Primary Skin Irritation Test

with T-3608

in Albino Rabbits

Experiment No.: 0984EB0368

Conducted At: Pathology and Toxicology
Riker Laboratories, Inc.
St. Paul, Minnesota

Dates Conducted: July 17, 1984 to July 20, 1984

Conducted By:

G. E. Hart 8/13/84
Date
Sr. Laboratory Technician
Acute Toxicology

K. D. O'Malley, BS 8/14/84
Date
Senior Toxicologist
Study Director

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Summary

The results of the primary skin irritation test conducted from July 17, 1984 to July 20, 1984 at Riker Laboratories, Inc., St. Paul, Minnesota indicate that T-3608 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-3608 to the skin of female albino rabbits. This study was conducted for research and development purposes and is, therefore, not regulated by the Food and Drug Administration's Good Laboratory Practice Regulation of 1978, although the standard operating procedures of this laboratory adhere to the general principles of this regulation. The raw data generated by the Study Director and the final report are stored in the conducting laboratory's archives.

Method and Results

Young albino rabbits of the New Zealand breed[a] were used in the evaluation of the primary skin irritating properties of the test article. The test procedure was modeled after that of Draize et al[b].

One day prior to the application of the test article, the hair was clipped from the back and flanks of each rabbit and two test sites selected lateral to the midline of the back approximately ten centimeters apart. One of the two sites was abraded by making four epidermal incisions, two perpendicular to the other two, while the other test site remained intact.

The test article (0.5 gm) was applied to each of the test sites on each rabbit and immediately covered with two-inch square gauze patches. The patches, which were placed directly over the test sites, were secured with gauze wrap. The trunk of each animal was then wrapped with impervious plastic sheeting[c] which held the patches in position during the one day exposure period.

At the end of one day, the plastic wrappings, patches, and all residual test article were removed[d]. One hour and 48 hours after removal of the test article, the intact and abraded test sites were examined and scored separately 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 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 were added.

[a] Hazleton Dutchland, Inc., Denver, PA
[b] Draize: Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics (1965).
[c] 10 x 12 x .002 Extra Clear polyethylene sleeves, PPC Industries, Inc., Wheeling, Illinois.
[d] The test article was removed with water.

These two values were totaled and divided by four 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:

Mean Primary Irritation Score (Range of Values)	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 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-3608

Animal Number	Irritation Scores for Abraded Skin Sites after Removal: 1 Hour Er.	1 Hour Ed.	48 Hours Er.	48 Hours Ed.	Irritation Scores for Intact Skin Sites after Removal: 1 Hour Er.	1 Hour Ed.	48 Hours Er.	48 Hours Ed.
4B1146	0	0	0	0	0	0	0	0
4B1149	0	0	0	0	0	0	0	0
4B1152	0	0	0	0	0	0	0	0
4B1155	0	0	0	0	0	0	0	0
4B1147	0	0	0	0	0	0	0	0
4B1150	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Subtotal			0.0				0.0	

Rating: Non-irritating

Primary Irritation Index: 0.0/8.0

Key: Er. = Erythema
Ed. = Edema

APPENDIX I
PROTOCOL

Riker Experiment No.: 0984EB0368

5.

TEST: Acute Primary Skin Irritation Test

SPONSOR: 3M Commercial Chemicals Division

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

TEST ARTICLE: T-3608

CONTROL ARTICLE: N/A

PROPOSED STARTING/COMPLETION DATE OF TEST: 7/84 - 10/84

TEST SYSTEM: Female New Zealand White Albino Rabbits

SOURCE: Haylton Distributed
Denver Pa

OBJECTIVE: To determine the irritation potential of the test article to the skin of 6 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 2 test sites selected lateral to the midline of the back approximately ten centimeters apart. 1 of the 2 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 grams) will be applied to 1 abraded and 1 intact site(s) on each animal, covered ~~with~~ and ~~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 1 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.

William C. McCormick 7/6/84
Sponsor Date

Karen D. Malley 7/13/84
Study Director Date

Form 19171-12-B-PWO

APPENDIX II

Principal Participating Personnel Involved in the Study

Name	Function
G. E. Hart	Sr. Laboratory Technician Acute Toxicology
K. D. O'Malley, BS	Senior Toxicologist Study Director
K. L. Ebbens, BS	Supervisor Toxicology Testing
G. C. Pecore	Supervisor Animal Laboratory

APPENDIX III

Composition 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.

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.