

Study Title

Eye Irritation Test in Rabbits of trans-1,2-Dichloroethylene

Author

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Study Completed On

April 18, 1988

Performing Laboratory

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Medical Research No.

8408-001

Laboratory Project ID

Haskell Laboratory Report No. 228-88

GENERAL INFORMATION

Material Tested: Ethene, 1,2-dichloro-, (E)-

Medical Research No.: 8408-001

Haskell No.: 17,159-02

Physical Form: Colorless liquid

Purity: 99.64%

Synonyms:

- trans-1,2-Dichloroethylene
- trans-Acetylene dichloride

Other Code: A product of PPG Industries, Inc.

Submitter's Notebook No.: E-49275-47

CAS Registry No.: 156-60-5

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: R. A. Gorski
Chemicals and Pigments Department
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In-Life Phase
Initiated - Completed: 3/22/88 - 3/25/88

Notebook: E-56699, pp. 16-25 and 57.

There are 11 pages in this report.

Distribution:

- K. D. Dastur (1)
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- R. A. Gorski (1)
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Eye Irritation Test in Rabbits of
trans-1,2-Dichloroethylene

SUMMARY

trans-1,2-Dichloroethylene (99.64% pure) was evaluated for acute eye irritation potential in 2 female rabbits. trans-1,2-Dichloroethylene produced severe corneal opacity in the washed eye. In addition, trans-1,2-dichloroethylene produced moderate iritis and conjunctival redness and copious blood-tinged discharge in both treated eyes, and moderate and mild chemosis in the washed and unwashed eye, respectively. Fluorescein stain examinations were positive for corneal injury in the washed eye and negative in the unwashed eye. Biomicroscopic examinations revealed moderate to severe corneal injury in the washed eye and no corneal injury in the unwashed eye. The treated eyes of both rabbits were normal by 3 days after treatment. Under the conditions of this study, trans-1,2-dichloroethylene was a severe eye irritant.

Work by:

Carol Finley 4/12/88
Carol Finley
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QUALITY ASSURANCE DOCUMENTATION

STUDY: MR 8408-001
H# 17,159-02

Eye Irritation Test in Rabbits of
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Because short-term studies are numerous and routine in nature, representative studies from this test type are audited quarterly to ensure the studies are designed and conducted in compliance with the Good Laboratory Practice Standards.

Reported by:

W. Troy Baxter

W. Troy Baxter
Quality Assurance Auditor

4-15-88

Date

INTRODUCTION

The purpose of this study was to evaluate the eye irritation potential of trans-1,2-dichloroethylene. 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 Rabbit Chow® #5322 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 study initiation, the eyes of 2 female 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 2806 and 3289 grams on the day of treatment.

A 0.01 mL aliquot of trans-1,2-dichloroethylene was introduced into the lower conjunctival sac of the right eyes of 2 female 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

trans-1,2-Dichloroethylene produced severe corneal opacity in the washed eye. In addition, trans-1,2-dichloroethylene produced moderate iritis and conjunctival redness and copious blood-tinged discharge (confirmed with Hemastix® reagent strips) in both treated eyes, and moderate and mild chemosis in the washed and unwashed eye, respectively. Fluorescein stain examinations were positive for corneal injury in the washed eye and negative in the unwashed eye. Biomicroscopic examinations revealed moderate to severe corneal injury in the washed eye and no corneal injury in the unwashed eye. The treated eyes of both rabbits were normal by 3 days after treatment. Individual eye irritation scores are presented in Tables III and IV. Under the conditions of this study, trans-1,2-dichloroethylene was a severe eye irritant.

TABLE I
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)
		Score equals A x B x 5	Total Maximum = 80
(2)	Iris		
	(A)	Values	
		Normal	0
		Folds above normal, congestion, swelling, circum-corneal 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.

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.

TABLE III

EYE IRRITATION REACTIONS OBSERVED IN
THE UNWASHED RABBIT EYE AFTER EXPOSURE TO
trans-1,2-DICHLOROETHYLENE

Rabbit Number 22476	1 Hour	4 Hours	1 Day	2 Days	3 Days
Cornea					
Opacity	0	0	0	0	0
Area	0	0	0	0	0
Iris	1 5	1	0	0	0
Conjunctiva					
Redness	1	2	2	1	0
Chemosis	2	2	0	0	0
Discharge	3(H+) 12	2(H+) 12	0	0	0
Biomic of Cornea	- 17	- 17	0	0	0

H+ = Hemastix® evaluation positive for blood.

Fluorescein examinations: negative for corneal injury at all intervals.

TABLE IV

EYE IRRITATION REACTIONS OBSERVED IN
THE WASHED RABBIT EYE AFTER EXPOSURE TO
trans-1,2-DICHLOROETHYLENE

Rabbit Number 22477	1 Hour	4 Hours	1 Day	2 Days	3 Days
Cornea					
Opacity	1	2	4	1	0
Area	2	2	1	1	0
	15	20	25	10	
Iris	1	1	1	0	0
	5	5	5		
Conjunctiva					
Redness	1	2	2	1	0
Chemosis	3	3	1	1	0
Discharge	3(H+)	3(H+)	0	0	0
	14	16	15	2	
Biomic of Cornea	-	-	4	2	0
	34	41	45	12	

H+ = Hemastix® evaluation positive for blood.

Fluorescein examinations: positive for corneal injury 1 day after treatment.