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Du Pont HLR 784-88

Study Title

Eye Irritation Test in Rabbits of

[redacted]

Author

William J. Brock

Study Completed On

December 28, 1988

Performing Laboratory

E. I. du Pont de Nemours and Company, Inc.
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P. O. Box 50
Newark, Delaware 19714

[redacted]

Laboratory Project ID

Haskell Laboratory Report No. 784-88

GENERAL INFORMATION

Material Tested: [redacted]

Medical Research No.: [redacted]

Haskell No.: 17,503

Physical Form: White powder

Purity: [redacted]

Contaminants: [redacted]

Synonyms: [redacted]

Submitter's Notebook No.: [redacted]

Stability: The test material was assumed to be stable under the conditions of administration.

Sponsor: Chemicals and Pigments Department
E. I. du Pont de Nemours and Company, Inc.
Wilmington, Delaware

Material Submitted By: [redacted]
Chemicals and Pigments Department
E. I. du Pont de Nemours and Company, Inc.
Jackson Laboratory
Deepwater, New Jersey

In-Life Phase
Initiated - Completed: 11/16/88 - 11/19/88

Notebook: [redacted]

There are 9 pages in this report.

Distribution: [redacted]

Eye Irritation Test in Rabbits of

[redacted]

SUMMARY

[redacted] was evaluated for acute eye irritation potential in 2 male rabbits. [redacted] ced no irritation in either the washed or unwashed rabbit eye. Fluorescein stain and biomicroscopic examinations were negative for corneal injury in both treated eyes throughout the study. Under the conditions of this study, [redacted] was not an eye irritant.

Work by: Carol Finlay 12/2/88
Carol Finlay
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Study Director: William J. Brock 12/2/88
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Reviewed and
Approved for Issue: William J. Brock 12/28/88
William J. Brock, Ph.D.
Study Director

WJB:alr:HLR109.10

QUALITY ASSURANCE DOCUMENTATION

STUDY: [redacted] Eye Irritation Test in Rabbits of [redacted]
H# 17,503

AUDITS:

Item Audited	Audit Date
Records and final report	12/12,19-21/88

SHORT-TERM AUDIT REPORT NUMBER: [redacted]
DATE FINDINGS REPORTED TO MANAGEMENT AND STUDY DIRECTOR: 12-21-88

Reported by: Stephen W. Records 12-28-88
Stephen W. Records — Date
Quality Assurance Auditor

INTRODUCTION

The purpose of this study was to evaluate the eye irritation potential of [redacted]. This study was conducted according to the applicable EPA Good Laboratory Practice Regulations. Areas of noncompliance are documented in the study records. No deviations existed that significantly affected the validity of the study.

MATERIALS AND METHODS

A. Animal Husbandry

Young adult male New Zealand White rabbits were received from Hare Marland, Hewitt, New Jersey. The rabbits were housed singly in suspended, stainless steel, wire-mesh cages. Each rabbit was assigned a unique identification number which was recorded on a card affixed to the cage. Purina Certified High Fiber Rabbit Chow® #5325 and water were available ad libitum. Rabbits were quarantined, weighed and observed for general health for approximately 2 weeks. Animal rooms were maintained on a timer-controlled, 12-hour light/12-hour dark cycle. Environmental conditions of the rooms were targeted for a temperature of 20°C ± 2°C and relative humidity of 50% ± 10%. Excursions outside these ranges were judged to have been of insufficient magnitude and/or duration to have adversely affected the validity of the study.

B. Protocol

On the day before study initiation, the eyes of 2 male New Zealand White rabbits were examined using fluorescein dye. Animals showing preexisting corneal or conjunctival injury or irritation were not used in this study. The rabbits weighed 3029 and 3405 grams on the day of treatment.

A 0.01 g aliquot of [redacted] was introduced into the lower conjunctival sac of the right eyes of 2 male New Zealand White rabbits. The left eyes served as controls. The treated and control eyes of 1 animal remained unwashed. Approximately 20 seconds after the test material was administered, both eyes of the remaining animal were rinsed for 1 minute with lukewarm tap water. Approximately 1 and 4 hours and 1, 2 and 3 days after treatment, the rabbits were examined for evidence of eye irritation.

