Project Number: WIL-12071

Sponsor: Great Lakes Chemical Corporation
P.O. Box 2200
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Primary Dermal Irritation Study
in Albino Rabbits with CN-322

FINAL REPORT

Date of Issuance: March 10, 1986

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I. SUMMARY

The test material CN-322 was applied to the intact dorsal skin of six female albino rabbits. One test site approximately one inch square was delineated on the back of each rabbit; 0.5 milliliter of CN-322 was applied to each site.

Doses were applied under one-inch square, two-ply gauze patches that were secured on all four sides with porous surgical tape. A gauze binder was applied and the entire trunk of the animal was wrapped with non-irritating tape. Approximately four hours after dosing the bandages were removed and the sites wiped with wet disposable paper towels.

The test sites were evaluated for dermal irritation in accordance with the method of Draize. Dermal readings were taken approximately thirty minutes after bandage removal and at approximately 24, 48 and 72 hours after dosing and daily thereafter through day 6 if irritation persisted. The Primary Irritation Index of CN-322 was calculated to be 0.4. Based on the data obtained, the test material CN-322 received a descriptive rating classification of mildly irritating according to the method of Draize.

II. INTRODUCTION AND OBJECTIVE

This report presents the data from a "Primary Dermal Irritation Study in Albino Rabbits with CN-322". The study, designated WIL-12071, was conducted in compliance with the Standard Operating Procedures of WIL Research Laboratories, Inc., the Good Laboratory Practice Regulations and the protocol, which was designed in compliance with the Environmental Protection Agency Guidelines for registering Industrial Chemicals in the U.S. (Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Humans and Domestic Animals; Section 81-5, issued November, 1982) and the Toxic Substances Control Act (TSCA) Health Effects Test Guidelines issued in August, 1982 and protocol amendment(s).

The objective of this study was to evaluate the irritative potential of the test material when administered as a single application to the intact skin of albino rabbits.

The study initiated with dosing on December 13, 1985 and was terminated on December 19, 1985. The study was conducted at WIL Research Laboratories, Inc., Ashland, Ohio.

III. EXPERIMENTAL DESIGN - MATERIALS AND METHODS

A. ANIMALS AND HOUSING

Eighty-four female young adult New Zealand White rabbits were received from Hazelton Research Products, Denver, Pennsylvania on October 1, 1985. Upon receipt each animal was observed by a qualified technician. Animals considered acceptable for study were weighed and identified uniquely by a plastic ear tag displaying the animal number. The rabbits were acclimated to laboratory conditions for a 73 day quarantine period. During this time, the animals were observed twice daily for mortality and general changes in appearance and behavior. Animals used on this study were selected from this group of rabbits.

The test animals were housed individually in wire-mesh cages suspended above cage board. Purina® Certified Rabbit Chow® #5322 and drinking water from on-site wells were provided ad libitum during the quarantine period and study. The basal diet utilized at WIL Research Laboratories, Inc. is a certified feed with appropriate analyses performed and provided by the manufacturer. Tap water supplying the facility is analyzed twice yearly according to Standard Operating Procedures. The results of these analyses are maintained at WIL Research Laboratories, Inc. and are available upon Sponsor request.

Throughout the quarantine period and study the animals were housed in an environmentally controlled room. Controls were set to maintain temperature at 67° ± 4° F and relative humidity at 40% or greater. Light timers were set to provide fluorescent illumination for a 12-hour light/12-hour dark photoperiod. Temperature and humidity were recorded once daily.

B. ASSIGNMENT OF ANIMALS TO STUDY

On the day prior to study initiation, eight female rabbits were selected for possible use on this study based on general appearance, behavior and body weights. At this time the hair was clipped from the back of each rabbit. On the day of study initiation, the rabbits were examined for general appearance, behavior and the condition of the shaved test area. One female was eliminated due physical abnormality and one female was arbitrarily eliminated. The remaining six rabbits were assigned to study. The rabbits weighed from 3509 to 4509 grams at study initiation.

