

AR 226-0205

Primary Skin Irritation Test
with T-3874
in Albino Rabbits



Experiment No:

0386EB0135

Conducted At:

Pathology and Toxicology
Riker Laboratories, Inc.
St. Paul, Minnesota

Dates Conducted:

March 18, 1986 to March 20, 1986

Conducted By:

Gene L. Harris 4/14/86
G. L. Harris, BS Date
Advanced Toxicologist
Study Director

Reviewed By:

C. F. Chesney 4/14/86
C. F. Chesney, D.V.M., Ph.D. Date
Manager, Pathology and Toxicology

dc: K. L. Ebbens
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000052

Summary

The results of the primary skin irritation test conducted from March 18, 1986 to March 20, 1986 at Riker Laboratories, Inc., St. Paul, Minnesota indicate that T-3874 is non-irritating (0.0/8.0) to the skin of female albino rabbits. Neither erythema nor edema were noted at any time during the study.

Introduction

The objective of this study was to determine the primary skin irritation potential of T-3874 to the skin of female albino rabbits. This test was conducted to meet the Department of Transportations requirements for primary skin irritation. The raw data generated by the Study Director and the final report are stored in the conducting laboratory's archives.

600053

Animals and Husbandry

Young New Zealand White Rabbits^a were used in the evaluation of the primary skin irritating properties of the test article. The rabbits were individually housed^b in stainless steel cages, and food^c and water were available ad libitum. All rabbits were individually identified with ear tags and considered to be in good health at study initiation. The rabbits were housed in a temperature and humidity controlled room. Room lighting was on a 12/12 hour light/dark cycle that was automatically timed.

Method and Results

The test procedure was modeled after that of Draize et al^d. One day prior to the application of the test article, the hair was clipped from the back and flanks of each rabbit and the test site was selected lateral to the midline of the back approximately ten centimeters apart.

The test article (0.5 ml) was applied to the intact test site on each rabbit and immediately covered with two-inch square gauze patches. The patch, which was placed directly over the test site, was secured with gauze wrap. The trunk of each animal was then wrapped with impervious plastic sheeting^e which held the patches in position during the four hour exposure period.

^a Hazleton Dutchland, Inc., Denver, PA

^b Animals were housed in accordance with recommendations contained in DHEW Publication No. 78-23 (NIH): Revised 1978 "Guide For the Care and Use of Laboratory Animals.

^c Purina Lab Rabbit Chow® and rabbits may be offered Alfalfa Cubes for additional roughage.

^d Draize: Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics (1965).

^e 10 x 12 x .002 Extra Clear polyethylene sleeves, PPC Industries, Inc., Wheeling, IL

At the end of four hours, the plastic wrappings, patches, and all residual test article were removed by washing with water. One hour and two days after removal of the test article, the abraded test site was examined and scored for erythema and edema on a graded scale of 0 - 4.

The average irritation produced was evaluated by adding the mean scores for erythema and edema of the abraded test site one hour and two days post removal of the test article. This value was divided by two to obtain the mean primary irritation index. The scoring criteria for erythema and edema are shown below.

Scoring Criteria for Skin Reactions

Reaction	Description	Score
Erythema	Barely perceptible (Edges of area not defined)	1
	Pale red in color and area definable	2
	Definite red in color and area well defined.	3
	Beet or crimson red in color	4
Edema	Barely perceptible (Edges of area not defined)	1
	Area definable but not raised more than 1 mm.	2
	Area well defined and raised approximately 1 mm.	3
	Area raised more than 1 mm.	4
Maximum Primary Irritation Score =		8

The following grading system was used to arrive at a descriptive primary skin irritation rating:

<u>Mean Primary Irritation Score</u> <u>(Range of Values)</u>	<u>Descriptive Rating</u>
0	Non-Irritating
0.1 - 0.5	Minimally Irritating
0.6 - 1.5	Slightly Irritating
1.6 - 3.0	Mildly Irritating
3.1 - 5.0	Moderately Irritating
5.1 - 6.5	Severely Irritating
6.6 - 8.0	Extremely Irritating

The rating for a test article may be increased if the reactions caused are beyond simple erythema and edema, e.g. necrosis, escharosis, hemorrhage. The results are presented in Table 1. The protocol, principal personnel involved in the study, composition characteristics and Quality Assurance statement are contained in Appendices I - IV.

