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

*Control kalebrodin
study*

FINAL REPORT

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**IITRI Project No. L8100
Study No. 291
Test Article No. 100**

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**

March 9, 1982

IIT RESEARCH INSTITUTE

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IITRI Project No. L8100

DERMAL SENSITIZATION STUDY OF
FORMALDEHYDE SOLUTION IN GUINEA PIGS

Study No. 291

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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 Rac, DVM, 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 3-9-82
Marcia Reckers, B.S. Date
Study Director
Life Sciences Research

Bruce K. Bernard 3-9-82
Bruce K. Bernard, Ph.D. Date
Program Director
Life Sciences Research

Josephine M. Reed 3-9-82
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. 291

Test Article No. 100

SUMMARY

FORMALDEHYDE SOLUTION at a concentration of 15% in NANOpure water, was applied in 0.5 ml doses to the upper left quadrant of the back 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.

Two of five controls and eight of ten treated guinea pigs exhibited Draize erythematous reactions greater than one during the study. No edematous reactions were observed in either group. The median scores for the control group were 0.0-1.0 and the median scores for the treated group were 1.0-4.0. Eight of the guinea pigs treated with test article had erythema scores greater than 3 on the Draize scale.

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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, 37% (Sargent Welch, lot KJKH) was received April 14, 1981. The test article is a clear liquid with a viscosity similar to water. The test article was stored in the original container at room temperature (approximately 22°C).

b. Dosage Formulation: The dosage formulation was 15% in NANOpure water. 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 425 g, were purchased from Elm Hill Breeding Labs, Chelmsford, MA for use in this study. All guinea pigs were held in quarantine for four weeks following receipt (5/19/81) 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 June 16, 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 (7/15/81), 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 (7/22/81).
4. Skin Examination: Twenty-four and 48 hours after removal of each challenge patch, the test sites were scored for edema and erythema according to 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 (7/24/81), 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. Two of five controls and eight of ten treated guinea pigs exhibited a positive reaction at least once during the study. A total number of 23 positive scores was obtained in the treated group. The median scores obtained in the control group were 0.0-1.0 and the median scores for the treated group 1.0-4.0. Edema was not observed in any guinea pig.

IV. EVALUATION

The number of positive erythema scores for the test article exceeded that for the comparative control group at every observation interval. Eight of the guinea pigs treated with test article had Draize erythema scores of 4.

V. QUALITY ASSURANCE

Laboratory operations were inspected on June 18 and July 10 and 22, 1981. The final draft report was audited on February 22, 1982. Audits and inspections were performed by Josephine M. Reed. Raw data generated during the study will be retained in the IITRI Life Sciences Archives as specified by government regulations.

TABLE I

SUMMATION OF INDIVIDUAL DERMAL SENSITIZATION SCORES

Study Number: 291 Test Article Number: 100
Test Article Name: FORMALDEHYDE SOLUTION

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

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

TABLE 2
COMPARISON OF DERMAL SENSITIZATION SCORES
Study Number: 291 Test Article Number: 100
Test Article Name: FORMALDEHYDE SOLUTION

	FIRST		CHALLENGE	
	24	48	24	48
HOURS FOLLOWING CHALLENGE:				
CONTROL				
Median Score:	0	0	1	1
Range:	0	0-1	0-2	0-4
Guinea Pigs Exhibiting a Positive Reaction ¹ :	0	0	2	2
TREATED				
Median Score:	1	1	4	4
Range:	0-2	0-2	0-4	0-4
Guinea Pigs Exhibiting a Positive Reaction ¹ :	4	3	8	8

Number of Positive reactions observed during the study:
Control: 4 Treated: 23

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

Control: 2 Treated: 8

¹) 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 291Test Article 100Score at 24 Hrs.

TREATED GROUP - CHALLENGE 1

Animal Number	Date	Time	Erythema	Edema	Initials
506	7/23/81	4:03PM	4	0	MR
507	7/23/81	4:03PM	2	0	MR
508	7/23/81	4:04PM	4	0	MR
509	7/23/81	4:05PM	0	0	MR
510	7/23/81	4:05PM	4	0	MR
511	7/23/81	4:05PM	4	0	MR
512	7/23/81	4:05PM	4	0	MR
513	7/23/81	4:06PM	0	0	MR
514	7/23/81	4:06PM	4	0	MR
515	7/23/81	4:06PM	4	0	MR

Read and Understood By M BeckaDate 7/24/81

DERMAL SENSITIZATION

Study Number 291Test Article 100Score at 48 Hrs.

