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PRIMARY DERMAL IRRITATION POTENTIAL OF COMPONENTS OF THE M-258A--ETC(U)
SEP 81 J T FRUIN, M A HANES
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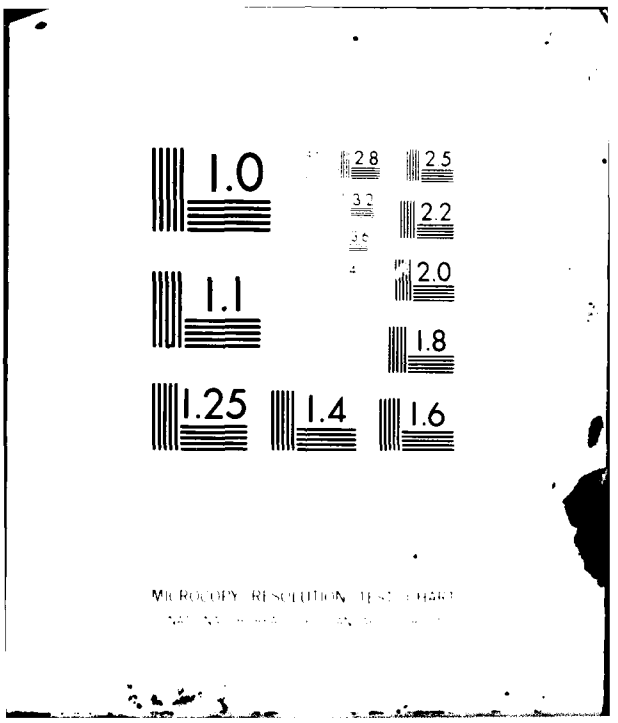
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MICROCOPY RESOLUTION TEST CHART

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

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

The primary dermal irritation potential of components of the Prototype M-258A-1 Decontamination Kit was assessed by using a modified Draize test. The test called for applying the components as they are intended to be applied under field conditions. Approximately 0.03 to 0.1 g of test substance was applied per dose site. Decon I and Decon I and II when applied together, caused moderate irritation after exposure and occlusion for 24 hours. Decon II caused mild irritation after exposure and occlusion for 24 hours.

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TECHNICAL NOTE NO. 81–18TN

PRIMARY DERMAL IRRITATION POTENTIAL OF COMPONENTS OF THE M-258A-1 DECONTAMINATION KIT (Study 4)

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and
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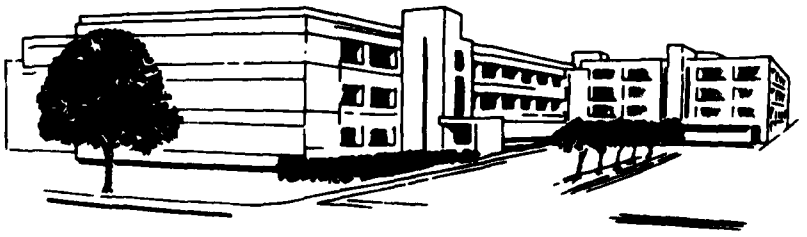
TOXICOLOGY GROUP,
DIVISION OF RESEARCH SUPPORT

SEPTEMBER 1981

Toxicology Series 11



LETTERMAN ARMY INSTITUTE OF RESEARCH PRESIDIO OF SAN FRANCISCO CALIFORNIA 94129

Toxicology Series 11

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.

This material has been reviewed by Letterman Army Institute of Research and there is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense. *(AR 360-5)*

(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: 81021

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

PRINCIPAL INVESTIGATOR: CPT Martha A. Hanes, DVM, VC

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. Decon I, consisting of a pad pre-wetted with hydroxyethane (ethanol) 72 $\pm$ 2% phenol 10 $\pm$ 0.5%, sodium hydroxide 5 + 0.5%, ammonium hydroxide 0.2 $\pm$ 0.05% and water was used to wipe the back of rabbits for 1 minute.

B. Decon II, consisting of a pad impregnated with a quantity of crystalline chloramine B and an equal quantity of liquid contained in breakable glass ampoules covered with nylon mesh. The liquid containes hydroxyethane (ethanol) 45 $\pm$ 2%, zinc chloride 5$\pm$0.5% and water. Just prior to dosing, the ampoules were broken and thus the chloramine B impregnated pad was saturated with liquid. Decon II was used to wipe the backs of rabbits for 2-3 min.

