Primary Skin Irritation Test

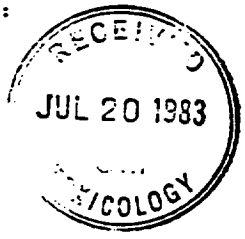
with T-3371

in Albino Rabbits

Experiment No.: 0883EB0079

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

Dates Conducted: March 1, 1983 to March 17, 1983



Conducted By: D. M. Markoe, Jr., BS — Date 6/30/83
Toxicologist
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Summary

The results of the ICAO skin irritation test conducted from March 1, 1983 to March 17,1983 at Riker Laboratories, Inc., St. Paul, Minnesota indicate that T-3371 produced irreversible tissue damage to the skin of female albino rabbits following a four hour, a one hour, and a three minute contact period. Moderate erythema and edema, as well as, chemical burn, eschar and necrosis were produced following all three contact periods. An endpoint, as required by ICAO, was not achieved due to the extreme irritation following each contact period.

Introduction

The objective of this study was to determine the ICAO skin irritation potential of T-3371 to the skin of female albino rabbits. This study is 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.

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 either a four hour, one hour or three minute[d] exposure period.

At the end of the exposure period, the plastic wrappings, patches, and all residual test article were removed[e]. One, 24 and 48 hours after removal of the test article, the test sites were examined for irreversible damage and scored separately for erythema and edema on a graded scale of 0 - 4 (Table 1).

The length of the exposure period is reduced until an endpoint of no irreversible damage is reached, if possible.

The results are presented in Tables 2-4. The protocol, principal personnel involved in the study, composition characteristics and Quality Assurance statement are contained in Appendices I - IV.

[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] Three animals per exposure group.
[e] The test article was removed with water.

Table 1

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

Table 2

Primary Skin Irritation Test - Albino Rabbits

with T-3371 (four hour contact)

Irritation Scores for Right Intact Skin Sites After Removal

Animal Number	Immediately ER	Immediately ED	24 Hours ER	24 Hours ED	48 Hours ER	48 Hours ED
3B358	2 E	4	2 EC	3	2 EN	2
3B350	2 E	4	2 EC	3	2 EN	2
3B353	2	4	2 EC	3	2 ENX	2

Irritation Scores for Left Intact Skin Sites After Removal

Animal Number	Immediately ER	Immediately ED	24 Hours ER	24 Hours ED	48 Hours ER	48 Hours ED
3B358	2 E	4	2 EC	3	2 EN	3
3B350	2 E	4	2 EC	3	2 EN	2
3B353	2	4	2 EC	3	2 ENX	3

Key: C = Chemical burn
E = Eschar
N = Necrosis
X = Epithelial sloughing
ED = Edema
ER = Erythema

Table 3

Primary Skin Irritation Test - Albino Rabbits

with T-3371 (one hour contact)

Irritation Scores for Right Intact Skin Sites After Removal

Animal Number	Immediately ER	Immediately ED	24 Hours ER	24 Hours ED	48 Hours ER	48 Hours ED
3B349	1	2	2 C	3	2 EN	3
3B384	1	1	2 C	2	2 EN	2
3B355	1	2	2 C	2	2 EN	2

Irritation Scores for Left Intact Skin Sites After Removal

Animal Number	Immediately ER	Immediately ED	24 Hours ER	24 Hours ED	48 Hours ER	48 Hours ED
3B349	1	2	2 C	3	2 EN	2
3B384	1	1	2 C	2	2 XE	2
3B355	1	2	2 C	2	2 NXE	2

Key: C = Chemical burn
E = Eschar
N = Necrosis
X = Epithelial sloughing
ED = Edema
ER = Erythema

Table 4

Primary Skin Irritation Test - Albino Rabbits

with T-3371 (three minute contact)

Irritation Scores for Right Intact Skin Sites After Removal

Animal Number	Immediately ER	ED	24 Hours ER	ED	48 Hours ER	ED
3B397	2 B	1	2 NOX	2	2 NOX	2
3B395	2 B	1	2 NO	2	2 NO	2
3B394	2 B	1	2 NOX	2	2 NOX	2

Irritation Scores for Left Intact Skin Sites After Removal

Animal Number	Immediately ER	ED	24 Hours ER	ED	48 Hours ER	ED
3B397	2 B	1	2 NOX	2	2 NOX	2
3B395	2 B	1	2 NO	2	2 NO	2
3B394	2 B	1	2 NO	2	2 NO	2

Key: B = Blancing
X = Epithelial sloughing
O = Eschar
N = Necrosis
ED = Edema
ER = Erythema

APPENDIX I Riker Experiment No.: _____

PROTOCOL 7.

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-7571

CONTROL ARTICLE: None

PROPOSED STARTING/COMPLETION DATE OF TEST: 2/83 - 5/83

TEST SYSTEM: Female New Zealand White Albino Rabbits

SOURCE: DUTCHLAND LABS, 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. 0 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 g) will be applied to 0 abraded and — 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~~ four 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:

1 hour contact on three rabbits
4 hour contact on remaining three rabbits

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.

* one sight: one hr. application, 2nd sight 4 hr. application.

[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

** Read each site upon removal of test substance and 1 and 2 days.

W. C. T. Conning 2/16/83
Sponsor Date

[signature] 2/22/83
Study Director Date

Form 19171-12-8-PWO

Riker Experiment No.: 0883EB0079

APPENDIX I (concluded)
Deviations and/or Amendments to Protocol

1. In addition to the four hour and one hour contact applications an additional application of three minute contact with three animals will be dosed.

D. M. Marbaid 3/3/83
Study Director Date

2. Due to a delay in report processing the proposed completion date should be amended to 6/83.

D. M. Marbaid 6/30/83
Study Director Date

3. _____

Study Director Date

4. _____

Study Director Date

5. _____

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

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.