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THE PRIMARY DERMAL IRRITATION RESULTING FROM THE ABRASIVE ACTIO--ETC(U)
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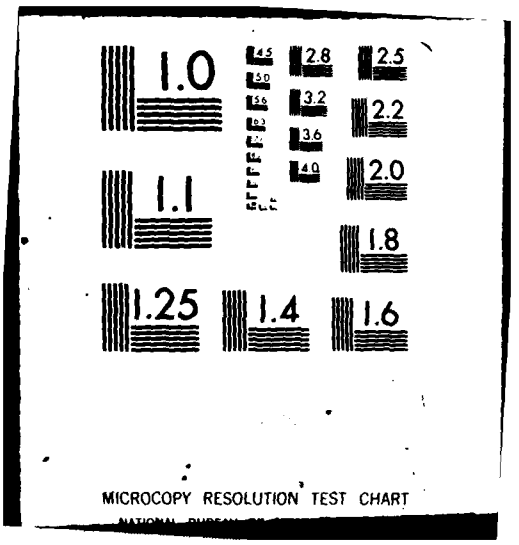
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MICROCOPY RESOLUTION TEST CHART

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REPORT DOCUMENTATION PAGE

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1. REPORT NUMBER: LAIR Technical Note No. 81-25TN	2. GOVT ACCESSION NO.: AD-A109887
3. RECIPIENT'S CATALOG NUMBER	
4. TITLE (and Subtitle): The Primary Dermal Irritation resulting from the abrasive action when using the M-258A-1 Decontamination Kit, Study 6	5. TYPE OF REPORT & PERIOD COVERED: Final, 30 June - 15 July 1981
	6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s): John T. Fruin, DVM, PhD, LTC VC	8. CONTRACT OR GRANT NUMBER(s): 19
9. PERFORMING ORGANIZATION NAME AND ADDRESS: Toxicology Group, Div. of Research Support, Letterman Army Institute of Research, Presidio of San Francisco, CA 94129	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS: Project 3516772.875, WU 302
11. CONTROLLING OFFICE NAME AND ADDRESS: U.S. Army Medical Research and Development Command, Fort Detrick, Frederick, MD 21701	12. REPORT DATE: September 1981 13. NUMBER OF PAGES: 18
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office)	15. SECURITY CLASS. (of this report): UNCLASSIFIED 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

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18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

M-258 Kit, Primary Dermal Irritation, Chemical Defense, Chemical Decontamination

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

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.

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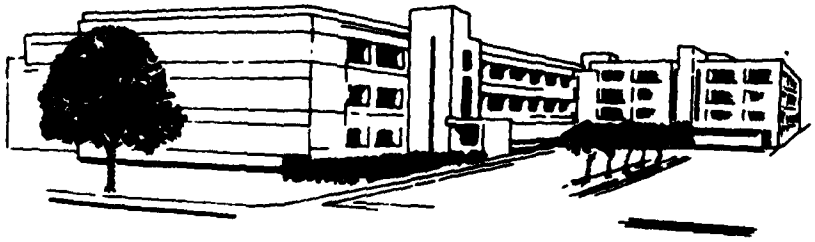
TECHNICAL NOTE NO. 81–25TN

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

JOHN T. FRUIN, DVM, PhD, LTC VC

TOXICOLOGY GROUP,
DIVISION OF RESEARCH SUPPORT

SEPTEMBER 1981 **Toxicology Series 14**



LETTERMAN ARMY INSTITUTE OF RESEARCH PRESIDIO OF SAN FRANCISCO CALIFORNIA 94129

TECHNICAL NOTE No. 81-25TN

In conducting the research described in this report, the investigation adhered to the "Guide for the Care and Use of Laboratory Animals," as promulgated by the Committee on Revision of the Guide for Laboratory Animal Facilities and Care, Institute of Laboratory Animal Resources, National Research Council.

Joshua Marshall 23 Sept 81
(Signature and date)

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: 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)

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 (occlusive modified Draize).

ACKNOWLEDGMENTS

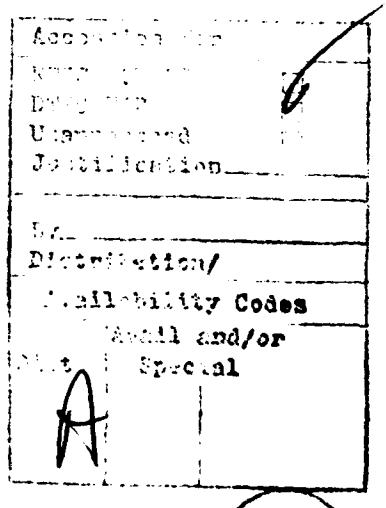
The authors wish to thank LTC Kenneth Black MD, MC; CPT Martha A. Hanes DVM, VC; SSG Lance White; PFC Evelyn Zimmerman; and Carolyn Lewis, MS; for assistance in performing the research, and for advice in scoring the irritation reactions. The authors also wish to thank E. Houston, PhD, MS; LTC R. Howarth, 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 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 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 $\pm$ 2

Physical state: clear liquid, colorless, and oderless

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: 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 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 $\pm$ 5 F (21 $\pm$ 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 . 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)

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. (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.

