Primary Skin Irritation Test

with T-3421

in Albino Rabbits

Experiment No.: 0883EB0288

Conducted At: Safety Evaluation Laboratory
Riker Laboratories, Inc.
St. Paul, Minnesota

Dates Conducted: June 15, 1983 to June 18, 1983

Conducted By:

D. M. Markoe, Jr. 8/5/83

D. M. Markoe, Jr., BS — Date
Toxicologist
Study Director

Reviewed By:

K. D. O'Malley 7/20/83

K. D. O'Malley, BS — Date
Senior Toxicologist
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W. C. McCormick

Summary

The results of the primary skin irritation test conducted from June 15, 1983 to June 18, 1983 at Riker Laboratories, Inc., St. Paul, Minnesota indicate that T-3421 is moderately irritating (3.2/8.0) to the skin of female albino rabbits. Mild erythema and edema were noted at the one hour evaluation following a one day occluded contact period. The erythema persisted at the 48 hour evaluation while the edema subsided slightly.

Introduction

The objective of this study was to determine the primary skin irritation potential of T-3421 to the skin of female albino rabbits. This study was conducted in accordance with the Food and Drug Administration's Good Laboratory Practice Regulation of 1978. 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 g) 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 acetone.

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-3421

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.
3B987	2	2	2	1	2	2	2	1
3B990	2	2	2	1	2	2	1	1
3B993	2	1	1	0	2	2	2	0
3B996	2	2	1	1	2	2	2	1
3B951	2	2	2	1	2	2	2	1
3B991	2	2	2	1	2	2	2	1
Mean	2.0	1.8	1.7	0.8	2.0	2.0	1.8	0.8
Subtotal			6.3				6.6	

Rating: Moderately irritating

Primary Irritation Index: 3.2/8.0

Key: Er. = Erythema
Ed. = Edema

APPENDIX I Riker Experiment No.: 0883EB0288

PROTOCOL

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-3421

CONTROL ARTICLE: NONE

PROPOSED STARTING/COMPLETION DATE OF TEST: 6/83 - 8/83

TEST SYSTEM: Female New Zealand White Albino Rabbits

SOURCE: DUTCHLAND LAB. 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 gauze and secured with tape. 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.

W. C. McCormick 6-9-83

Sponsor Date

Study Director Date

APPENDIX II

Principal Participating Personnel Involved in the Study

Name	Function
D. M. Markoe, Jr., BS	Toxicologist Study Director
K. L. Ebbens, BS	Supervisor Toxicology Testing
K. D. O'Malley, BS	Senior Toxicologist Acute Toxicology
G. C. Pecore	Supervisor Animal Laboratory

APPENDIX III

Test and/or Control Article Characterization

for KTZ-15 (CC834-4)
T-3421

1. The identity strength, uniformity, composition, purity or other pertinent characterizations of the test and/or control substances have been determined and documented as of 25 May 83

2. The method of synthesis or origin of the test and control substances, including their amount and the method of bioassay (if applicable) is documented.

yes V no ____

3. The stability of the test and/or control substances have been determined or will be determined as of 25 Jun 83 or end of Test

The above information and documentation are located in the sponsor's records.

D. Ricker 5/25/83
Sponsor Date

cc L.D. Winter 236-2B
W.C. McCormick 220-2E
W.H. Pearlman 223-65E
D. Pauly 236-1

APPENDIX IV

QUALITY ASSURANCE STATEMENT

Acute Toxicology Laboratory Studies

Study No.: 082303222

This short term study was audited by Compliance Audit and the final report examined against the raw data on August 17, 1983. The results of the audit were reported to the study director and to management on August 17, 1983.

In addition to the data audit, different significant phases for studies underway in the Acute Toxicology Laboratory are inspected weekly on a recurring cycle, and the facilities are examined by Compliance Audit on a three month schedule.

Gail E. Van Buskirk
Compliance Audit

August 17, 1983
Date