At each observation the treated eyes were examined using illumination and magnification and scored for ocular reactions using the Draize scale (presented in Table I). The untreated eye of each animal was also examined and used for comparison. Any unusual effects, e.g., pannus, blistering of the conjunctiva, ulceration or other effects indicative of corrosive action were also noted. Fluorescein dye was used to evaluate corneal ulceration and irritation starting at the 1-day observation and at each subsequent observation. Biomicroscopic examinations for corneal injury were conducted at the 1-day observation and each subsequent observation. Treated eyes were scored according to the system presented in Table II.

C. Records Retention

All raw data and the final report will be stored in the archives of Haskell Laboratory for Toxicology and Industrial Medicine, E. I. du Pont de Nemours and Company, Inc., Newark, Delaware or in the Du Pont Records Management Center, Wilmington, Delaware.

RESULTS AND CONCLUSIONS

[redacted] produced no irritation in either treated rabbit eye. Fluorescein stain and biomicroscopic examinations were negative for corneal injury in both treated eyes throughout the study. Under the conditions of this study, [redacted] was not an eye irritant.

TABLE I

DRAIZE[1] SCALE FOR SCORING OCULAR LESIONS

(1)	Cornea	
	(A) Opacity-degree of density (area most dense taken for reading)	
	No opacity	0
	Scattered or diffuse area, details of iris clearly visible	1 (Slight)
	Easily discernible translucent areas, details of iris slightly obscured	2 (Mild)
	Opalescent areas, no details of iris visible, size of pupil barely discernible	3 (Moderate)
	Opaque, iris invisible	4 (Severe)
	(B) Area of cornea involved	
	One quarter (or less) but not zero	1 (Localized)
	Greater than one quarter, but less than half	2 (Small)
	Greater than one half, but less than three quarters	3 (Moderate)
	Greater than three quarters, up to whole area	4 (Generalized)
	Score equals A x B x 5	Total Maximum = 80
(2)	Iris	
	(A) Values	
	Normal	0
	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 (Moderate)
	No reaction to light, hemorrhage, gross destruction (any or all of these)	2 (Severe)
	Score equals A x 5	Total Maximum = 10
(3)	Conjunctiva	
	(A) Redness (refers to palpebral and bulbar conjunctiva excluding cornea and iris)	
	Vessels normal	0
	Vessels definitely injected above normal	1 (Mild)
	More diffuse, deeper crimson red, individual vessels not easily discernible	2 (Moderate)
	Diffuse beefy red	3 (Severe)

TABLE I (Cont'd)

DRAIZE SCALE FOR SCORING OCULAR LESIONS

(B)	Chemosis	
	No swelling	0
	Any swelling above normal (includes nictitating membrane)	1 (Slight)
	Obvious swelling with partial eversion of lids	2 (Mild)
	Swelling with lids about half closed	3 (Moderate)
	Swelling with lids about half closed to completely closed	4 (Severe)
(C)	Discharge	
	No discharge	0
	Any amount different from normal (does not include small amounts observed in inner canthus of normal animals)	1 (Minimal)
	Discharge with moistening of the lids and hairs just adjacent to lids	2 (Moderate)
	Discharge with moistening of the lids and hairs, and considerable area around the eye	3 (Copious)

Score equals (A + B + C) x 2 Total Maximum = 20

The maximum total score is the sum of all scores obtained for the cornea, iris and conjunctiva. Total maximum score possible = 110.

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[1] Draize, J. H., "Dermal Toxicity." Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics. The Editorial Committee of the Association of Food and Drug Officials of the United States, Austin, Texas, 1959, pp. 46-59.

TABLE II

BIOMICROSCOPE CLASSIFICATIONS OF CORNEAL INJURY
(Biomic of Cornea)

0 = No injury; cornea within normal limits.

Slight (1) = Epithelial changes visible only with biomicroscope (may include localized area of mild injury).

Mild (2) = Opacity visible with ophthalmoscope or light but showing epithelial changes only with biomicroscope (may include localized area of moderate injury).

Moderate (3) = Opacity visible with ophthalmoscope or light but showing epithelial and stromal changes with biomicroscope (may include localized area of severe injury).

Moderate to Severe (4) = Opacity visible with ophthalmoscope or light but showing epithelial and stromal changes and endothelial relucency with unremarkable swelling. This type of injury shows evidence of healing (reversible damage) within 14 days.

Severe (5) = Opaqueness or opacity visible with ophthalmoscope or light but showing epithelial and stromal changes and endothelial relucency and swelling or other distortion. This type of injury does not show evidence of healing (permanent damage) within 14 days.

- = No biomicroscope evaluation performed.