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DATA EVALUATION REPORT

STUDY TYPE: Primary Eye Irritation- Rabbits

TOX. CHEM. NO.: 663-P

MRID NO.: 412906-24

GUIDELINE NO.: 81-4

TEST MATERIAL: DPX-43898-26 (brown solid granule); (purity--5.3% by analysis)

SYNONYMS: FORTRESS 5G

STUDY NUMBER: HLR711-88

SPONSOR: E.I.duPONT de NEMOURS and CO.,INC.
WILMINGTON, DELAWARE

TESTING FACILITY: HASKELL LABORATORY for TOXICOLOGY and INDUSTRIAL MEDICINE
NEWARK, DELAWARE

TITLE of REPORT: PRIMARY EYE IRRITATION STUDY with DPX-43898-26 in RABBITS

STUDY DATES: 10/4/88 to 10/7/88

REPORT ISSUED: 10/24/88

CONCLUSION: Based on the data presented, DPX-43898-26 caused conjunctival irritation and corneal opacity which subsided in less than 72 hours following the instillation of the test material in the conjunctival sacs of six New Zealand White rabbits.

Toxicity Category: III

Classification: Core guideline

MATERIALS: Six female New Zealand White rabbits weighing from 2359 to 2762 grams and having no evidence of preexisting corneal or conjuctival lesions were used as the test animals. DPX-43898-26, containing 5% of the active ingredient, 0,0- diethyl 0-(1,2,2,2-tetrachloroethyl) phosphorothioate, served as the test material.

METHODS: The eyes of 6 New Zealand White rabbits were examined for corneal and/or conjunctival lesions using a flourescein dye. Aliquots of approximataly 89 mg of DPX-43898-26 were introduced into the lower left conjunctival sacs. Treated eyes were left unwashed. The weight of the test substance used in the study corresponds to a 0.1mL volume. The right eye served as the control. Rabbits were examined for evidence of eye irritation at approximately 1, 24, 48, and 72 hours post instillation. Eyes were examined and scored for ocular reactions using the Draize scale, under which criteria for determining the severity of ocular lesions are established (See Table I taken from the study report).

The untreated eye in each rabbit was used for comparison and any unusual effects were noted. Biomicroscopic examinations for corneal injury were conducted at the 24, 48 and 72 hour observation intervals. Corneal injury was assessed using biomicroscopic classifications (See Table II taken from the study report).

STATISTICAL ANALYSIS: Mean values were calculated on the eye irritation scores.

QUALITY ASSURANCE: A statement of compliance with EPA's Good Laboratory Practice Regulations, dated November 9,1988, has been included in the submission.

RESULTS: DPX-43898-26 produced slight corneal opacity, mild conjunctival redness and chemosis in all six rabbits. One rabbit had a blood tinged ocular discharge in addition to the other lesions.

No biomicroscopic lesions were found in the corneas of five of the six rabbits. Scores of zero were assigned for this parameter in the unaffected animals. One rabbit was assigned a classification score of 2. This score meant that the corneal opacity was visible with the ophthalmoscope or light and the epithelial changes could only be detected with the use of the biomicroscope. This condition was present at 24 and 48 hours post- treatment, but was not evident at the 72 hour observation interval.

The following results were obtained using the Draize test:

ANIMAL#	CORNEA opacity/area	IRIS	CONJUNCTIVA R/C/D	TOTAL SCORE
23332 a.	1/4	0	1/2/0	26
23331 a.	1/4	0	1/2/0	26
b.	0	0	1/0/0	2
23336 a.	1/4	0	1/2/0	26
b.	0	0	1/0/0	2
23335 a.	1/4	0	1/2/0	26
b.	1/2	0	1/1/0	14
c.	1/1	0	1/0/0	7
23385 a.	1/4	0	1/2/2	30
b.	0	0	1/0/0	2
c.	0	0	1/0/0	0
23386 a.	1/4	0	1/2/0	26

a= 1 hour interval b= 24 hour interval c= 72 hour interval
R= redness C= chemosis D= discharge

No signs of irritation were reported after the one hour observation interval in animals 23332 and 23386. No signs of irritation were observed after the 24 hour observation interval in animals 23331 and 23336. No lesions were observed after the 48 hour observation interval in animals 23335 and 23385. The mean scores for irritation at 1, 24, 48 and 72 hours were 26.7, 3.3, 1.5 and 0, respectively.

DISCUSSION: Based on the results from this study, DPX-43898-26 caused corneal opacity and conjunctival irritation in all treated rabbits, but both conditions subsided in less than 72 hours. The study was conducted in accordance with Subdivision F Guidelines for primary eye irritation (81-4).

The study is classified as core guideline.

TABLE I

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)
Score equals A x B x 5	Total Maximum = 80	
(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)
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.

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[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.