C. TEST MATERIAL RECEIPT AND IDENTIFICATION

The test material CN-322 was received from Great Lakes Chemical Corporation, West Lafayette, Indiana on November 26, 1985 as follows:

LABEL IDENTIFICATION	LOT NUMBER	NO. CONTAINERS RECEIVED	GROSS WEIGHT	PHYSICAL DESCRIPTION
CN-322 Ref. No. 1223-30-D1 11/18/85	1223-30-D1	1 bottle	821 g	Amber viscous liquid

Test material stability information is the responsibility of the Sponsor.

D. TEST MATERIAL DISPENSATION

A sufficient amount of test material to dose all animals was transferred from its original container into a labeled clear bottle which was covered and transported to the animal room for dosing.

E. TEST MATERIAL ADMINISTRATION

Prior to dosing, the test sites were delineated with four dots made with an indelible marker (approximately one inch square). Each 0.5 milliliter dose of the test material was applied to intact skin under one-inch square gauze patches that were secured on all four sides with Micropore® Tape. The sites were then covered with gauze bandaging that was secured with several wrappings of Dermiform® Tape. Plastic restraint collars were applied and remained on the rabbits for the duration of the exposure period.

Approximately four hours after dosing, the bandages were removed and the sites wiped with wet disposable paper towels.

F. OBSERVATIONS

1. MORTALITY

The rabbits were observed for mortality twice daily (morning and afternoon) for the duration of the study.

2. DERMAL IRRITATION

Examination for dermal irritation was done in accordance with the method of Draize (Table 3). Other findings, if present, were noted.

Dermal readings were taken at approximately thirty minutes after bandage removal (4.5 hours post-dose) and 24, 48, 72 and 96 hours and 5 and 6 days after dosing.

3. BODY WEIGHTS

Individual body weights were obtained and recorded on study day 0 and at terminal sacrifice.

G. DATA RETENTION

All raw data generated during the conduct of this investigation, including that information stored and processed by the WIL Computer Data Management System, a copy of the final report and the test material retention sample are retained in the Archives at WIL Research Laboratories, Inc., Ashland, Ohio.

IV. RESULTS

A. OBSERVATIONS

1. MORTALITY

None of the rabbits died during the study period.

2. DERMAL IRRITATION (Table 1)

Dermal irritation was limited to very slight erythema. There was no edema or other dermal findings.

The Primary Irritation Index of CN-322 was calculated to be 0.4. Based on this value, the test material CN-322 received a descriptive rating classification of mildly irritating.

3. BODY WEIGHTS (Table 2)

There were no remarkable changes or differences observed in body weights during the study period.

V. DISCUSSION AND CONCLUSIONS

The Primary Irritation Index of CN-322 was calculated to be 0.4.

Based on the data obtained, the test material CN-322 received a descriptive rating classification mildly irritating according to the method of Draize.

There were no remarkable body weight changes.

Dennis J. Naas

Dennis J. Naas, B.S.
Study Director

3/10/86
Date

VI. PERSONNEL AND REPORT SUBMISSION

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VII. QUALITY ASSURANCE UNIT STATEMENT

Primary Dermal Irritation Study
in Albino Rabbits with CN-322

Dates of Inspection(s)	Date(s) Findings Reported to Study Director
March 4, 1986	March 4, 1986

This study was inspected in accordance with the Good Laboratory Practice Regulations and the Standard Operating Procedures of WIL Research Laboratories, Inc. The study was conducted in compliance with Good Laboratory Practice Regulations, the Standard Operating Procedures of WIL Research Laboratories, Inc., the protocol and protocol amendment(s). To the best of the signatory's knowledge there were no significant deviations from the Good Laboratory Practice Regulations which affected the quality or integrity of the study. Quality Assurance findings, derived from the inspection(s) during the conduct of the study and from the inspection of the final report, are documented and have been reported to the study director. A status report is submitted to management monthly.

The raw data and a copy of the final report will be kept in the Archives at WIL Research Laboratories, Inc.

