

Study Title

Eye Irritation Test with [REDACTED] in Rabbits

Author

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Study Completed On

February 13, 1992

Performing Laboratory

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

Laboratory Project ID

Haskell Laboratory Report No. 809-91

GENERAL INFORMATION

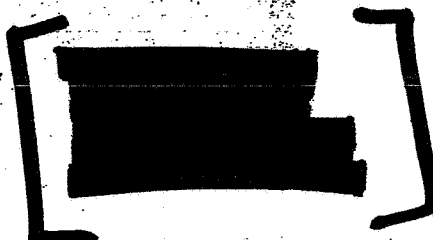
Substance Tested: [REDACTED]
Medical Research No.: [REDACTED]
Haskell No.: 19,173
Haskell Test Code No.: [REDACTED]
Physical Form: Slightly yellow liquid dispersion
Composition: [REDACTED]
Purity: [REDACTED]
Synonym: [REDACTED]
Submitter's Notebook No.: [REDACTED]
Stability: In the absence of visible evidence to the contrary, the test substance was assumed to be stable under the conditions of administration.
Sponsor: Du Pont Chemicals
E. I. du Pont de Nemours and Company
Wilmington, Delaware
Substance Submitted By: [REDACTED]
Du Pont Chemicals
E. I. du Pont de Nemours and Company
Chambers Works
Deepwater, New Jersey
Study Initiated - Completed: 11/15/91 - 2/13/92
In-Life Phase
Initiated - Completed: 11/19/91 - 11/22/91
Notebook: [REDACTED]

There are 12 pages in this report.

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GENERAL INFORMATION (CONT'D)

Distribution:



Eye Irritation Test with [REDACTED] in Rabbits

SUMMARY

[REDACTED] was evaluated for acute eye irritation potential in 2 rabbits. The eyes of the rabbits were examined on the day of treatment and on days 1, 2, and 3 following treatment.

The test substance produced mild conjunctival redness in the treated unwashed eye. No irritation was observed in the treated washed eye. Fluorescein stain examinations were negative for corneal injury, and biomicroscopic examinations revealed no corneal damage in either treated eye. The treated unwashed eye was normal by 3 days following treatment.

Under the conditions of this study, [REDACTED] was a mild eye irritant.

Work by:

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Acknowledgment: Bryan W. Crossley also participated in the conduct of this study.

JWS/lmr

QUALITY ASSURANCE DOCUMENTATION

Dates of Inspection:

Conduct - 11/20/91

Records, Report(s) - 1/21/92

Findings reported to:

Study Director - 1/24/92

Management - 2/11/92

Reported by:

James Mackay II
James Mackay II
Quality Assurance Auditor

2/12/92
Date

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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 affected the validity of the study.

MATERIALS AND METHODS

A. Animal Husbandry

Young adult male and 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 $20^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and relative humidity of $50\% \pm 10\%$. 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 prior to treatment, the eyes of one female and one male New Zealand White 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 weighed 3608 and 3660 grams, respectively, on the day of treatment.

Approximately 0.01 mL of [REDACTED] was introduced into the lower conjunctival sac of each left eye. The right eye of each rabbit was not treated with the test substance and served as a control. The treated and control eyes of 1 animal remained unwashed. Approximately 20 seconds after the test substance was administered, both eyes of the remaining rabbit were rinsed for approximately 1 minute with room temperature water. 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 according to 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. 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, Newark, Delaware or in the Du Pont Records Management Center, Wilmington, Delaware.

RESULTS

[REDACTED] produced mild conjunctival redness in the treated unwashed eye. No irritation was observed in the treated washed eye. Fluorescein stain examinations were negative for corneal injury, and biomicroscopic examinations revealed no corneal damage in either treated eye. The treated unwashed eye was normal by 3 days following treatment. Individual eye irritation scores are presented in Tables 3 and 4.

CONCLUSION

Under the conditions of this study, [REDACTED] was a mild eye irritant.

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TABLE 1
DRAIZE¹ 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)	

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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.

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TABLE 2

BIOMICROSCOPE CLASSIFICATIONS OF CORNEAL INJURY

- 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**

Rabbit Number 26667	1 Hour	4 Hours	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	1	1	0
Chemosis	0	0	0	0	0
Discharge	0	0	0	0	0
Biomicroscopic Examination of Cornea	-	-	0	0	0

Fluorescein examinations: negative for corneal injury on days 1-3.

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TABLE 4**EYE IRRITATION REACTIONS OBSERVED IN THE
WASHED RABBIT EYE AFTER TREATMENT WITH**

Rabbit Number 26583	1 Hour	4 Hours	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	0	0	0	0	0
Chemosis	0	0	0	0	0
Discharge	0	0	0	0	0
Biomicroscopic Examination of Cornea	-	-	0	0	0

Fluorescein examinations: negative for corneal injury on days 1-3.

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