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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

HASKELL LABORATORY REPORT NO. HLO-387-84 [redacted]

| Material tested* | Haskell No. | Other Codes |
|---|---|---|
| [redacted] | 15,388 | [redacted] |

Study Initiated/Completed
6/11/84 - 6/18/84

Material Submitted by
[redacted]
Polymer Products Department
Washington Works

## EYE IRRITATION TEST IN RABBITS

Haskell Evaluation: Haskell Standard Operating Procedure for eye irritation testing was followed [redacted] Details are given in the appendix. In the unwashed eye, [redacted] produced moderate conjurctival redness, slight conjunctival chemosis, and slight corneal dulling with clearing by seven days. In the washed eye, [redacted] produced mild conjunctival redness with clearing by three days. When tested by this procedure, [redacted] is a moderate eye irritant.

*Purity: [redacted]

*Composition: [redacted]

*Synonyms: [redacted]

Report by:

Carol S. Auletta/Donna L. Blaszcak
Bio/dynamics Inc.

Reviewed by:

George W. Lovett, M.D.
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Associate Director

GWL/egg

Date Issued: August 30, 1984
Haskell Lab. Report No. HLO-387-84
Appendix attached: 10 pp, Bio/dynamics Project No. 5227-84
Total pages in this report: 12

Bio/dynamics Inc.

Division of Biology and Safety Evaluation

PROJECT NO.: 5227-84

# EYE IRRITATION STUDY IN RABBITS

TEST MATERIAL: HL 15,388

Submitted to: E.I. du Pont de Nemours & Company
Haskell Laboratory for Toxicology and
Industrial Medicine
Elkton Road, P.O. Box 50
Newark, Delaware 19711

Attn: [redacted]

Date: August 13, 1984

## I. INTRODUCTION

This study was conducted for E.I. du Pont de Nemours & Company to evaluate the ocular irritation produced by HL 15,388 in rabbits. The study was performed at Bio/dynamics, Inc., Mettlers Road, East Millstone, New Jersey 08873.

This report has been reviewed by the Quality Assurance Unit of Bio/dynamics, Inc. to assure its conformance with the protocol and raw data. All raw data, the original study protocol and final report will be retained on file in the Bio/dynamics Archives.

## II. EXPERIMENTAL DESIGN

| No. of Rabbits | Amount of Material | Eyes Washed/ Unwashed |
|---|---|---|
| 1 | 10 mg | Unwashed |
| 1 | 10 mg | Washed |

## III. DATES OF STUDY:

| | |
|---|---|
| Animal Receipt: | April 30, 1984 |
| Initiation (Dosing): | June 11, 1984 |
| Termination (Last Observation): | June 18, 1984 |

## IV. STUDY PERSONNEL:

| | |
|---|---|
| Study Director: | Carol S. Auletta, B.A., D.A.B.T. |
| Laboratory Supervisor: | Donna L. Blaszcak, B.S., AALAS R.L.A.T. |
| Technician in Charge: | Mary Webb, B.S., AALAS |
| Study Monitor (Report Preparation): | Deborah Metting, B.A. |

## V. STUDY CONDUCT

This study was conducted following Good Laboratory Practices.

## VI. MATERIALS

| | |
|---|---|
| A. Test Animals: | Albino Rabbits |
| Breed: | New Zealand White |
| Reason for Selection: | Standard laboratory animal for ocular irritation studies. The New Zealand White breed was used because of its availability and because of the existing historical data base for comparative evaluation. |