TREATED GROUP - CHALLENGE 1

Animal Number	Date	Time	Erythema	Edema	Initials
506	7/24/81	3:54 PM	4	0	MR
507	7/24/81	3:54 PM	4	0	MR
508	7/24/81	3:54 PM	4	0	MR
509	7/24/81	3:57 PM	1	0	MR
510	7/24/81	3:57 PM	4	0	MR
511	7/24/81	3:58 PM	4	0	MR
512	7/24/81	3:58 PM	4	0	MR
513	7/24/81	3:58 PM	0	0	MR
514	7/24/81	3:58 PM	4	0	MR
515	7/24/81	3:59 PM	4	0	MR

Read and Understood By M BeckerDate 7/24/81

DERMAL SENSITIZATION

Study Number 291Test Article 100Score at 24 Hrs.

TREATED GROUP - CHALLENGE 2

Animal Number	Date	Time	Erythema	Edema	Initials
506	7-16-81	2:54 PM	2	0	MR
507	7-16-81	2:55 PM	2	0	MR
508	7-16-81	2:55 PM	2	0	MR
509	7-16-81	2:55 PM	0	0	MR
510	7-16-81	2:55 PM	1	0	MR
511	7-16-81	2:55 PM	1	0	MR
512	7-16-81	2:56 PM	2	0	MR
513	7-16-81	2:56 PM	0	0	MR
514	7-16-81	2:56 PM	1	0	MR
515	7-16-81	2:57 PM	1	0	MR

Read and Understood By M. B.Date 7-16-81

DERMAL SENSITIZATION

Study Number 291Test Article 100Score at 48 Hrs.

TREATED GROUP - CHALLENGE 2

Animal Number	Date	Time	Erythema	Edema	Initials
506	7-17-81	2:58PM	2	0	MR
507	7-17-81	2:59PM	1	0	MR
508	7-17-81	2:59PM	2	0	MR
509	7-17-81	3:00PM	0	0	MR
510	7-17-81	3:00PM	1	0	MR
511	7-17-81	3:01PM	1	0	MR
512	7-17-81	3:01PM	2	0	MR
513	7-17-81	3:03PM	0	0	MR
514	7-17-81	3:02PM	0	0	MR
515	7-17-81	3:03PM	1	0	MR

Read and Understood By MR BeckerDate 7/17/81

DERMAL SENSITIZATION

Study Number 291Test Article 100Score at 24 Hrs.

CONTROL GROUP - CHALLENGE 1

Animal Number	Date	Time	Erythema	Edema	Initials
501	7-16-81	2:53PM	0	0	MR
502	7-16-81	2:53PM	0	0	MR
503	7-16-81	2:53PM	0	0	MR
504	7-16-81	2:54PM	0	0	MR
505	7-16-81	2:54PM	0	0	MR

Read and Understood By MBDate 7-16-81

DERMAL SENSITIZATION

Study Number 291Test Article 100Score at 48 Hrs.

CONTROL GROUP - CHALLENGE 1

Animal Number	Date	Time	Erythema	Edema	Initials
501	7-17-81	2:56 PM	0	0	MR
502	7-17-81	2:56 PM	0	0	MR
503	7-17-81	2:57 PM	0	0	MR
504	7-17-81	2:57 PM	0	0	MR
505	7-17-81	2:57 PM	1	0	MR

Read and Understood By M BeckaDate 7/17/81

DERMAL SENSITIZATION

Study Number 291Test Article 100Score at 24 Hrs.

CONTROL GROUP - CHALLENGE 2

Animal Number	Date	Time	Erythema	Edema	Initials
501	7/23/81	4:00 PM	1	0	MR
502	7/23/81	4:01 PM	2	0	MR
503	7/23/81	4:02 PM	0	0	MR
504	7/23/81	4:02 PM	1	0	MR
505	7/23/81	4:02 PM	2	0	MR

Read and Understood By MR BeckoDate 7/24/81

DERMAL SENSITIZATION

Study Number 291Test Article 100Score at 48 Hrs.

CONTROL GROUP - CHALLENGE 2

Animal Number	Date	Time	Erythema	Edema	Initials
501	7/24/81	3:54 PM	1	0	MR
502	7/24/81	3:54 PM	4	0	MR
503	7/24/81	3:55 PM	0	0	MR
504	7/24/81	3:55 PM	1	0	MR
505	7/24/81	3:55 PM	4	0	MR

Read and Understood By m BeckaDate 7/24/81