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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. Exposure sites were not occluded. Scores were below those considered to be caused by a primary irritant.		

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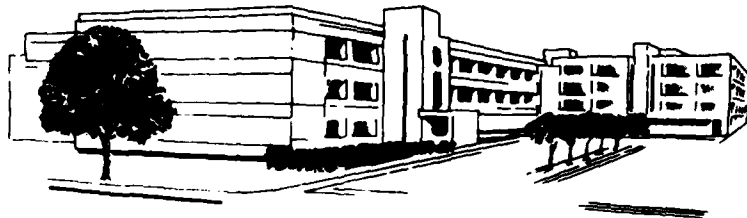
**PRIMARY DERMAL IRRITATION RESULTING FROM THE ABRASIVE
ACTION WHEN USING THE M-258A-1 DECONTAMINATION KIT (Study 7)**

JOHN T. FRUIN, DVM, PhD, LTC VC

**TOXICOLOGY GROUP,
DIVISION OF RESEARCH SUPPORT**

SEPTEMBER 1981

Toxicology Series 15



LETTERMAN ARMY INSTITUTE OF RESEARCH PRESIDIO OF SAN FRANCISCO CALIFORNIA 94129

PREFACE

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: 81024

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)

WORK UNIT: 302 Studies on Potential Dermal Irritation of M-258A-1
Kit.

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 (non-occlusive modified Draize).

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Signatures of Principal Scientists Involved
In The Study

I, the undersigned, believe the study, GLP number 81024, 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 11 Sept 81

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



DEPARTMENT OF THE ARMY
LETTERMAN ARMY INSTITUTE OF RESEARCH
PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129

REPLY TO
ATTENTION OF:

SGRD-ULZ-QA

22 July 1981

MEMORANDUM FOR RECORD

SUBJECT: Report of GLP Compliance

I hereby certify that in relation to LAIR GLP study 81024 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 7)

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. In addition the exposure sites were not bandaged as specified in SOP-OP-STX-34. Chemical analysis were not conducted except for measuring pH. Chemicals were prepared on the day of dosing and chemical composition was assumed to be that of the formular printed on the outer container. Compound was assumed to be stable under conditions of storage and use. Purity of compound was assumed to be that printed on the container.

Chemical Data

Chemical Name: Physiologic Saline

CAS: N/A

Molecular Structure: H₂O and NaCl

Molecular Weight: 18.016 and 58.454

pH: 5.0 ± 2

Physical state: clear liquid, colorless, and oderless

Boiling point: 100 C

Compound density: 1.0

Contaminates: unknown

Formulation: 99.1% H₂O 0.9% NaCl

Manufacturer: Traverol Laboratories, Deerfield, IL 60015

Manufacturer Lot No: 2C655S1

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 left exposed to the air.

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: $50 \pm 5\%$.

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.

RESULTS

Scoring (SOP-OP-STX-34)

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)

Erythema and Eschar Formation

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate-to-severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injurious in depth)	4
Possible total erythema score	4*

Edema Formation

No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (edges raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4
Possible total edema score	4*

Possible total score for primary irritation 8

* 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.

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

TABLE 2

PRIMARY DERMAL IRRITATION INDEX FOR THE M-258A-1 DECONTAMINATION KITS

Treatment	Intact Score*	Abraded Score	Combined Score	Category
Wipe 1 minute	0.0	0.17	0.08	I
Wipe 3 minutes	0.0	0.17	0.08	I
Wipe 4 minutes	0.0	0.0	0.0	I
Control	0.0	0.0	0.0	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
2. FRUIN, J.T. and M.A. HANES. The Primary Dermal Irritation Potential of Components of the M-258A-1 Decontamination Kit (Study 1). Institute Report No. 101 San Francisco, CA: Letterman Army Institute of Research, 1981
3. McCREESH, A.H. and M. STEINBERG. Dermato-toxicology and Pharmacology Washington, DC: Hemisphere Publishing Corp., 1977

Summary of Primary Skin Irritation Test Data

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APPENDIX A-3 Saline 4 min	12
APPENDIX A-4 Control	13
	APPENDIX A

TABLE A-1

Summary of Primary Skin Irritation Test Data

GLP Study No. 81024 Chemical Name Conc Solvent Amt Applied Code
 Date of Application 1 July 1981 Saline 1 m:n NA NA 0.03-0.1 ml A
 Principal Investigator LTC Fruin