C. Decon I and Decon II were used to wipe the same area of the back for 1 and 2-3 minutes, respectively.

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 potential of the test substance used as listed above.

ACKNOWLEDGMENTS

The authors wish to thank LTC Kenneth Black MD, MC; SP5 Lance White; SP4 Thomas Kellner, BS; PFC Evelyn Zimmerman; Carolyn Lewis, MS; for assistance in performing the research, and for advice in scoring the irritation reactions. The authors also wish to thank M. Mershon, VMD; LTC (P) E. Houston, PhD, MS; LTC R. Howarth, VMD, VC, of the U.S. Army Medical Research Institute of Chemical Defense, Aberdeen Proving Grounds, MD, for providing prototype M-258A-1 Decontamination Kits and background information.

Signatures of Principal Scientists Involved In The Study

We, the undersigned, believe the study, GLP Study number 81021, 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.

Martha A. Hanes 2 Sept 81

MARTHA A. HANES, DVM / DATE
CPT, VC
Principal Investigator

John T. Fruin 2 Sept 81

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

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 81021 the following inspections were made:

11 June 1981
16 June 1981
19 June 1981

Routine inspections with no adverse findings are reported quarterly, thus these inspections are also included in the July 1981 report to management and the Study Director.

JOHN C. JOHNSON
CPT, MS
Quality Assurance Officer

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 using the standard method to apply the test compound produced evidence of severe irritation potential. Further testing was determined to be necessary to determine the kits irritation potential under conditions of proposed field usage.

Deviation from standards

Rather than applying liquid test substance on gauze, liquid impregnated pads from the M-258A-1 Decontamination Kit were cut into approximately one inch squares. Decon I squares were used to wipe the test area on the backs of rabbits for 1 minute. Decon II squares were used similarly, except the wiping was for 2 minutes. For Decon I plus Decon II the test site was first wiped for 1 minute with Decon I and then for 2 minutes with Decon II.

In addition, the exposure sites were not bandaged as specified in SOP-OP-STX-34. Chemical analyses were not conducted except for measuring pH. The pH of Decon I was 10.7 - 10.8, Decon II was 6.5 - 6.6 and combined Decon I and II was 10.6 - 10.7. Chemical composition was considered to be that printed on the outer container for the prototype M-258A-1 Decontamination Kit (Table 1 and 2). The compound was assumed to be stable under conditions of storage and use. Compound purity was unknown.

TABLE 1 (3)

CHEMICAL ANALYSIS OF DECON I
(pH = 10.7 - 10.8)

Component	ETOH	H_2O	Phenol	NaOH	NH_4OH
%	72%±2%	q.s.	10±0.5%	5.0±0.5%	0.2±0.05%
Name	ethanol	water	phenol	sodium hydroxide	ammonium hydroxide
Molecular Structure	C_2H_6O	H_2O	C_6H_6O	NaOH	NH_4OH
Molecular Weight	46.07	18.016	94.12	40.01	35.036

TABLE 2 (3)

CHEMICAL ANALYSIS OF DECON II
(pH = 6.5 - 6.6)

	*LIQUID PORTION			*SOLID PORTION
Component	ETOH	H_2O	$ZnCl_2$	Chloramine B
%	45±2%	50±2.5%	5±0.5%	100%
Name	ethanol	water	zinc chloride	Chloramine B (N-Chlorobenzene-sulfamido-sodium)
Molecular Structure	C_2H_6O	H_2O	ZnI_2	C_6H_5Cl $NNaO_2S$
Molecular Weight	46.07	18.016	136.29	213.64

* Equal quantities of liquid and solid are mixed to form Decon II.

Objective of Study

The objective of this study was to determine the primary dermal irritation potential of the Prototype M-258A-1 Decontamination Kit as it is expected to be used in the field.

METHODS

Historical Listing of Study Events

11 June 1981	Animals were weighed and sites for exposure were randomized.
15 June 1981	Animals were close clipped and areas marked.
16 June 1981	Animals were weighed and dosed.
16-30 June 1981	Animals were observed daily, only significant or abnormal observations were recorded.
17 June 1981	Bandages removed, 24-hr postexposure score.
19 June 1981	72-hr postexposure score.
23 June 1981	7-day postexposure score, weight taken.
30 June 1981	Animals were scored, (14 day after exposure) and weights taken. Animals were removed from the study.

