

**DERMAL SENSITIZATION STUDY OF
FORMALDEHYDE SOLUTION
IN GUINEA PIGS**

RECEIVED
FEB 19 1982
TOXICOLOGY

FINAL REPORT

**IITRI Project No. L8100
Study No. 309
Test Article No. 100**

FILE COPY

Contractor:

**IIT Research Institute
Life Sciences Research
10 West 35th Street
Chicago, IL 60616**

Sponsor:

**Standard Oil Co. (Ind)
200 E. Randolph Drive
Chicago, IL 60601**

February 5, 1982

IIT RESEARCH INSTITUTE

iitri


IITRI Project No. L8100


DERMAL SENSITIZATION STUDY OF
FORMALDEHYDE SOLUTION IN GUINEA PIGS
Study No. 309
Test Article No. 100

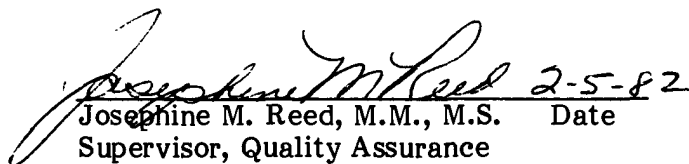
This report describes a dermal sensitization study conducted by IIT Research Institute for the Standard Oil Company (Indiana).

Marcia Reckers, B.S., Associate Toxicologist, served as study director and was responsible for the overall conduct of the study. Vladislava S. Rac, D.V.M., Senior Pathologist, served as study pathologist. Michael Becka, Technician, was responsible for the collection of test data. Calvin Reaves, Experimentalist, was responsible for animal care personnel. Josephine M. Reed, M.M., M.S., Supervisor, Quality Assurance, was responsible for the quality assurance program.

This report was prepared by Marcia Reckers.


Marcia Reckers, B.S. Date
Study Director
Life Sciences Research


Bruce K. Bernard, Ph.D. Date
Program Director
Life Sciences Research


Josephine M. Reed, M.M., M.S. Date
Supervisor, Quality Assurance
Life Sciences Research

IIT RESEARCH INSTITUTE

DERMAL SENSITIZATION STUDY OF
FORMALDEHYDE SOLUTION IN GUINEA PIGS
Study No. 309
Test Article No. 100

SUMMARY

FORMALDEHYDE SOLUTION at a concentration of 15% was applied in 0.5 ml doses to the upper left quadrant of the backs of ten guinea pigs once per week during an induction period of 3 weeks. Two and 3 weeks following the induction period, the lower left quadrant of the back of ten treated guinea pigs and five control guinea pigs was challenged with 0.5 ml of the dosage formulation. All guinea pigs were scored for edema and erythema 24 and 48 hours following administration of each challenge dose.

None of the controls and ten of ten treated guinea pigs exhibited positive Draize erythematous reactions greater than one during the study. No edematous reactions were observed in either group. The median score obtained in the control group was 0.0 and the range of median scores obtained in the treated group was 0-2. Four of the guinea pigs treated with test article had Draize erythema scores in excess of 2.

TABLE OF CONTENTS

	Page
I. INTRODUCTION	5
II. MATERIALS AND METHODS	5-7
a. Test Article	5
b. Dosage Formulation	5
c. Animals.....	5
d. Food and Water	5
e. Environment.....	5
f. Method	5-6
g. Evaluation	7
III. RESULTS	7
a. Mortality	7
b. Skin Effects	7
IV. EVALUATION	7
V. QUALITY ASSURANCE.....	7
VI. TABLES	
Table I Summation of Individual Dermal Sensitization Scores	T-1
Table II Comparison of Dermal Sensitization Scores	T-2
VII. APPENDICES	
Appendix I Scale for Scoring Skin Lesions	A-1
Appendix II Individual Irritation Scores	A-2 - A-9

DERMAL SENSITIZATION STUDY OF
FORMALDEHYDE SOLUTION IN GUINEA PIGS

I. INTRODUCTION

The purpose of this study was to determine the dermal sensitizing capability of FORMALDEHYDE SOLUTION in guinea pigs following repeated skin application.

