Acute Ocular Irritation Test

with T-3494

in Albino Rabbits

Experiment No.: 0884EB0011

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

Dates Conducted: January 3, 1984 to January 10, 1984

Conducted By: D. M. Markoe, Jr. 1/24/84
D. M. Markoe, Jr., BS — Date
Toxicologist
Study Director

Reviewed By: Karen D. O'Malley 1/24/84
K. D. O'Malley, BS — Date
Senior Toxicologist
Acute Toxicology

dc: M. T. Case
K. L. Ebbens
F. D. Griffith
W. C. McCormick

Summary

The results of the acute ocular irritation test conducted from January 3, 1984 to January 10, 1984 at Riker Laboratories, Inc., St. Paul, Minnesota indicate that T-3494 is minimally irritating (3.3/110.0) to the eye of the female albino rabbit. Neither corneal opacity nor iritis were produced during the study. Minimal conjunctivitis was noted at the one hour evaluation and subsided by the two day evaluation.

Introduction

The objective of this study was to determine the acute ocular irritation properties of T-3494 when instilled into the eye 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 to evaluate the ocular irritating properties of the test article. The test method was modeled after that of Draize et al[b].

The test article was instilled into the conjunctival sac of the right eye of each rabbit according to the treatment procedure presented in Table 1 with the left eye of each animal serving as a control. At each scoring interval, the cornea, iris and palpebral conjunctiva were examined and graded for irritation and injury according to a standard scoring system[b]. The maximum possible score at any one examination and scoring period 110 points, which indicates maximal irritation and damage to all three ocular tissues (cornea, iris, conjunctiva) while a score of zero indicates no irritation (Table 2). In this scoring system, special emphasis is placed upon irritation or damage to the cornea, while less emphasis is placed upon damage to the iris and conjunctiva.

After completion of the test, the scores were analyzed, and a descriptive eye irritation rating was assigned to the test article. The criteria used for assignment of the descriptive rating were the frequency, the extent and the persistence of irritation or damage which occurred to the three ocular tissues (Table 3). The individual results are presented in Table 4.

[a] Hazleton Dutchland, Inc., Denver, PA
[b] Draize: Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics (1965).

The rating is arrived at by selecting the maximum mean irritation score at one hour, one, two or three days after instillation. If the rate of dissipation of injury does not meet the requirements defined for the descriptive rating appropriate for a particular numerical score, the descriptive rating is raised by one or more levels. The rating system is presented in Table 3. The protocol, principal personnel involved in the study, composition characteristics and Quality Assurance statement are contained in Appendices I - IV.

Table 1

Eye Irritation Test - Albino Rabbits

Treatment Procedure

Test Article	Number of Animals Evaluated	Form Administered	Quantity of Test Article Administered	Contact Period (seconds)	Volume of Wash (tap water)	Evaluation Time Post Dose Administration
T-3494	6	solid	0.1 gm	unlimited	none	1 Hour, 1, 2, 3 and 7 Days

Table 2

Eye Irritation Test - Albino Rabbits

Scale of Weighted Scores for
Grading the Severity of Ocular Lesions

Ocular Tissues	Description	Draize Grade
Conjunctiva	Redness (A)	
	Redness (refers to palpebral conjunctiva only). Vessels definitely injected above normal.	1
	More diffuse, deeper crimson red, individual vessels not easily discernible.	2
	Diffuse beefy red.	3
	Chemosis (B)	
	Any swelling above normal (included nictitating membrane).	1
	Obvious swelling with partial eversion of the lids.	2
	Swelling with lids about half-closed.	3
	Swelling with lids about half-closed to completely closed.	4
	Discharge (C)	
	Any amount different from normal (Does not include small amount observed in inner canthus of normal animals).	1
	Discharge with moistening of the lids and hairs just adjacent to the lids.	2
	Discharge with moistening of the lids and hairs and considerable area around eye.	3
	Score (A + B + C) x 2 Total maximum = 20	
Cornea	Opacity (A)	
	Opacity - Degree of density (area which is most dense is taken for reading).	
	Scattered or diffuse area, details of iris clearly visible.	1
	Easily discernible translucent areas, details of iris slightly obscured.	2
	Opalescent areas, no details of iris visible, size of pupil barely discernible.	3
	Opaque, iris invisible.	4
	Area of Cornea Involved (B)	
	One quarter (or less) but not zero.	1
	Greater than one-quarter, but less than one-half.	2
	Greater than one-half, but less than three-quarters.	3
	Greater than three-quarters, up to whole area.	4
	Score equals A x B x 5 Total maximum = 80	
Iris	Values (A)	
	Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still reacting to light (sluggish reaction is positive).	1
	No reaction to light, hemorrhage, gross destruction (any or all of these).	2
	Score equals A x 5 Total maximum = 10	

Note: The maximum total score is the sum of all scores obtained for the conjunctiva.