Treatment	Intact Score*	Abraded Score	Combined Score	Category
Wipe 1 minute	0.25	0.25	0.25	I
Wipe 3 minutes	0.33	0.83	0.58	I
Wipe 4 minutes	0.50	0.86	0.75	I
Control	0.50	0.00	0.25	I

* 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

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

APPENDIX A

TABLE A-1
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 1 min	NA	NA	0.03-0.1 ml	A

Principal Investigator LTC FRUIN

Irritation Scores

		Intact Skin Sites				Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
F8100086	IV	0	0	0	0					
F8100087						III	1	0	0	0
F8100088	IV	0	0	0	0					
F8100092	I	0	0	0	0					
F8100097	IV	2	0	0	0					
F8100099						II	0	0	0	0
Total:		a 2	b 0	a 0	b 0		a 1	b 0	a 0	b 0
		a+b 2		a+b 0			a+b 1		a+b 0	

C^I + = 2

C^A + = 1

Intact Score = C^I / 2xNo. of Sites on test 2/(2x4) = 0.25

Abraded Score = C^A / 2xNo. of Sites on test 1/(2x2) = .25

Total Score = $\frac{C^I+C^A}{2 \times \text{No. of Sites on test}}$ 3/(2x6) = .25

Primary Skin Irritation Index Category I

Remarks:

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

		Intact Skin Sites				Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
F8100086						III	0	0	0	0
F8100087	IV	1	1	0	0					
F8100088	I	0	0	0	0					
F8100092						II	0	0	0	0
F8100097						III	3	2	0	0
F8100099	IV	0	0	0	0					
Total:		a 1	b 1	a 0	b 0		a 3	b 2	a 0	b 0
		a+b 2		a+b 0			a+b 5		a+b 0	

C^I + = 2

C^A + = 5

Intact Score = C^I / 2xNo. of Sites on test 2/6 = .33

Abraded Score = C^A / 2xNo. of Sites on test 5/6 = .83

Total Score = $\frac{C^I+C^A}{2 \times \text{No. of Sites on test}}$ 7/12 = .58

Primary Skin Irritation Index Category I

Remarks:

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

		Intact Skin Sites				Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
F8100086						II	0	0	0	0
F8100087	I	1	0	1	0					
F8100088						II	2	0	0	0
F8100092						III	0	0	0	0
F8100097						II	3	2	0	0
F8100099	I	0	0	0	0					
Total:		a 1	b 0	a 1	b 0		a 5	b 2	a 0	b 0
		a+b 1		a+b 1			a+b 7		a+b 0	

C^I + = 2

C^A + = 7

Intact Score = C^I / 2xNo. of Sites on test 2/(2x2) = 0.50

Abraded Score = C^A / 2xNo. of Sites on test 7/(2x4) = 0.86

Total Score = $\frac{C^I + C^A}{2 \times \text{No. of Sites on test}}$ 9/12 = .75

Primary Skin Irritation Index Category I

Remarks:

TABLE A-4
Summary of Primary Skin Irritation Test Data

GLP Study No. 81023	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 1 July 1981	Control	NA	NA	0.03-0.1 ml	D

Principal Investigator LTC FRUIN

Irritation Scores

		Intact Skin Sites					Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
F8100086	I	1	0	0	0					
F8100087						II	0	0	0	0
F8100088						III	0	0	0	0
F8100092	IV	0	0	0	0					
F8100097	I	2	0	0	0					
F8100099						III	0	0	0	0
Total:		a 3	b 0	a 0	b 0		a 0	b 0	a 0	b 0
		a+b 3		a+b 0			a+b 0		a+b 0	

C^I + = 3

C^A + = 0

Intact Score = C^I / 2xNo. of Sites on test 3/(2x3) = .50

Abraded Score = C^A / 2xNo. of Sites on test 0/(2x3) = .00

Total Score = $\frac{C^I+C^A}{2}$ x No. of Sites on test 3/(2x6) = .25

Primary Skin Irritation Index Category I

Remarks: