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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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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)  The 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 approximately 0.04 g of freshly prepared material to be held in contact with the skin of rabbits for 24 hr. Both components, Decon I and Decon II when applied separately and together, caused little irritation after exposure for 24 hr. Further testing of these components is recommended to determine if they present a significant hazard under field conditions.		

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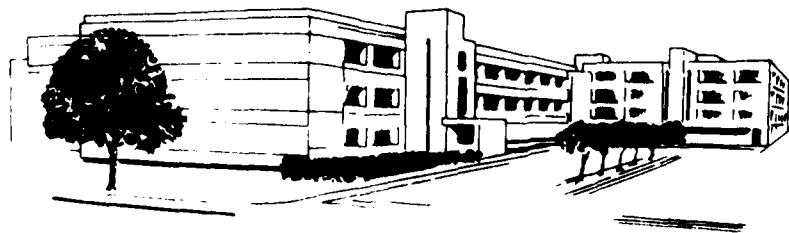
**PRIMARY DERMAL IRRITATION POTENTIAL OF COMPONENTS  
OF THE M-258A-1 DECONTAMINATION KIT (Study 3)**

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*and*  
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**TOXICOLOGY GROUP,  
DIVISION OF RESEARCH SUPPORT**

**SEPTEMBER 1981**

**Toxicology Series 9**



**LETTERMAN ARMY INSTITUTE OF RESEARCH PRESIDIO OF SAN FRANCISCO CALIFORNIA 94129**

Toxicology Series 9

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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)

*J. M. H. Marshall, Jr. 8 Sept 81*  
(Signature and date)



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Signatures of Principal Scientists Involved  
In The Study

We, the undersigned, believe the study, GLP number 81019, 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.

<i>Martha A. Hanes 21 Aug 81</i>	<i>John T. Fruin 2 Sept 81</i>
MARTHA A. HANES, DVM / DATE	JOHN T. FRUIN, DVM, PhD / DATE
CPT, VC	LTC (P), VC
Principal Investigator	Study Director



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REF: 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 81019 the following inspections were made:

11 June 1981  
15 June 1981  
16 June 1981  
18 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.

A handwritten signature in cursive script, reading "John C. Johnson", is positioned above the typed name.

JOHN C. JOHNSON  
CPT, MS  
Quality Assurance Officer

PRIMARY DERMAL IRRITATION POTENTIAL OF COMPONENTS  
OF THE M-258A-1 DECONTAMINATION KIT (Study 3)

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 kits irritation potential using freshly prepared material. The reason for this was to insure that dermal irritation was not the result of chemical deterioration.

Deviation from standards

Rather than applying 0.5 ml of liquid test substance, the amount was reduced to the amount needed to wet on square inch of close clipped rabbit skin.

Chemical analysis were not conducted except for measuring pH. Purity is unknown. Chemicals were prepared in accordance with the components and concentrations available from the M-258A-1 Kit Manufacturers. Division of Cutaneous Hazards was responsible for the preparation. Tables 1 and 2 list the components and their concentration. Freshly prepared compounds are assumed to be stable, for the duration of the test, but no tests were conducted.

TABLE 1 (3)

CHEMICAL ANALYSIS OF DECON I  
(pH = 10.6 - 10.7)

Component	ETOH	H <sub>2</sub> O	Phenol	NaOH	NH <sub>4</sub> OH
%	72 $\pm$ 2%	q.s.	10 $\pm$ 0.5%	5.0 $\pm$ 0.5%	0.2 $\pm$ 0.05%
Name	ethanol	water	phenol	sodium hydroxide	ammonium hydroxide
Molecular Structure	C <sub>2</sub> H <sub>6</sub> O	H <sub>2</sub> O	C <sub>6</sub> H <sub>6</sub> O	NaOH	NH <sub>4</sub> OH
Molecular Weight	46.07	18.016	94.12	40.01	35.036

TABLE 2 (3)

CHEMICAL ANALYSIS OF DECON II  
(pH = 6.1 - 6.2)

Component	*LIQUID PORTION			*SOLID PORTION
	ETOH	H <sub>2</sub> O	ZnCl <sub>2</sub>	Chloramine B
%	45 $\pm$ 2%	50 $\pm$ 2.5%	5 $\pm$ 0.5%	100%
Name	ethanol	water	zinc chloride	Chloramine B (N-Chlorobenzene-sulfamido-sodium)
Molecular Structure	C <sub>2</sub> H <sub>6</sub> O	H <sub>2</sub> O	ZnCl <sub>2</sub>	C <sub>6</sub> H <sub>5</sub> Cl NNaO <sub>2</sub> S
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 freshly prepared compounds used in the M-258

Decontamination Kit. The quantity of material used was that needed to wet a one-square-inch area of clipped rabbit skin.

#### METHODS

##### Historical Listing of Study Events

4 June 1981	Animals were clipped and held for study.
9 June 1981	Animals were weighed.
11 June 1981	Sites for exposure were randomized. Animals were clipped and areas marked.
15 June 1981	Animals were dosed and weighed.
15-29 June 1981	Animals were observed daily, only significant or abnormal observations were recorded.
16 June 1981	Bandages removed, 24-hr post-exposure score.
18 June 1981	72-hr post-exposure score.
22 June 1981	7-day post-exposure score, weight taken.
29 June 1981	Animals were scored (14-day post-exposure) and weights taken. Animals were removed from the study.

##### Animal Data

Animal: New Zealand White Rabbits

Sex: Male

Source: Elkhorn Rabbitry

##### Pre-test Conditioning:

- A. Transferred from GLP Study 81005, a primary eye irritation study. Animals were rested for 3 weeks after the last eye treatment
- 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: 75 ± 5 F (24 ± 3 C)

Relative Humidity: 50 ± 10%

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

#### Dosing Levels

- A. Decon I: 0.04 ml
- B. Decon II: 0.04 ml
- C. Decon I and II: 0.02 ml and 0.02 ml, respectively
- D. Control: A dry square inch gauze pad was taped to the animal.

#### 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. 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. A plastic strip held on by elastic tape was placed around the animal to retard evaporation, and to insure skin contact by the test substance. The test substance was in contact with the skin for 24 hours. At the end of the exposure period the wrapping was removed, the skin wiped if material was adherent and scored.

## 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 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.

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	0.5	0.83	0.67	I
Decon II	0.0	0.5	0.25	I
Decon I+II	0.33	0.08	0.25	I
Control	0.17	0.17	0.17	I

DISCUSSION

Decon I, and II separately, and combined were significantly less irritating when applied in appropriate quantities expected under field conditions. Compounds producing combined averages of 2 or less are considered non-irritating (provided the intact score is by itself less than 0.5) and placed in Category I.

In the study, the quantity of material used to dose was the amount needed to wet one-square-inch of clipped skin absorbed on a cotton gauze pad. Some of the compound is trapped in the cotton gauze material and is not in contact with the skin. Results from simulated usage should be given more consideration in the evaluation of the kit.

CONCLUSIONS

The modified Draize test demonstrated the irritation potential

of the Prototype M-258A-1 Decontamination Kit Components, when freshly prepared, are less irritating when applied in a lower quantity. This supports the possibility of compound instability. Damage may have been produced by some breakdown product in earlier studies conducted (see Toxicology Series 6). The effect of age on the components should be scrutinized.

#### RECOMMENDATIONS

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

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Summary of Primary Skin Irritation Test Data

	Page
APPENDIX A-1 Decon I	12
APPENDIX A-2 Decon II	13
APPENDIX A-3 Decon I and II	14
APPENDIX A-4 Control	15

APPENDIX A

APPENDIX A-1

Summary of Primary Skin Irritation Test Data

GLP Study No. 81019 Chemical Name Decon I Conc 100% Solvent NA Amt Applied 0.4 ml Code A  
 Date of Application 15 June 1981  
 Principal Investigator CPT HANES

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
F8100043	I	0	0	0	0					
F8100050	IV	0	0	0	0					
F8100051						III	1	2	0	0
F8100055						II	1	1	0	0
F8100056	I	0	0	2	1					
F8100075						III	0	0	0	0
Total:		a	b	a	b		a	b	a	b
		0	0	2	1		2	3	0	0
		a+b		a+b			a+b		a+b	
		0		3			5		0	
		CI +				CA +				
		3				5				

Intact Score =  $\frac{CI}{2 \times \text{No. of Sites on test}}$   $\frac{3}{(2 \times 3)} = 0.5$

