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Du Pont HLR 385-89

Study Title

Eye Irritation Test with [redacted] in Rabbits

Author

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Study Completed On

July 31, 1989

Performing Laboratory

E. I. du Pont de Nemours and Company, Inc.
Haskell Laboratory for Toxicology and Industrial Medicine
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[redacted]

Laboratory Project ID

Haskell Laboratory Report No. 385-89

GENERAL INFORMATION

Material Tested:	[redacted]
Medical Research No.:	[redacted]
Haskell No.:	17,869
Physical Form:	Milky liquid dispersion
Purity:	[redacted]
Composition:	[redacted]
Synonyms:	[redacted]
Other Code:	[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:	6/13/89 - 6/16/89
Notebook:	[redacted]

There are 11 pages in this report.

Distribution: [redacted]

Eye Irritation Test with MPD-7352A in Rabbits

SUMMARY

[redacted] was evaluated for acute eye irritation potential in 2 young adult rabbits. Both rabbits were dosed with a single 0.01 mL aliquot of test material in 1 eye. In 1 rabbit the treated eye was washed after treatment. In the other rabbit the treated eye was not washed. The contralateral eye of each rabbit served as a control. Both eyes of each rabbit were examined using illumination and magnification at 1 and 4 hours, and 1, 2 and 3 days following treatment. Biomicroscopic and fluorescein stain examinations were also conducted on post-treatment days 1, 2 and 3.

[redacted] produced mild conjunctival redness, slight chemosis and minimal blood-tinged discharge by 1 hour after treatment in 1 rabbit. Conjunctival redness only was observed in this animal at 4 hours. Similar ocular responses were observed in the second rabbit at 1 and 4 hours after treatment with the addition of moderate iritis and slight generalized opacity. Fluorescein stain and biomicroscopic examinations were neg ve for corneal injury in both treated eyes throughout the study. The treated eyes of both rabbits were normal by 1 day following study initiation.

Under the conditions of this study [redacted] was a moderate eye irritant.

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Study Director

DEM:alr:HLR119.12

QUALITY ASSURANCE DOCUMENTATION

STUDY: [redacted] Eye Irritation Test with [redacted] in Rabbits
H# 17,869

AUDITS:

Items Audited	Audit Dates
Test System Identification and Housing	6/13/89

SHORT-TERM AUDIT REPORT NUMBER: [redacted]
DATE FINDINGS REPORTED TO MANAGEMENT AND STUDY DIRECTOR: 6/13/89

Reported by: William J. Lynam — 6/31/89
William J. Lynam
Quality Assurance Auditor
Date

INTRODUCTION

The purpose of this study was to evaluate the acute eye irritation potential of [redacted] in young adult rabbits. 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 female 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 of study initiation, the eyes of 2 female rabbits were examined using illumination, magnification and fluorescein dye. These animals were selected for this study as they showed no evidence of preexisting corneal or conjunctival injury or irritation and were judged to be in good health. These rabbits were approximately 14 weeks old and weighed 3067 and 3086 grams, respectively, on the day of treatment.

A 0.01 mL aliquot of [redacted] was introduced into the lower conjunctival sac of each right eye of 2 female rabbits. The left eye of each rabbit was not treated with the test material and served as a control. The [redacted] treated and control eyes of 1 animal remained unwashed. Approximately 20 seconds after the test material was administered, both eyes of the remaining rabbit were rinsed for approximately 1 minute with water at room temperature.

Each rabbit was observed for approximately 30 to 60 seconds before being returned to its cage and any abnormal behavior was noted.

Approximately 1 and 4 hours, and 1, 2 and 3 days after [redacted] was administered, the rabbits were examined for evidence of eye irritation. At each of these observation periods eyes were examined using illumination and magnification and scored for ocular reactions using the Draize scale (presented in Table 1). Eyes were also observed for any unusual responses to treatment such as pannus, blistering of the conjunctiva, ulceration or other effects indicative of corrosive action. Hemastix® reagent strips were used to detect occult blood in discharge from the eye. Biomicroscopic and fluorescein stain examinations were also conducted at post-treatment days 1, 2 and 3. The eyes were scored according to the method of classification presented in Table 2. Control eyes were not scored. These untreated eyes were used for comparison and were considered "normal" relative to the treated eye.

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 mild conjunctival redness, slight chemosis and minimal blood-tinged discharge by 1 hour after treatment in 1 rabbit. Conjunctival redness only was observed in this animal at 4 hours. Similar ocular responses were observed in the second rabbit at 1 and 4 hours after treatment with the addition of moderate iritis and slight generalized opacity. Fluorescein stain and biomicroscopic examinations were negative for corneal injury in both treated eyes throughout the study. The treated eyes of both rabbits were normal by 1 day after study initiation. Individual eye irritation scores are presented in Tables 3 and 4.

Under the conditions of this study, [redacted] was moderate eye irritant.

TABLE 1

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)
(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)
(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 1 (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)

[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 2

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.

TABLE 3

EYE IRRITATION REACTIONS OBSERVED IN THE UNWASHED RABBIT EYE AFTER TREATMENT WITH [redacted]

Rabbit Number 23931	1 hr	4 hr	1 day	2 days	3 days
Cornea					
Opacity	0	1	0	0	0
Area	0	4	0	0	0
Iris	1	1	0	0	0
Conjunctiva					
Redness	1	1	0	0	0
Chemosis	1	1	0	0	0
Discharge	0	0	0	0	0
Biomic of Cornea	-	-	0	0	0

Fluorescein examinations: Negative for corneal injury at all observation periods.

TABLE 4

EYE IRRITATION REACTIONS OBSERVED IN THE WASHED RABBIT EYE AFTER TREATMENT WITH [redacted]

Rabbit Number 23932	1 hr	4 hr	1 day	2 days	3 days
Cornea					
Opacity	0	0	0	0	0
Area	0	0	0	0	0
Iris	0	0	0	0	0
Conjunctiva					
Redness	1	1	0	0	0
Chemosis	1	0	0	0	0
Discharge	1(H+)	0	0	0	0
Biomic of Cornea	-	-	0	0	0

Fluorescein examinations: Negative for corneal injury at all observation periods.

H+ = Hemastix® evaluation was positive for blood.