VI. MATERIALS (cont.)

| | |
|---|---|
| Supplier: | Hazleton-Dutchland, Inc.<br>Denver, Pennsylvania |
| Number: | Two (2 males) |
| Age: | Young adults |
| Equilibration Period: | 42 days |
| Observations: | All animals were checked for viability twice daily during the equilibration period. Prior to assignment to study all animals were examined to ascertain suitability for study. |
| Husbandry: | Currently acceptable practices of good animal husbandry were followed, e.g., Guide for the Care and Use of Laboratory Animals; DHEW Publication No. (NIH) 78-23 Revised 1978. |
| Housing: | Individually housed |
| Cages: | Suspended, stainless steel |
| Environmental Conditions: | Temperature: 60-70°F is considered an acceptable temperature range for rabbits; room temperature was monitored and recorded twice daily and maintained within this range to the maximum extent possible.<br><br>Humidity: 30-70% is considered an acceptable humidity range for rabbits; room humidity was monitored and recorded daily and maintained within this range to the maximum extent possible.<br><br>Light cycle: 12 hours light, 12 hours dark (controlled by an automatic timer) |
| Food: | Lab Rabbit Chow HF (Purina #5326), ad libitum |
| Water: | Automatic watering system, ad libitum Municipal water supply (Elizabethtown Water Co.) |

V. MATERIALS (cont.)

| | |
|---|---|
| Identification: | Each animal was identified with a monel ear tag bearing a unique number prior to testing. |
| Selection: | Animals were randomly placed in cages upon receipt and were placed on study as available at the time of study initiation. Animals considered unsuitable for study because of poor health or ocular abnormalities were excluded from selection. |

B. Test Material: HL 15,388

Description: White powder

Date of Receipt: May 21, 1984

Received from: E.I. du Pont de Nemours & Company

Storage: Room temperature

VII. METHODS

A. Duration of Study:

A single dose was administered followed by a 3 to 7 day observation period.

B. Route of Administration:

Ocular

C. Justification for Route of Administration:

The study is intended to provide information on the health hazards likely to arise from a short-term accidental exposure to the test material by the ocular route.

D. Preparation of Animals:

On the day before dosing, both eyes of each animal were examined using fluorescein dye to check for presence of corneal ulceration. Just prior to test substance application, the eyes were examined again, but without fluorescein. Animals showing pre-existing corneal or conjunctival injury or irritation were not placed on study.

E. Preparation of Test Material:

The test material was administered as received; no mixture was required.

VII. METHODS (cont.)

F. Administration of Test Substance:

1. Dose:

10 mg

2. Administration:

The appropriate amount of the test material was introduced into the lower conjunctival sac of the right eye of each animal. The upper and lower lids were gently held together for one second prior to releasing to prevent loss of material. The contralateral eye served as the control.

3. Wash:

The treated and control eye of one animal remained unwashed. Twenty seconds after the test substance was administered, both eyes of the remaining animal was rinsed for one minute with lukewarm water.

VIII. EXPERIMENTAL EVALUATION

A. Viability Check:

Twice Daily

B. Evaluation of Ocular Irritation:

1. Intervals:

Approximately 1 and 4 hours and 1, 2, 3 and 7 days after treatment, or until no signs of irritation were present.

2. Methods:

At each interval the treated and control eyes were examined and scored for ocular reactions according to the Draize scale (see Appendix A). Fluorescein dye was used to confirm presence or absence of corneal ulceration in treated eyes starting with the 24 hour observation and at each subsequent observation. Unusual effects such as pannus, blistering of the conjunctiva, ulceration and other effects indicative of corrosive action were also noted when present.

IX. RESULTS AND DISCUSSION

Individual ocular observations are presented in Table I; the scoring system used is presented in Appendix A. A summary of 1) responses considered positiv according to 16 CFR 1500.42 [CONSUMER PRODUCT SAFETY COMMISSION, Federal Hazardous Substances Act Regulations, Test for Eye Irritants] and 2) Maximum Draize Scores is presented in Table II.

HL 15.388 produced mild but reversible ocular irritation in both the washed and unwashed eyes. Both eyes had mild to moderate conjunctival irritation (redness, chemosis) and slight corneal and/or iridial changes. Both of the animals were free of ocular irritation within 3 to 7 days after instillation of the test material.

Responses in the non-rinsed eye were similar to those in the rinsed eye. Therefore, rinsing of the eye after instillation of the test material did not appear to have had a beneficial effect.