Animal Data

Animal: New Zealand White Rabbits

Sex: Female

Source: Elkhorn Rabbitry

Pre-test Conditioning:

A. Transferred from Clinical Investigation, and had not been on study

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

Body Weight Range: 3-4 kg

Condition of animals at start of study: normal

Identification System: Ear marked as per SOP-OP-AGR-1

Environmental Conditions

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

Diet: Purina Certified Rabbit Chow 5322 approximately 110 g 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 ± 10%

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

Dosing Levels

A. Approximately 0.03-0.1 g Decon I

B. Approximately 0.03-0.1 g Decon II

C. Approximately 0.03-0.1 g and 0.3-0.1 g of Decon I and Decon II respectively.

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 by 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). The test substance impregnated pads were wiped over the test sites for 1,2 and 3 minutes (see deviation to standards). An Elizabethan collar was placed around each animals neck to keep animals from self-mutilating the treatment sites.

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 3). 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 3

EVALUATION OF SKIN REACTIONS (4)

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 aproximately 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 0.51-2 are considered mildly irritating (Category II), if the intact score is greater than 0.5, whereas those with indexes from 2 to 5 are moderate irritants (Category III). (Category assignment and interpretation, A.H. McCreesh, 1980, personnel communication).

Category IV irritants are compounds producing moderate to severe primary irritation of intact skin surrounding an abrasion. In addition, these compounds produce necrosis, vesiculation, ulceration and/or eschars. (Category assignment and interpretation, A.H. McCreesh, personnel communication, 1980.) Table 4 demonstrates the primary irritation indexes for the exposed areas.

TABLE 4

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

Chemical	Intact Score	Abraded Score	Combined Score	Category
Decon I	1.00	3.33	2.17	II
Decon II	0.67	1.33	1.00	II
Decon I+II	4.50	3.00	3.75	III
Control	0.00	0.00	0.00	I

DISCUSSION

Decon I, Decon II, and Decon I+II showed moderate irritation potential. Decon II showed mild irritation. The irritation demonstrated by this test was much less than demonstrated previously by the standard test (2).

CONCLUSIONS

The modified Draize test presented here may provide more accurate data concerning the potential hazard of the M-258A-1 Decontamination Kit to the soldier in the field.

RECOMMENDATIONS

Recommendations will be made after the current series of studies is 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. WINDHOLZ, M. (Editor). The Merck Index. Ninth Edition. Ragway, NJ: Merck and Co. 1976

4. 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

APPENDIX A-1

Summary of Primary Skin Irritation Test Data

GLP Study No. 81021	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 16 June 1981	Decon I	N/A	N/A	0.03-0.1 g	A

Principal Investigator CPT HANES

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
F8100048	I	0	0	0	0					
F8100078						II	2	3	0	0
F8100081						III	2	2	1	1
F8100082	IV	2	1	0	0					
F8100083	I	1	1	1	0					
F8100084						II	2	4	1	2
Total:		a 3	b 2	a 1	b 0		a 6	b 9	a 2	b 3
		a+b 5		a+b 1			a+b 15		a+b 5	
				C^I 6	+				C^A 20	+

Intact Score = C^I / 2xNo. of Sites on test 6/(2x3) = 1.00

Abraded Score = $\frac{C^A}{C^I+C^A}$ / 2xNo. of Sites on test 20/(2x3) = 3.33

Total Score = $\frac{}{2 \times}$ No. of Sites on test 26/(2x6) = 2.17

Primary Skin Irritation Index Category III

Remarks:

APPENDIX A-2

Summary of Primary Skin Irritation Test Data

GLP Study No. 81021	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 16 June 1981	Decon II	NA	NA	0.03-0.1 g	B

Principal Investigator CPT HANES

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
F8100048						II	1	1	0	0
F8100078	I	1	1	0	0					
F8100081	IV	1	0	0	0					
F8100082						III	1	1	1	0
F8100083						II	1	1	1	0
F8100084	I	0	0	1	0					
Total:		a_2	b_1	a_1	b_0		a_3	b_3	a_2	b_0
		a+b 3		a+b 1			a+b 6		a+b 2	