Table 1
Primary Skin Irritation Test - Albino Rabbits
with T-3874

Irritation Scores for Intact Skin Sites after Removal:				
Animal Number	1 Hour		Day 2	
	Er.	Ed.	Er.	Ed.
6B0394	0	0	0	0
6B0397	0	0	0	0
6B0389	0	0	0	0
6B0392	0	0	0	0
6B0395	0	0	0	0
6B0398	0	0	0	0
Mean	0.0	0.0	0.0	0.0
Subtotal		0.0		
Rating: Non-irritating				
Primary Irritation Index: 0.0/8.0				
Key: Er. = Erythema				
Ed. = Edema				

000057

TEST: Acute Primary Skin Irritation Test

SPONSOR: 3M Commercial Chemical

Division

CONDUCTED BY: Safety Evaluation Laboratory, Riker Laboratories, Inc., St. Paul, Minnesota

TEST ARTICLE: T-3874

CONTROL ARTICLE: None

PROPOSED STARTING/COMPLETION DATE OF TEST: 3/86 - 4/86

TEST SYSTEM: Female New Zealand White Albino Rabbits

SOURCE: HAZLETON - DUTCHLAND
DENVER, PA

OBJECTIVE: To determine the irritation potential of the test article to the skin of six animals. Rabbits were selected as the test system due to their historical use, sensitivity to irritants, ease of handling and general availability.

METHOD: The animals will be housed in standard wire-mesh cages in temperature and humidity controlled rooms with food^a and water offered *ad libitum*. Each animal will be assigned a numbered ear tag, which will correspond to a card affixed to the outside of the cage. Prior to the application of the test article, the hair will be clipped from the back and flanks of each animal and one test sites selected lateral to the midline of the back approximately ten centimeters apart. None of the one sites will be abraded by making four epidermal incisions, two perpendicular to the other two, while the other test site(s) will remain intact. The test article (0.5 ml) will be applied to no abraded and one intact site(s) on each animal, covered with gauze and secured with gauze. The trunk of each animal will then be wrapped with impervious plastic sheeting which will occlude the test article during the 4 day exposure period. One hour and 48 hours after removal of the test article, the intact and abraded test sites will be examined and scored separately for erythema and edema on a graded scale of 0 to 4^b. The average irritation produced will be evaluated by adding the mean scores for erythema and edema of the intact test sites one and 48 hours post removal of the test article. Similarly, the mean scores for erythema and edema of the abraded test sites will be added. These two values will be totaled and divided by four to obtain the mean primary irritation index and then assigned a descriptive primary skin irritation rating as follows:

Mean Primary Irritation Score	Descriptive Rating
0	Non-irritating
0.1 - 0.5	Minimally Irritating
0.6 - 1.5	Slightly Irritating
1.6 - 3.0	Mildly Irritating
3.1 - 5.0	Moderately Irritating
5.1 - 6.5	Severely Irritating
6.6 - 8.0	Extremely Irritating

The rating for a test article may be increased if the reaction caused is beyond erythema and edema and are deemed to be of importance in the interpretation of the results. All raw data generated by the study director and the final report will be stored in the Riker Laboratories' Archive, St. Paul, Minnesota.

^a Purina Rabbit Chow, Ralston Purina Co., St. Louis, Missouri

^b Draize: Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics (1965)

Published by the Editorial Committee of the Association of Food and Drug Officials of the United States.

^c 4-hour exposure period; for DOT see attached from 49CFR173.

[Signature]
Sponsor

3/27/86

Date

[Signature]
Study Director

2/28/86

Date

000058

APPENDIX IIPrincipal Participating Personnel Involved in the Study

<u>Name</u>	<u>Function</u>
G. L. Harris, BS	Advanced Toxicologist Study Director
G. E. Hart	Sr. Laboratory Technician Acute Toxicology
K. L. Ebbens, BS	Supervisor Toxicology Testing
G. C. Pecore	Supervisor Animal Laboratory

000059

APPENDIX IIIComposition Characteristics

This study is not regulated by the Good Laboratory Practice Act of 1978 and therefore information pertaining to composition characteristics is not applicable for inclusion in this study.

000060

APPENDIX IV
Quality Assurance Statement

This study is not officially regulated by the Good Laboratory Practice Regulation of 1978, and therefore a statement signed and prepared by the Compliance Audit department is not applicable.

The standard operating procedures of this laboratory does adhere to the general principles of this regulation. The Compliance Audit department does inspect different significant phases for studies underway in the Acute Toxicology Laboratory on a recurring cycle, and the facilities are examined on a three month schedule. In addition a select number of Research & Development studies are routinely picked at random from the Archives by the Compliance Audit department for review.

000061