</td>
<td>0</td>
<td>III</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>F8100087</td>
<td>IV</td>
<td>0</td>
<td>0</td>
<td>III</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100088</td>
<td>IV</td>
<td>0</td>
<td>0</td>
<td>III</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100092</td>
<td>I</td>
<td>0</td>
<td>0</td>
<td>III</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100097</td>
<td>IV</td>
<td>0</td>
<td>0</td>
<td>III</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Total: a+b = 2

Intact Score = $c_1^{1/2} \times$ No. of Sites on test

Abraded Score = $c_{A}^{1/2} \times$ No. of Sites on test

Total Score = 2 x No. of Sites on test

Primary Skin Irritation Index Category 1

Remarks:

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### TABLE A-2
Summary of Primary Skin Irritation Test Data

GLP Study No. 81023  
Chemical Name  
Conc  
Solvent  
Amt Applied  
Code  

Date of Application 1 July 1981  
Saline 3 min  
NA  
NA  
0.03-0.1 ml  
B  

Principal Investigator LTC FRUIN  

### Irritation Scores

<table>
<thead>
<tr>
<th>Rabbit No.</th>
<th>Site</th>
<th>Erythema 24 hr</th>
<th>Edema 24 hr</th>
<th>Site</th>
<th>Erythema 24 hr</th>
<th>Edema 24 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>F8100086</td>
<td></td>
<td></td>
<td></td>
<td>III</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100087</td>
<td>IV</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100088</td>
<td>I</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100092</td>
<td></td>
<td></td>
<td></td>
<td>II</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100097</td>
<td></td>
<td></td>
<td></td>
<td>III</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>F8100099</td>
<td>IV</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Total:  

\[
\begin{align*}
\text{Intact Score} &= \frac{C^I}{2 \times \text{No. of Sites on test}} \\
\text{Abraded Score} &= \frac{C^A}{2 \times \text{No. of Sites on test}} \\
\text{Total Score} &= \frac{2}{2} 	imes 7112
\end{align*}
\]

Primary Skin Irritation Index Category I  
Remarks:  

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TABLE A-3
Summary of Primary Skin Irritation Test Data

GLP Study No. 81023
Chemical Name | Conc | Solvent | Amt Applied | Code
--- | --- | --- | --- | ---
Date of Application 1 July 1981 | Saline 4 min | NA | NA | 0.03-0.1 ml | C
Principal Investigator LTC FRUIN

### Irritation Scores

<table>
<thead>
<tr>
<th>Rabbit No.</th>
<th>Site</th>
<th>Intact Skin Sites</th>
<th>Abraded Skin Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Erythema 24 hr</td>
<td>Edema 24 hr</td>
</tr>
<tr>
<td></td>
<td></td>
<td>72 hr</td>
<td>72 hr</td>
</tr>
<tr>
<td>F8100086</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100087</td>
<td>I</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>F8100088</td>
<td>F8100092</td>
<td>III</td>
<td>0</td>
</tr>
<tr>
<td>F8100097</td>
<td>II</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>F8100099</td>
<td>I</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Total:  
Intact Score = $\frac{C_I}{2 \times \text{No. of Sites on test}}$  
Abraded Score = $\frac{C_A}{2 \times \text{No. of Sites on test}}$  
Total Score = $2 \times \text{No. of Sites on test}$

Primary Skin Irritation Index Category I

Remarks:
**TABLE A-4**
Summary of Primary Skin Irritation Test Data

GLP Study No. 81023

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Conc</th>
<th>Solvent</th>
<th>Amt Applied</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.03-0.1 m</td>
<td>NA</td>
<td>NA</td>
<td>D</td>
</tr>
</tbody>
</table>

Date of Application: 1 July 1981
Principal Investigator: LTC FRUIN

### Irritation Scores

<table>
<thead>
<tr>
<th>Rabbit No.</th>
<th>Site</th>
<th>Erythema (24 hr, 72 hr)</th>
<th>Edema (24 hr, 72 hr)</th>
<th>Site</th>
<th>Erythema (24 hr, 72 hr)</th>
<th>Edema (24 hr, 72 hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F8100086</td>
<td>I</td>
<td>1</td>
<td>0</td>
<td>II</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100087</td>
<td>I</td>
<td>0</td>
<td>0</td>
<td>III</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100088</td>
<td>IV</td>
<td>0</td>
<td>0</td>
<td>IV</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100092</td>
<td>I</td>
<td>2</td>
<td>0</td>
<td>III</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100097</td>
<td>I</td>
<td>0</td>
<td>0</td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F8100099</td>
<td>I</td>
<td>0</td>
<td>0</td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Total:

- Intact: \( a+b = 3 \) \( a = 0 \), \( b = 0 \)
- Abraded: \( a+b = 0 \) \( a = 0 \), \( b = 0 \)

\[
\text{Intact Score} = \frac{C_I}{2 \times \text{No. of Sites on test}} = \frac{3}{2 \times 3} = .50
\]

\[
\text{Abraded Score} = \frac{C_A}{2 \times \text{No. of Sites on test}} = \frac{0}{2 \times 3} = .00
\]

\[
\text{Total Score} = \frac{C_I + C_A}{2 \times \text{No. of Sites on test}} = \frac{3}{2 \times 3} = .25
\]

**Primary Skin Irritation Index** Category I

**Remarks:**

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