II. MATERIALS AND METHODS

a. Test Article: FORMALDEHYDE SOLUTION (Sargent Welch, lot no. KTKH) was received April 4, 1981. The test article is a clear liquid. The test article was stored in the original container at room temperature (approximately 22°C).

b. Dosage Formulation: The dosage formulation was 15%. It was found during a preliminary study in guinea pigs, that this concentration produced a Draize score of 1 or less in control guinea pigs, receiving a single application.

c. Animals: Adult male Hartley Guinea Pigs weighing approximately 325 g, were purchased from Elm Hill Breeding Labs, Chelmsford, MA for use in this study. All guinea pigs were held in quarantine for approximately 1-1/2 weeks following receipt (7/16/81) and examined carefully to insure their health and suitability as test subjects. Guinea pigs selected for the study were identified by a unique numbered metal tag inserted through the pinna of the right ear and by a cage card.

d. Food and Water: Guinea Pig Chow 5025 (Ralston Purina Co., St. Louis, MO) and water supplied from a reverse-osmosis purifier by an automatic watering system were available **ad libitum**.

e. Environment: The individual stainless steel cages measured 25.0 x 17.8 x 41.2 cm and conformed to the upper limit weight range recommended in the **Guide for the Care and Use of Laboratory Animals**, DHEW, (NIH) No. 78-23. Deotized animal cage board (DACB, Upjohn Company, Kalamazoo, MI) was provided beneath the suspended cages. Air conditioned animal rooms were maintained at approximately 22°C and 40% relative humidity. Fluorescent lighting was provided on the basis of a 12 hour diurnal cycle.

f. Method:

1. Animals: Fifteen male guinea pigs were used in this study. Ten guinea pigs were treated and five guinea pigs were used as controls.

2. Skin Preparation: Twenty-four hours prior to test article application the backs of the treated guinea pigs were clipped free of hair. The upper left quadrant was clipped for the induction applications and the lower left quadrant was clipped for the challenge applications. Hair from the lower left quadrant was clipped from the backs of the control guinea pigs 24 hours prior to the challenge applications.
3. Dosing:
 - a) Induction: A 0.5 ml quantity of the dosage formulation was applied to the upper left quadrant of ten guinea pigs once/week for a period of 3 weeks beginning on July 28, 1981. The test article was covered by a 3/4" x 1" patch (Webril^R Appli-Pad, the Kendall Co.), held in place with impermeable plastic tape (Blenderm^R, 3 M Company) and elastic adhesive bandage (Elastoplast^R, Beiersdorf, Inc.). All wrapping materials were removed 6 hours after each application.
 - b) Challenge: Two weeks following the administration of the last induction phase dose (8/26/81), a 0.5 ml quantity of the dosage formulation was applied to the lower left quadrant of the back of the ten treated and the five previously untreated control guinea pigs. The test article was covered by a 3/4" x 1" patch, (Webril^R Appli-Pad, the Kendall Co.) held in place with impermeable plastic tape (Blenderm^R, 3M Company) and elastic adhesive bandage (Elastoplast^R, Beiersdorf, Inc.). All wrapping materials were removed 6 hours after each application. A second challenge dose was administered in an identical manner 1 week later (9/2/81).
4. Skin Examination: Twenty-four and 48 hours after removal of each challenge patch, the test sites were graded for edema and erythema using the method of Draize (Appendix I). Guinea pigs were clipped if necessary prior to scoring.
5. Observations: All guinea pigs were observed daily for mortality and morbidity.
6. Body Weights: Body weights were not measured.
7. Animal Disposition: After the final observation September 4, 1981, the guinea pigs were sacrificed humanely and discarded without necropsy.

g. Evaluation: A reaction with a Draize score of 2 or greater in the treated animals is considered a positive reaction. The concentration of test article used was intended to produce a Draize reaction of 1 or less in the control animals.

III. RESULTS

a. Mortality: No deaths were observed during the study.

b. Skin Effects: The individual erythema and edema scores (Appendix II) are summarized in Table I. None of the controls and ten of ten treated guinea pigs exhibited a positive reaction at least once during the study. A total number of 19 positive scores were obtained in the treated group. The range of individual erythema scores obtained in the control and treated groups were 0 and 0-4, respectively. Similarly, the range of median scores obtained were 0 and 0-2, respectively. No edema was observed in any guinea pig.