Abraded Score =  $\frac{CA}{2 \times \text{No. of Sites on test}}$   $\frac{5}{(2 \times 3)} = 0.83$

Total Score =  $\frac{CI+CA}{2 \times \text{No. of Sites on test}}$   $\frac{8}{(2 \times 6)} = 0.67$

Primary Skin Irritation Index Category I

Remarks:

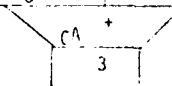
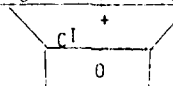
APPENDIX A-2

Summary of Primary Skin Irritation Test Data

GLP Study No. B1019 Chemical Name Decon II Conc. 100 Solvent NA Amt. Applied 0.4 ml  
 Date of Application 15 June 1981 Principal Investigator CPT HANFS

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
F8100043						II	1	1	0	0
F8100050	I	0	0	0	0					
F8100051	IV	0	0	0	0					
F8100055						III	0	0	0	0
F8100056						II	0	1	0	0
F8100075	I	0	0	0	0					
Total:		a	b	a	b	a	b	a	b	
		0	0	0	0	1	2	0	0	
		a+b	a+b	a+b	a+b	a+b	a+b	a+b	a+b	
		0	0	0	0	3	3	0	0	



Intact Score =  $\frac{C^I}{2 \times \text{No. of Sites on test}}$   $\frac{0}{(2 \times 3)} = 0.0$   
 Abraded Score =  $\frac{C^A}{2 \times \text{No. of Sites on test}}$   $\frac{3}{(2 \times 3)} = 0.5$   
 Total Score =  $\frac{C^I + C^A}{2 \times \text{No. of Sites on test}}$   $\frac{3}{(2 \times 6)} = 0.25$   
 Primary Skin Irritation Index Category I

Remarks:

APPENDIX A-3

Summary of Primary Skin Irritation Test Data

GLP Study No. 81019 Chemical Name Decon I + II Conc. 100% Solvent NA Amt Applied 0.02 ml Site I  
 Date of Application 15 June 1981 0.02 ml II C  
 Principal Investigator CPT HANES

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
F8100043						III	0	0	0	0
F8100050						II	0	1	0	0
F8100051	I	0	0	0	0					
F8100055	IV	1	1	0	0					
F8100056						III	0	0	0	0
F8100075	IV	0	0	0	0					
Total:		a	b	a	b		a	b	a	b
		1	1	0	0		0	1	0	0
		a+b	a+b	a+b	a+b		a+b	a+b	a+b	a+b
		2	2	0	0		1	1	0	0
		c <sup>I</sup> +				c <sup>A</sup> +				
		2				1				

Intact Score =  $\frac{c^I}{2 \times \text{No. of Sites on test}} = \frac{2}{(2 \times 3)} = 0.33$

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

Total Score =  $\frac{c^I + c^A}{2 \times \text{No. of Sites on test}} = \frac{3}{(2 \times 6)} = 0.25$

Primary Skin Irritation Index Category I

Remarks: \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

APPENDIX A-4

Summary of Primary Skin Irritation Test Data

GLP Study No. 81019 Chemical Name Control Conc.  Solvent  Amt. Applied  Date  
 Date of Application 15 June 1981 Control    0  
 Principal Investigator CPT HAMES

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
F8100043	IV	0	0	0	0					
F8100050						III	0	0	0	0
F8100051						II	1	0	0	0
F8100055	I	0	0	0	0					
F8100056	IV	1	0	0	0					
F8100075						II	0	0	0	0
Total:		<sup>a</sup> 1	<sup>b</sup> 0	<sup>a</sup> 0	<sup>b</sup> 0		<sup>a</sup> 1	<sup>b</sup> 0	<sup>a</sup> 0	<sup>b</sup> 0
		<sup>a+b</sup> 1		<sup>a+b</sup> 0			<sup>a+b</sup> 1		<sup>a+b</sup> 0	



Intact Score =  $\frac{C^I}{2 \times \text{No. of Sites on test}} = \frac{1}{(2 \times 3)} = 0.17$

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

Total Score =  $\frac{C^I + C^A}{2 \times \text{No. of Sites on test}} = \frac{2}{(2 \times 6)} = 0.17$

Primary Skin Irritation Index Category I

Remarks:  
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