Table 3

Eye Irritation Test - Albino Rabbits

Classification of Test Materials
Based on Eye Irritation Properties

Rating	Range	Definition
Non-Irritating	0.0 - 0.5	To maintain this rating, all scores by the one day reading must be zero; otherwise, increase rating one level.
Practically Non-Irritating	>0.5 - 2.5	To maintain this rating, all scores by the one day reading must be zero; otherwise, increase rating one level.
Minimally Irritating	>2.5 - 15.0	To maintain this rating, all scores by the three day reading must be zero; otherwise, increase rating one level.
Mildly Irritating	>15.0 - 25.0	To maintain this rating, all scores by the seven day reading must be zero; otherwise, increase rating one level.
Moderately Irritating	>25.0 - 50.0	To maintain this rating, scores by seven days must be $\leq$ 10 for 60% or more of the animals. Also, mean seven day score must be $\leq$ 20. If seven day mean score is $\leq$ 20 but < 60% of animals show scores < 10, then no animal among those showing scores > 10 can exceed a score of 30 if rating is to be maintained; otherwise raise rating one level.
Severely Irritating	>50.0 - 80.0	To maintain this rating, scores by seven days must be $\leq$ 30 for 60% or more of the animals. Also, mean seven day score must be $\leq$ 40. If seven day mean score $\leq$ 40 but < 60% of the animals show scores $\leq$ 30, then no animal among those showing scores > 30 can exceed a score of 60 if rating is to be maintained; otherwise, raise rating one level.
Extremely Irritating	>80.0 - 110.0	

TABLE 4

EYE IRRITATION TEST - ALBINO RABBITS

with T-3494

RESULTS

Tissue	Examination Period	ANIMAL NUMBERS						Means
		3B2037	3B2036	3B2035	3B2040	3B2039	3B2038	
Cornea (D-A)	1 Hour	0	0	0	0	0	0	0.0
Iris		0	0	0	0	0	0	0.0
Conjunctiva (RSD)		4(2-0-0)	4(2-0-0)	4(2-0-0)	2(1-0-0)	4(2-0-0)	2(1-0-0)	3.3
	Total	4	4	4	2	4	2	3.3
Cornea (D-A)	1 Day	0	0	0	0	0	0	0.0
Iris		0	0	0	0	0	0	0.0
Conjunctiva (RSD)		0	2(1-0-0)	2(1-0-0)	0	0	0	0.7
	Total	0	2	2	0	0	0	0.7
Cornea (D-A)	2 Days	0	0	0	0	0	0	0.0
Iris		0	0	0	0	0	0	0.0
Conjunctiva (RSD)		0	0	0	0	0	0	0.0
	Total	0	0	0	0	0	0	0.0
Cornea (D-A)	3 Days	0	0	0	0	0	0	0.0
Iris		0	0	0	0	0	0	0.0
Conjunctiva (RSD)		0	0	0	0	0	0	0.0
	Total	0	0	0	0	0	0	0.0
Cornea (D-A)	7 Days	0	0	0	0	0	0	0.0
Iris		0	0	0	0	0	0	0.0
Conjunctiva (RSD)		0	0	0	0	0	0	0.0
	Total	0	0	0	0	0	0	0.0

Riker Experiment No.: _____

APPENDIX I

PROTOCOL

TEST: Acute Ocular Irritation Test

SPONSOR: 3M Commercial Chemicals Division

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

TEST ARTICLE: T-3494

CONTROL ARTICLE: _____

PROPOSED STARTING/COMPLETION DATE OF TEST: 1/-4 - 4/4

TEST SYSTEM: Female New Zealand White Albino Rabbits

SOURCE: _____

OBJECTIVE: The objective of this test will be to determine the irritation potential of the test article to the ocular tissu (cornea, iris and conjunctiva) of _____ albino rabbits. Rabbits were selected as the test syst for their sensitivity to irritants, historical use, ease of handling and general availability.

METHOD: The animals will be housed in standard wire-mesh cages in temperature and humidity control rooms with food[a] and water offered *ad libitum*. Each animal will be assigned a numbered ear which will correspond to a card affixed to the outside of the cage. The test article will be instilled the conjunctival sac of the right eye at a dose of 0.1 _____ with the contralateral eye of each ani serving as a control. At _____ hours and 1, 2, 4 _____ c (additional scoring intervals may be added to further characterize the ocular reactions), the tissues be examined and graded for irritation and injury according to a standard scoring system of Dr *et al*[b]. After completion of the test, the scores will be analyzed, and a descriptive eye irritation r assigned to the test article. Eye examinations may be carried out with the aid of sodium fluores If deemed necessary by the study director, washed eye procedures entailing a 5 and 30 se contact period with a _____ wash over a _____ period will be conducted 3 animals per procedure. All raw data generated by the study director and the final report w stored in the Riker Laboratories' Archive, St. Paul, Minnesota.

[a] Purina Rabbit Chow, Ralston-Purina, St. Louis, Missouri

[b] Draise: Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics (1965) Published by the Editorial Committee of The Association of Food and Drug Officials of the United States.

_____ _____ _____

Sponsor Date Study Director

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.