IV. EVALUATION

The erythema scores for the test article exceeded the comparative control scores at every observation interval. Four of the guinea pigs treated with the test article had Draize erythema scores of 3 or greater.

V. QUALITY ASSURANCE

Laboratory operations were inspected on August 4, 20 and 26, 1981. The final report was audited on January 21, 1982. All inspections and audits were performed by Josephine M. Reed. Raw data generated during the course of this study will be retained in the IITRI Life Sciences archives as specified by government regulations.

VI. TABLES

TABLE 1

SUMMATION OF INDIVIDUAL SENSITIZATION SCORES

Study Number: 309 Test Article Number: 100
 Test Article Name: FORMALDEHYDE SOLUTION

HOURS FOLLOWING CHALLENGE:		FIRST		CHALLENGE*		SECOND	
		24	48	24	48	24	48
SKIN REACTIONS:		Erythema	Edema	Erythema	Edema	Erythema	Edema
TREATMENT GROUP		SCORES					
CONTROL	0	5/5	5/5	5/5	5/5	5/5	5/5
	1	0	0	0	0	0	0
	2	0	0	0	0	0	0
	3	0	0	0	0	0	0
	4	0	0	0	0	0	0
TREATED	0	8/10	10/10	7/10	10/10	10/10	10/10
	1	0	0	1/10	0	0	0
	2	2/10	0	2/10	0	0	0
	3	0	0	0	0	0	0
	4	0	0	0	0	0	0

*Number of guinea pigs showing a given response/number of animals in a group.

TABLE 2

COMPARISON OF DERMAL SENSITIZATION SCORES

Study Number: 309 Test Article Number: 100
 Test Article Name: FORMALDEHYDE SOLUTION

	HOURS FOLLOWING CHALLENGE	CHALLENGE		
		FIRST	SECOND	THIRD
	24	48	24	48
CONTROL				
Median Score:	0	0	0	0
Range:	0	0	0-1	0
Guinea Pigs Exhibiting a Positive Reaction ¹ :	0	0	0	0
TREATED				
Median Score:	0	0	2	2
Range:	0-2	0-2	1-4	0-4
Guinea Pigs Exhibiting a Positive Reaction ¹ :	2	2	7	8

Number of positive reactions observed during the study:

Control: 0 Treated: 19

Number of guinea pigs exhibiting a positive reaction at any interval during the study:

Control: 0 Treated: 10

¹ A positive reaction is a Draize score of 2 or greater.

VII. APPENDICES

APPENDIX 1

SCALE FOR SCORING SKIN LESIONS*

Evaluation of Skin Reactions

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 1.0 mm)	3
Severe edema (raised more than 1.0 mm extending beyond the area of exposure)	4

Draize, J.H., Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics, Assoc. Food and Drug Officials of the U.S., Austin, Texas, 1959.

DERMAL SENSITIZATION

Study Number 309Test Article 100Score at 24 Hrs.

TREATED

FIRST CHALLENGE

Animal Number	Date	Time	Erythema	Edema	Initials
846	8/27/81	4:12PM	0	0	MB
847	8/27/81	4:13PM	0	0	MB
848	8/27/81	4:13PM	2	0	MB
849	8/27/81	4:14PM	0	0	MB
850	8/27/81	4:14PM	0	0	MB
851	8/27/81	4:15PM	0	0	MB
852	8/27/81	4:15PM	0	0	MB
853	8/27/81	4:16PM	0	0	MB
854	8/27/81	4:16PM	0	0	MB
855	8/27/81	4:17PM	2	0	MB

Read and Understood By M. ReckersDate 9/8/81

DERMAL SENSITIZATION

Study Number 309Test Article 100Score at 48 Hrs.TREATEDFIRST CHALLENGE

Animal Number	Date	Time	Erythema	Edema	Initials
846	8/28/81	4:10P	0	0	MB
847	8/28/81	4:10P	1	0	MB
848	8/28/81	4:10P	2	0	MB
849	8/28/81	4:11P	0	0	MB
850	8/28/81	4:11P	0	0	MB
851	8/28/81	4:12P	0	0	MB
852	8/28/81	4:12P	0	0	MB
853	8/28/81	4:13P	0	0	MB
854	8/28/81	4:13P	0	0	MB
855	8/28/81	4:14PM	2	0	MB

Read and Understood By M. ReckersDate 9/8/81

DERMAL SENSITIZATION

Study Number 309Test Article 100Score at 24 Hrs.