Irritation Scores

Rabbit No.	Site	Intact Skin Sites				Abraded Skin Sites				
		Erythema		Edema		Site	Erythema		Edema	
		24 hr	72 hr	24 hr	72 hr			24 hr	72 hr	24 hr
F8100091						III	0	0	0	0
F8100093	I	0	0	0	0					
F8100094						II	1	0	0	0
F8100095						III	0	0	0	0
F8100096	IV	0	0	0	0					
F8100098	I	0	0	0	0					
Total:		a 0	b 0	a 0	b 0		a 1	b 0	a 0	b 0
		a+b 0		a+b 0			a+b 1		a+b 0	
		CI + 0				CA + 1				

Intact Score = $\frac{CI}{2 \times \text{No. of Sites on test}}$ $\frac{0}{(2 \times 3)} = 0.0$

Abraded Score = $\frac{CA}{2 \times \text{No. of Sites on test}}$ $\frac{1}{(2 \times 3)} = 0.17$

Total Score = $\frac{CI+CA}{2 \times \text{No. of Sites on test}}$ $\frac{1}{(2 \times 6)} = 0.08$

Primary Skin Irritation Index Category I

Remarks: _____

TABLE A-2

Summary of Primary Skin Irritation Test Data

GLP Study No. 81024 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

Rabbit No.	Site	Intact Skin Sites				Abraded Skin Sites				
		Erythema		Edema		Site	Erythema		Edema	
		24 hr	72 hr	24 hr	72 hr			24 hr	72 hr	24 hr
F8100091	I	0	0	0	0					
F8100093						II	1	0	0	0
F8100094						III	0	0	0	0
F8100095	IV	0	0	0	0					
F8100096	I	0	0	0	0					
F8100098						II	0	0	0	0
Total:		a	b	a	b		a	b	a	b
		0	0	0	0		1	0	0	0
		a+b		a+b			a+b		a+b	
		0		0			1		0	

$$\frac{CI + 0}{0} = 0$$

$$\frac{CA + 1}{1} = 1$$

Intact Score = $\frac{CI}{2 \times \text{No. of Sites on test}}$ $\frac{0}{(2 \times 3)} = 0.0$

Abraded Score = $\frac{CA}{2 \times \text{No. of Sites on test}}$ $\frac{1}{(2 \times 3)} = 0.17$

Total Score = $\frac{CI + CA}{2 \times \text{No. of Sites on test}}$ $\frac{1}{(2 \times 6)} = 0.08$

Primary Skin Irritation Index Category I

Remarks: _____

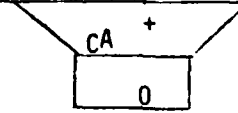
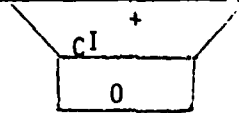
TABLE A-4

Summary of Primary Skin Irritation Test Data

GLP Study No. 81024 Chemical Name Control Conc NA Solvent NA Amt Applied 0.03-0.1 ml Code D
 Date of Application 1 July 1981
 Principal Investigator LTC Fruin

Irritation Scores

Rabbit No.	Site	Intact Skin Sites				Abraded Skin Sites				
		Erythema		Edema		Site	Erythema		Edema	
		24 hr	72 hr	24 hr	72 hr			24 hr	72 hr	24 hr
F8100091						II	0	0	0	0
F8100093	IV	0	0	0	0					
F8100094	I	0	0	0	0					
F8100095						II	0	0	0	0
F8100096						III	0	0	0	0
F8100098	IV	0	0	0	0					
Total:		a	b	a	b		a	b	a	b
		0	0	0	0		0	0	0	0
		a+b		a+b			a+b		a+b	
		0		0			0		0	



Intact Score = $\frac{C^I}{2 \times \text{No. of Sites on test}}$ $\frac{0}{(2 \times 3)} = .00$

Abraded Score = $\frac{C^A}{2 \times \text{No. of Sites on test}}$ $\frac{0}{(2 \times 3)} = .00$

Total Score = $\frac{C^I + C^A}{2 \times \text{No. of Sites on test}}$ $\frac{0}{(2 \times 6)} = .00$

Primary Skin Irritation Index Category I

Remarks: _____

**DAI
ILM**