Carol S. Auletta, B.A., D.A.B.T.
Study Director
Manager, Acute Toxicology

8/13/84
Date

Ira W. Daly, Ph.D., D.A.B.T.
Director of Toxicology

8/13/84
Date

## KEY TO FOOTNOTES

[a]Scores given are for treated eyes. Unless otherwise noted, control (untreated) eyes had negative scores for all parameters. Scored according to Draize Scale presented in Appendix A.

*Twenty seconds after dosing, both eyes were rinsed with lukewarm water for one minute.

f-Observation confirmed with fluorescein.

M-Male

F-Female

TABLE I

EYE IRRITATION STUDY IN RABBITS

TEST MATERIAL: HL 15,388

INDIVIDUAL OCULAR SCORES[a]

| | Time After Administration | | | | | | Positive Score |
|---|---|---|---|---|---|---|---|
| | Hours | | Days | | | | 24, 48, 72 Hr. |
| | 1 | 4 | 1 | 2 | 3 | 7 | (per 16 CFR 1500.42) |
| Animal No. 38[illegible]3 M | | | | | | | |
| 1. Conjunctivae | | | | | | | |
| A. Redness | 1 | 1 | 2 | 1 | 1 | 0 | Yes |
| B. Chemosis | 1 | 2 | 1 | 1 | 0 | 0 | No |
| C. Discharge | 0 | 0 | 0 | 0 | 0 | 0 | |
| D. Necrosis(N)/ Ulceration(U) | 0 | 0 | 0 | 0 | 0 | 0 | No |
| Score | 4 | 6 | 6 | 4 | 2 | 0 | |
| 2. Iris | 0 | 0 | 0 | 0 | 0 | 0 | No |
| Score | 0 | 0 | 0 | 0 | 0 | 0 | |
| 3. Cornea | | | | | | | |
| A. Opacity | + | + | 0 | 0 | 0 | 0 | No |
| B. Area | 2 | 2 | 0 | 0 | 0 | 0 | |
| C. Stippling | 2 | 2 | 0 | 0 | 0 | 0 | |
| D. Ulceration | 0 | 0 | 0f | 0f | 0f | 0f | No |
| Score | 0 | 0 | 0 | 0 | 0 | 0 | |
| Other | - | - | - | - | - | - | |
| Total Score | 4 | 6 | 6 | 4 | 2 | 0 | |
| Animal No. 3899 M* | | | | | | | |
| 1. Conjunctivae | | | | | | | |
| A. Redness | 1 | 1 | 1 | 1 | 0 | | No |
| B. Chemosis | 1 | 1 | 0 | 0 | 0 | | No |
| C. Discharge | 0 | 0 | 0 | 0 | 0 | | |
| D. Necrosis(N)/ Ulceration(U) | 0 | 0 | 0 | 0 | 0 | | No |
| Score | 4 | 4 | 2 | 2 | 0 | | |
| 2. Iris | + | 0 | 0 | 0 | 0 | | No |
| Score | 0 | 0 | 0 | 0 | 0 | | |
| 3. Cornea | | | | | | | |
| A. Opacity | 0 | 0 | 0 | 0 | 0 | | No |
| B. Area | 0 | 0 | 0 | 0 | 0 | | |
| C. Stippling | 1 | 0 | 0 | 0 | 0 | | |
| D. Ulceration | 0 | 0 | 0f | 0f | 0f | | No |
| Score | 0 | 0 | 0 | 0 | 0 | | |
| Other | - | - | - | - | - | | |
| Total Score | 4 | 4 | 2 | 2 | 0 | | |

Key to footnotes presented on page 6.

