TRADE SECRET

Study Title

H-23004: EYE IRRITATION TEST IN RABBITS

LABORATORY PROJECT ID: HL-1998-01312

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STUDY COMPLETED ON: January 28, 1998

PERFORMING LABORATORY: E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P.O. Box 50
Newark, Delaware 19714-0050

WORK REQUEST NUMBER: [redacted]

CERTIFICATION

Study Director:

Issued by: Tracy A. Filliben 1/28/98

Tracy A. Filliben
Toxicology Associate

Date

STUDY INFORMATION

Substance Tested: [redacted]

Synonyms/Codes: • H-23004

Haskell Number: 23004

Submitter's Notebook Number(s): [redacted]

Composition: [redacted]

Known Impurities: [redacted]

Physical Characteristics: [redacted]

Stability: The test substance appeared to be stable under the conditions of the study; no evidence of instability was observed.

Sponsor: E. I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

Study Initiated/Completed: January 5, 1998 / (see report cover page)

In-Life Initiated/Completed: January 6, 1998 / January 9, 1998

STUDY PERSONNEL

Manager:	Judith C. Stadler, Ph.D.
Study Director:	Tracy A. Filliben
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SUMMARY

H-23004 was evaluated for acute eye irritation potential in 2 New Zealand White rabbits. Approximately 0.01 mL of the test substance was instilled into the lower conjunctival sac of the right eye of each rabbit. Approximately 20 seconds after instillation, the treated and control eyes of 1 rabbit were washed. The treated and control eyes of the remaining rabbit were not washed. The eyes of the rabbits were examined on the day of treatment and on days 1, 2, and 3 following treatment.

H-23004 produced mild conjunctival redness in the treated unwashed rabbit eye. No ocular irritation was observed in the treated washed rabbit eye. The treated unwashed rabbit eye was normal by 4 hours after treatment. No clinical signs of toxicity were observed during the study. Individual eye irritation scores are presented in Tables 2 and 3.

Under the conditions of this study, H-23004 was a mild transient eye irritant.

INTRODUCTION

The purpose of this study was to evaluate the acute eye irritation potential of H-23004 in young adult New Zealand White rabbits.

MATERIALS AND METHODS

A. Animal Husbandry

Young adult male HM:(NZW)fBR New Zealand White rabbits were received from Hare Marland. 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. The last 3 digits of the identification number were written on the inside of each rabbit's ear with a water insoluble marker. The rabbits were offered approximately 125 grams of Purina® Certified High Fiber Rabbit Chow® #5325 daily during the study. Water was available *ad libitum.*

Haskell Laboratory has an animal health monitoring program. This program is monitored and administered by the Laboratory Veterinarian. Water samples are periodically analyzed for total bacterial counts and for the presence of coliforms, lead, and other contaminants. Additionally, samples from freshly washed cages and cage racks are periodically analyzed to ensure adequate sanitation by the cagewashers. Data from this program are maintained separately from study records. Animal feed is certified by the manufacturer to meet specified nutritional requirements and to be free of a list of specified contaminants. On the basis of these analyses, there is no evidence suggesting that contaminants were present in the feed or water in amounts which may have interfered with the results of this study.

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 ± 1°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 treatment, the eyes of 2 male New Zealand White rabbits were examined using illumination, magnification, and fluorescein dye. Animals used on this study were free of pre-existing corneal or conjunctival injury or irritation and were judged to be in good health. The rabbits weighed 2939 or 3208 grams on the day of treatment.

Approximately 0.01 mL of H-23004 was introduced into the lower conjunctival sac of each right eye. The left eye of each rabbit was not treated with the test substance and served as a control.

Approximately 20 seconds after the test substance was administered, both eyes of 1 rabbit were rinsed for approximately 1 minute with room temperature water. The treated and control eyes of the remaining rabbit were not washed. 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 H-23004 was administered, the rabbits were examined for evidence of eye irritation and for clinical signs of toxicity. 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. Control eyes were not scored. These untreated eyes were used for comparison and were considered "normal" relative to the treated eye.

RESULTS AND DISCUSSION

H-23004 produced mild conjunctival redness in the treated unwashed rabbit eye. No ocular irritation was observed in the treated washed rabbit eye. The treated unwashed rabbit eye was normal by 4 hours after treatment. No clinical signs of toxicity were observed during the study. Individual eye irritation scores are presented in Tables 2 and 3.

CONCLUSIONS

Under the conditions of this study, H-23004 was a mild eye irritant.

If these test scores are to be used for EEC/OECD classification, according to the guide to the labeling of dangerous substances published in the Official Journal of European Communities (EEC Directive 93/21, Annex VI), H-23004 probably should not be classified as an irritant unless further data proves otherwise.

RECORDS RETENTION

All study records, raw data, and the final report are retained at Haskell Laboratory, Newark, Delaware, or at Iron Mountain, 200 Todds Lane, Wilmington, Delaware 19802 (formerly known as the E. I. du Pont de Nemours and Company Records Management Center).

TABLE 1

DRAIZE[a] 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 (Continued)

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)

a 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

EYE IRRITATION REACTIONS OBSERVED
IN THE RABBIT EYE UNWASHED AFTER TREATMENT

RABBIT NUMBER 32415	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	0	0	0	0
Chemosis	0	0	0	0	0
Discharge	0	0	0	0	0

TABLE 3

EYE IRRITATION REACTIONS OBSERVED
IN THE RABBIT EYE WASHED AFTER TREATMENT

RABBIT NUMBER 32416	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