Study Title

Eye Irritation Test with H-21987 in Rabbits

Laboratory Project ID

Haskell Laboratory Report No. 606-96

Author

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Performing Laboratory

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
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GENERAL INFORMATION

Substance Tested: [redacted]

Synonyms:
- H-21987
- [redacted]

Physical Form: Tan liquid dispersion

Composition: [redacted]

Known Impurities: [redacted]

Purity: [redacted]

Structure: [redacted]

Submitter's Notebook No.: [redacted]

CAS Registry No.: [redacted]

Sponsor: DuPont Specialty Chemicals
E. I. du Pont de Nemours and Company
Wilmington, Delaware

Study Initiated - Completed: 8/5/96 - 8/28/96

In Life Phase
Initiated - Completed: 8/6/96 -8/9/96

GENERAL INFORMATION (Continued)

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 at Iron Mountain, 200 Todds, Lane, Wilmington, Delaware (formerly DuPont Records Management Center).

SUMMARY

H-21987 was evaluated for acute eye irritation potential in 2 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-21987 produced mild conjunctival redness in the treated unwashed eye. Moderate iritis, moderate conjunctival redness, and slight conjunctival chemosis were observed in the eye washed after treatment. The treated unwashed eye was normal by 1 day, and the treated washed eye was normal by 3 days after instillation of the test substance.

Under the conditions of this study, H-21987 was a moderate eye irritant.

SIGNATURE PAGE

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Acknowledgement: Barry Fritz also participated in the conduct of this study.

CF/lmp

INTRODUCTION

The purpose of this study was to evaluate the acute eye irritation potential of H-21987 in young adult rabbits.

MATERIALS AND METHODS

A. Animal Husbandry

Young adult male HM:(NZW)fBR 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. 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 assure 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. These rabbits weighed 3070 or 3405 grams on the day of treatment.

Approximately 0.01 mL of H-21987 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. In the absence of visible evidence to the contrary, the test substance was assumed to be stable under the conditions of administration.

Approximately 1 and 4 hours, and 1, 2, and 3 days after H-21987 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

No clinical signs of toxicity were observed during the study. H-21987 produced mild conjunctival redness in the treated unwashed eye. Moderate iritis, moderate conjunctival redness, and slight conjunctival chemosis were observed in the eye washed after treatment. The treated unwashed eye was normal by 1 day, and the treated washed eye was normal by 3 days after instillation of the test substance. Individual eye irritation scores are presented in Tables 2 and 3.

CONCLUSION

Under the conditions of this study, H-21987 was a moderate 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-21987 probably could be classified as "NON-IRRITANT" until further data is available.

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, 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)
(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

EYE IRRITATION REACTIONS OBSERVED IN THE UNWASHED RABBIT EYE

Rabbit Number 31071	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	0	0	0
Chemosis	0	0	0	0	0
Discharge	0	0	0	0	0

TABLE 3

EYE IRRITATION REACTIONS OBSERVED IN THE WASHED RABBIT EYE

Rabbit Number 31068	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	1	0	0	0
Conjunctiva					
Redness	1	2	1	1	0
Chemosis	1	1	0	0	0
Discharge	0	0	0	0	0