Ralph Anderson — 3/10/86

Ralph Anderson, B.S.
Director - Quality Assurance

Date

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TABLES 1-3

TABLE 1

PRIMARY DERMAL IRRITATION STUDY IN ALBINO RABBITS WITH CN-322

INDIVIDUAL DERMAL SCORES AND SCORE CALCULATION

PROJECT NO.: WIL-12071
SPONSOR: GREAT LAKES CHEMICAL CORPORATION

ANIMAL NO./SEX		ERYTHEMA		EDEMA		ERYTHEMA		EDEMA	
		4.5H	24H	4.5H	24H	48H	72H	48H	72H
2919	F	1	1	0	0	1	0	0	0
2922	F	0	0	0	0	0	0	0	0
2918	F	0	0	0	0	1	1	0	0
2946	F	1	1	0	0	1	1	0	0
2947	F	0	0	0	0	1	1	0	0
2969	F	0	0	0	0	0	0	0	0
TOTAL		2	2	0	0	4	3	0	0

Primary Irritation Index (PII) = Sum of the averages of the erythema scores and the edema scores at 24 and 72 hours after dosing.

H - Hours
F - Female

PII = (2 + 3)/12 + (0 + 0)/12
PII = 5/12 + 0/12
PII = 0.4 + 0.0
PII = 0.4

TABLE 1

PRIMARY DERMAL IRRITATION STUDY IN ALBINO RABBITS WITH CN-322

INDIVIDUAL DERMAL SCORES

PROJECT NO.: WIL-12071
SPONSOR: GREAT LAKES CHEMICAL CORPORATION

ANIMAL NO./SEX		ERYTHEMA		EDEMA		ERYTHEMA		EDEMA	
		96H	5D	96H	5D	6D	7D	6D	7D
2919	F	*		*					
2922	F	*		*					
2918	F	1	0	0	0	*		*	
2946	F	1	1	0	0	0	*	0	*
2947	F	1	0	0	0	*		*	
2969	F	*		*					
TOTAL		3	1	0	0	0		0	

H - Hours
D - Days
F - Female

* - Animal no longer on study

TABLE 2

PRIMARY DERMAL IRRITATION STUDY
IN ALBINO RABBITS WITH CN-322

INDIVIDUAL BODY WEIGHTS (GRAMS)

Group	Number	Sex	Day 0	Terminal (Time)
0.5 ml/site	2919	F	4341	4344 (Day 3)
	2922	F	4509	4470 (Day 3)
	2918	F	4324	4439 (Day 5)
	2946	F	4171	4228 (Day 6)
	2947	F	3509	3570 (Day 5)
	2969	F	4004	3986 (Day 3)

TABLE 3

PRIMARY DERMAL IRRITATION STUDY
IN ALBINO RABBITS WITH CN-322

SCORING CRITERIA FOR DERMAL REACTIONS

Evaluation of Dermal Reactions*

Value	
	Erythema and Eschar Formation
0	No erythema
1	Very slight erythema (barely perceptible, edges of area not well defined)
2	Slight erythema (pale red in color and edges definable)
3	Moderate to severe erythema (definite red in color and area well defined)
4	Severe erythema (beet or crimson red) to slight eschar formation (injuries in depth)
4	Total possible erythema score
	Edema Formation
0	No edema
1	Very slight edema (barely perceptible, edges of area not well defined)
2	Slight edema (edges of area well defined by definite raising)
3	Moderate edema (raised approximately 1 mm)
4	Severe edema (raised more than 1 mm and extending beyond area of exposure)
4	Total possible edema score
8	Total possible Primary Irritation Score

DESCRIPTIVE RATINGS

Mean Primary Dermal Irritation Index

Range of Values	Descriptive Rating
0	Nonirritating
0.1 - 1.9	Mildly Irritating
2.0 - 5.9	Moderately Irritating
6.0 - 8.0	Severely Irritating

*Draize, J. H., 1965. The Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics. Dermal Toxicity, Pp. 46-59. Assoc. of Food and Drug Officials of the U. S., Topeka, Kansas.