TABLE II

EYE IRRITATION STUDY IN RABBITS

TEST MATERIAL: HL 15,388

SUMMARY OF RESPONSES AND MAXIMUM DRAIZE SCORES

| | Positive (+) or Negative (-) Scores[a] | | | | | | Maximum Draize Score | | Time Clear[b] |
|---|---|---|---|---|---|---|---|---|---|
| | Cornea | | Iris | Conjunctivae | | | | | |
| Animal Number | Opacity | Ulceration | | Redness | Chemosis | Necrosis or Ulceration | Score | First Time Obtained | |
| Unwashed | | | | | | | | | |
| 3893 M | - | - | - | + | - | - | 6 | 4 Hour | Day 7 |
| Washed | | | | | | | | | |
| 3899 M | - | - | - | - | - | - | 4 | 1 Hour | Day 3 |

[a]Reference for positive and negative scores (24, 48 and 72 hours):
1. 16 CFR 1500.42
2. Illustrated Guide for Grading Eye Irritation by Hazardous Substances. (U.S. Government Printing Office, Washington, D.C. 02402)

[b]Time clear is time that eye was free of all irritation.

Appendix A
Standard Eye Irritation Grading Scale[1]

| | VALUE |
|---|---|
| **I. CORNEA** | |
| **A. Opacity - degree of density** (area most dense taken for reading) | |
| No Opacity | 0 |
| Slight dulling of normal luster | +** |
| Scattered or diffuse areas of opacity (other than slight dulling of normal luster), 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 * |
| **B. Total area of cornea involved:** (Total area exhibiting any opacity, regardless of degree) | |
| One quarter (or less) but not zero | 1 |
| Greater than one quarter, but less than half | 2 |
| Greater than half, but less than three quarters | 3 |
| Greater than three quarters, up to whole area | 4 |
| Corneal Score[2]: A X B X 5 (Maximum Score = 80) | |
| **C. Stippling** - (appearance of pinpoint roughening)** | |
| No stippling | 0 |
| One quarter (or less) but not zero | 1 |
| Greater than one quarter, but less than half | 2 |
| Greater than half, but less than three quarters | 3 |
| Greater than three quarters, up to whole area | 4 |
| **D. Ulceration** - (absence of a gross patch of corneal epithelium)** | |
| No ulceration | 0 |
| One quarter (or less) but not zero | 1 * |
| Greater than one quarter, but less than half | 2 * |
| Greater than half, but less than three quarters | 3 * |
| Greater than three quarters, up to whole area | 4 * |
| **II. IRIS** | |
| **A. Values** | |
| Normal | 0 |
| Slight deepening of the rugae or slight hyperemia of the circumcorneal blood vessels | + |
| Markedly deepened 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 * |
| Iris Score[2]: A X 5 (Maximum Score = 10) | |
| **III. CONJUNCTIVAE** | |
| **A. Redness** (refers to palpebral and bulbar conjunctivae excluding cornea and iris) | |
| Vessels normal | 0 |
| Some vessels definitely injected above normal | 1 |
| Diffuse, crimson red, individual vessels not easily discernible | 2 * |
| Diffuse beefy red | 3 * |
| **B. Chemosis** | |
| No swelling | 0 |
| Any swelling above normal (includes nictitating membrane) | 1 |
| Obvious swelling with partial eversion of lids | 2 * |
| Swelling with lids about half closed | 3 * |
| Swelling with lids more than half closed | 4 * |
| **C. Discharge** | |
| No discharge | 0 |
| Any amount different from normal (does not include small amounts observed in inner canthus of normal animals) | 1 |
| Discharge with moistening of the lids and hairs just adjacent to lids | 2 |
| Discharge with moistening of the lids and hairs and considerable area around eye | 3 |
| **D. Necrosis or Ulceration** of palpebral and bulbar conjunctivae or nictitating membrane | |
| Not present | 0 |
| Necrosis present | N * |
| Ulceration present | U * |
| Conjunctivae Score[2]: (A + B + C) X 2 (Maximum Score = 20) | |

[1]Draize, J.H. 1959. The Appraisal of Chemicals in Foods, Drugs, and Cosmetics, p. 51, Association of Food and Drug Officials of the United States, Austin, Texas.
[2]Total Draize score is the sum of the three scores obtained (cornea, iris, conjunctivae).
*Score considered positive under 16 CFR 1500.42
**Not included in Draize grading system, values assigned if finding present.