TREATED			SECOND CHALLENGE		
Animal Number	Date	Time	Erythema	Edema	Initials
846	9/3/81	3:39PM	3	0	MR
847	9/3/81	3:41PM	3	0	MR
848	9/3/81	3:41PM	4	0	MR
849	9/3/81	3:41PM	2	0	MR
850	9/3/81	3:42PM	4	0	MR
851	9/3/81	3:43PM	1	0	MR
852	9/3/81	3:43PM	1	0	MR
853	9/3/81	3:44PM	2	0	MR
854	9/3/81	3:45PM	1	0	MR
855	9/3/81	3:45PM	2	0	MR

Read and Understood By ML BickelDate 9-8-81

DERMAL SENSITIZATION

Study Number 309Test Article 100Score at 48
MR Hrs.

TREATED *SECOND CHALLENGE*

Animal Number	Date	Time	Erythema	Edema	Initials
846	9/4/81	3:31 PM	3	0	MR
847	9/4/81	3:31 PM	3	0	MR
848	9/4/81	3:31 PM	4	0	MR
849	9/4/81	3:32 PM	2	0	MR
850	9/4/81	3:32	4	0	MR
851	9/4/81	3:32	2	0	MR
852	9/4/81	3:33	0	0	MR
853	9/4/81	3:33	2	0	MR
854	9/4/81	3:33	0	0	MR
855	9/4/81	3:34	2	0	MR

Read and Understood By TK BeckerDate 9-8-81

DERMAL SENSITIZATION

Study Number 309Test Article 100Score at 24 Hrs.

CONTROL			FIRST CHALLENGE		
Animal Number	Date	Time	Erythema	Edema	Initials
866	8/27/81	4:10 PM	0	0	MB
867	8/27/81	4:10 PM	0	0	MB
868	8/27/81	4:11 PM	0	0	MB
869	8/27/81	4:11 PM	0	0	MB
870	8/27/81	4:12 PM	0	0	MB

Read and Understood By M. ReckersDate 9/8/81

DERMAL SENSITIZATION

Study Number 309Test Article 100Score at 48 Hrs.

CONTROL			FIRST CHALLENGE		
Animal Number	Date	Time	Erythema	Edema	Initials
866	8/28/81	4:07P	0	0	MB
867	8/28/81	4:07P	0	0	MB
868	8/28/81	4:05P	0	0	MB
869	8/28/81	4:05P	0	0	MB
870	8/28/81	4:09P	0	0	MB

Read and Understood By M. BeckersDate 9/8/81

DERMAL SENSITIZATION

Study Number 309Test Article 100Score at 24 Hrs.

CONTROL			SECOND CHALLENGE		
Animal Number	Date	Time	Erythema	Edema	Initials
871	9/3/81	3:38PM	0	0	MR
872	9/3/81	3:38PM	0	0	MR
873	9/3/81	3:38PM	0	0	MR
874	9/3/81	3:38PM	1	0	MR
875	9/3/81	3:38PM	0	0	MR

Read and Understood By MR BaskaDate 9-8-81

DERMAL SENSITIZATION

Study Number 309Test Article 100Score at 48 Hrs.

CONTROL			SECOND CHALLENGE		
Animal Number	Date	Time	Erythema	Edema	Initials
871	9/4/81	3:30PM	0	0	MR
872	9/4/81	3:30PM	0	0	MR
873	9/4/81	3:30PM	0	0	MR
874	9/4/81	3:30PM	0	0	MR
875	9/4/81	3:30PM	0	0	MR

Read and Understood By M. BeckeDate 7-8-81