

International Research and Development Corporation

SPONSOR: Pittsburgh Plate Glass Company
Chemical Division

COMPOUNDS: Methylchloroform, Tri-Ethane 324, Control
Methylchloroform, Tri-Ethane 324 +
0.3% Epichlorohydrin
Methylchloroform, Tri-Ethane 324 +
1.5% Epichlorohydrin
Methylchloroform, Tri-Ethane 324 +
7.5% Epichlorohydrin

SUBJECT: Primary Skin Irritation Study in the
Albino Rabbit.



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Date: August 25, 1965

159-003

SL 031154

I. SYNOPSIS

None of the agents tested produced primary skin irritation in the albino rabbit. There did not appear to be any difference in the reactions observed between the 4 test compounds when evaluated in the manner described in this report.

II. COMPOUNDS

The test compounds were received from the Pittsburgh Plate Glass Company, Pittsburgh, Pennsylvania, on July 28, 1965. The compounds were all clear, volatile liquids enclosed in glass containers and labeled as follows:

Methylchloroform, Sample No. 61708-32-271-2546, Tri-Ethane
324 Control

Methylchloroform, Sample No. 61708-32-271-2547, Tri-Ethane
324 + 0.3% Epichlorohydrin

Methylchloroform, Sample No. 61708-32-271-2548, Tri-Ethane
324 + 1.5% Epichlorohydrin

Methylchloroform, Sample No. 61708-32-271-2549, Tri-Ethane
324 + 7.5% Epichlorohydrin

III. METHOD

A total of 6 albino rabbits, undifferentiated as to sex and ranging in weight from 2063 to 2672 grams, were used for this study. The animals were divided into 2 groups of 3 rabbits each. The dorsal skin of each rabbit was prepared by clipping the hair from 2 areas on each side of the spine. The areas clipped were approximately 2 inches square. In addition, the clipped areas of the skin of the rabbits in one of the 2 groups was abraded by producing shallow incisions with a scalpel blade.

The respective test compounds were applied as received once only in a total of 0.5 milliliter to the prepared areas on the skin of each rabbit. The areas of application were then covered with dental dam and gauze and the body of each rabbit was overwrapped with elastic bandage. The rabbits were confined in individual holders during the above procedure, and for 24 hours thereafter to permit percutaneous absorption and to prevent oral ingestion of the compounds.

At the end of the 24-hour period of confinement in the holders, the bandages were removed, the back of each rabbit was washed with tepid tap water and the areas of application examined for evidence of dermal irritation. The rabbits were then placed in individual cages with food and water available ad libitum. At the end of 72 hours, the areas of application were again examined for evidence of dermal irritation.

All skin reactions were graded according to the scale on the following page.

The values for erythema and eschar formation at 24 and 72 hours for the intact skin animals were added to similar values obtained for the abraded animals (a total of 4 values).

Similarly, the values for edema at 24 and 72 hours for intact and abraded skin animals were added together (a total of 4 values). The

primary irritant score is the sum of the 8 values divided by 4. As scored by this method, a primary irritant is one which results in a score of 5 or greater.

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Evaluation of Skin Reactions

	<u>Value*</u>
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 (injuries in depth)	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 (raised approximately 1 millimeter)	3
Severe edema (raised more than 1 millimeter and extending beyond the area of exposure)	4

* The "value" recorded for each reading is the average value of the six or more animals subjected to the test.

IV. RESULTS

The results obtained from the 4 test compounds appear in Tables 1-4. Slight to well defined erythema was observed in all rabbits at the 24-hour reading for all of the test compounds. Very little erythema was observed at the 72-hour reading. No edema was observed at either period of examination.

As scored by the manner described herein, none of the test compounds could be considered to be primary skin irritants. In addition, there was no discernible difference between the compounds in the degree of irritation observed.

MEIHYLCHLOROFORM, TRI-ETHANE 324, CONTROL:
Primary Skin Irritation Study in the Albino Rabbit.

TABLE 1. Evaluation of Primary Skin Reactions in the Albino Rabbit.

Dermal Irritation	<u>Exposure Time</u> Hours	<u>Exposure Unit</u> Value
<u>Erythema and Eschar Formation:</u>		
Intact skin	24	2.0
Do	72	0.3
Abraded skin	24	2.0
Do	72	0.3
	Subtotal	4.6
<u>Edema Formation:</u>		
Intact skin	24	0
Do	72	0
Abraded skin	24	0
Do	72	0
	Subtotal	0
	Total	4.6

Primary Irritation Score: 4.6 divided by 4 = 1.14

Ref.: Paragraph 191.11 of Federal Hazardous Substances Labeling Act.

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METHYLCHLOROFORM, TRI-ETHANE 324 + 0.3% EPICHLOROHYDRIN:
Primary Skin Irritation Study in the Albino Rabbit.

TABLE 2. Evaluation of Primary Skin Reactions in the Albino Rabbit.

<u>Dermal Irritation</u>	<u>Exposure Time</u> Hours	<u>Exposure Unit</u> Value
<u>Erythema and Eschar Formation:</u>		
Intact skin	24	2
Do	72	0
Abraded skin	24	2
Do	72	0
	Subtotal	4
<u>Edema Formation:</u>		
Intact skin	24	0
Do	72	0
Abraded skin	24	0
Do	72	0
	Subtotal	0
	Total	4

Primary Irritation Score: 4 divided by 4 = 1

Ref.: Paragraph 191.11 of Federal Hazardous Substances Labeling Act.

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METHYLCHLOROFORM, TRI-ETHANE 324 + 1.5% EPICHLOROHYDRIN:
Primary Skin Irritation Study in the Albino Rabbit.

TABLE 3. Evaluation of Primary Skin Reactions in the Albino Rabbit.

Dermal Irritation	Exposure Time Hours	Exposure Unit Value
<u>Erythema and Eschar Formation:</u>		
Intact skin	24	2
Do	72	0
Abraded skin	24	2
Do	72	0.3
	Subtotal	4.3
<u>Edema Formation:</u>		
Intact skin	24	0
Do	72	0
Abraded skin	24	0
Do	72	0
	Subtotal	0
	Total	4.3

Primary Irritation Score: 4.3 divided by 4 = 1.07

Ref.: Paragraph 191.11 of Federal Hazardous Substances Labeling Act.

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METHYLCHLOROFORM, TRI-ETHANE 324 + 7.5% EPICHLOROHYDRIN:
Primary Skin Irritation Study in the Albino Rabbit.

TABLE 4. Evaluation of Primary Skin Reactions in the Albino Rabbit.

Dermal Irritation	<u>Exposure Time</u> Hours	<u>Exposure Unit</u> Value
<u>Erythema and Eschar Formation:</u>		
Intact skin	24	1.3
Do	72	0
Abraded skin	24	1.7
Do	72	0.3
	Subtotal	3.3
<u>Edema Formation:</u>		
Intact skin	24	0
Do	72	0
Abraded skin	24	0
Do	72	0
	Subtotal	0
	Total	3.3

Primary Irritation Score: 3.3 divided by 4 = 0.8

Ref.: Paragraph 191.11 of Federal Hazardous Substances Labeling Act.

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