C^I + = 4

C^A + = 8

Intact Score = C^I / 2xNo. of Sites on test 4/(2x3) = 0.67

Abraded Score = C^A / 2xNo. of Sites on test 8/(2x3) = 1.33

Total Score = $\frac{C^I+C^A}{2 \times \text{No. of Sites on test}}$ 12/(2x6) = 1.00

Primary Skin Irritation Index Category II

Remarks:

APPENDIX A-3

Summary of Primary Skin Irritation Test Data

GLP Study No. 81021	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 16 June 1981	Decon I + II	NA	NA	0.03-0.1 g of ea I + II	C

Principal Investigator CPT HANES

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
F8100048						III	1	2	1	0
F8100078	IV	2	3	0	0					
F8100081	I	3	3	2	2					
F8100082						II	2	3	0	2
F8100083						III	3	2	1	1
F8100084	IV	2	4	1	2					
Total:		a 7	b 10	a 3	b 4		a 6	b 7	a 2	b 3
		a+b 17		a+b 7			a+b 13		a+b 5	
				C^I + 24					C^A + 18	

Intact Score = C^I / 2xNo. of Sites on test 24/(2x3) = 4.00

Abraded Score = $\frac{C^A}{C^I+C^A}$ / 2xNo. of Sites on test 18/(2x3) = 3.00

Total Score = $\frac{}{2 \times}$ No. of Sites on test 42/(2x6) = 3.50

Primary Skin Irritation Index Category III

Remarks:

APPENDIX A-4

Summary of Primary Skin Irritation Test Data

GLP Study No. 81021	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 16 June 1981	Control	NA	NA	none	0

Principal Investigator CPT HANES

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
F8100048	IV	0	0	0	0						
F8100078							III	0	0	0	0
F8100081							II	0	0	0	0
F8100082	I	0	0	0	0						
F8100083	IV	0	0	0	0						
F8100084							III	0	0	0	0
Total:		a 0	b 0	a 0	b 0			a 0	b 0	a 0	b 0
		a+b 0		a+b 0				a+b 0		a+b 0	

C^I = 0 + C^A = 0

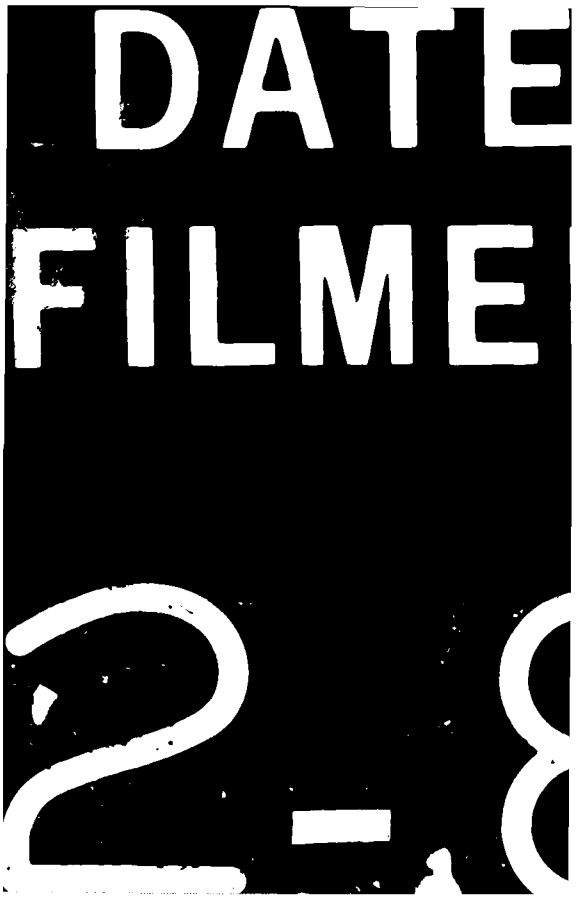
Intact Score = C^I / 2xNo. of Sites on test 0/(2x3) = 0

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

Total Score = $\frac{C^I+C^A}{2}$ x No. of Sites on test 0/(2x6) = 0

Primary Skin Irritation Index Category I

Remarks: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