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REPORT

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ACUTE EYE IRRITATION STUDY IN THE RABBIT

GU PROJECT NO. (b) (4)

TINUVIN 770

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1. INTRODUCTION

At the request of the Plastics & Additives Division an acute study in rabbits was conducted. The purpose was to determine the eye irritating potency of (b) (4)

This report presents the results of the laboratory investigation as compiled by the undersigned.

Study Director

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2. SUMMARY AND CONCLUSIONS

Under the conditions of the present experiment (b) (4) was found to cause moderate irritation when applied to the rabbit eye mucosa.

The calculated primary irritation index was :

41.5 in unrinsed eyes

17.4 in rinsed eyes

3. PERSONNEL

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4. MATERIALS AND METHODS

4.1 Test Article

Code No

(b) (4)

Batch No.

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Stability

stable

Description

solid

Generic name

not applicable

Content of Active Ingredient

data not available

Test Article Received:

01.06.82

4.2 Experimental Animals

Rationale

The albino rabbit has been selected for this test as being a standard species for the determination of an acute eye irritation.

Species and Strain

New Zealand White Rabbits checked for normal ophthalmic conditions.

Source

Kleintierfarm Madoerin AG, CH-4414
Puellinsdorf

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Initial Body Weight Range

2 - 3 kgs

Number of animal and sex

3 male / 3 female

Individual Identification

ear numbers

Husbandry

Animals were housed individually in metal cages.

The animal room was air conditioned: temperature $22\pm 3^{\circ}$ C, relative humidity $55\pm 15\%$; 12 hours light/day, approximately 15 air changes/h.

Adaptation period

4 days

Diet

Rabbit food, NAFAG, No. 814 Tox, NAFAG AG, Gossau, SG (Switzerland), and water were provided ad libitum.

4.3 Design

Basis

The procedure used is based, but not in every part identical with the Proposed Guidelines of the United States Environmental Protection Agency (EPA) Paragraph 163.81-5 "Primary eye irritation study", Federal Register, Vol. 43 No. 163 August 22, 1978.

Application of the substance

The test material in an amount of 0.1 ml was inserted in the conjunctival sac of the left eye of the rabbits and the lids were gently closed for 15

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seconds. The right eye was not treated and served as an untreated control. In 3 of the 6 rabbits approximately 30 seconds after the treatment the treated eye was flushed with 10 ml of sterile physiological saline.

The eye irritation was assessed with a slit-lamp at 24, 48, 72 hours and 4 and 7 days after treatment and was scored for each individual rabbit as outlined in table 1.

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Score for eye irritation in rabbits (Table 1)

CORNEA

A	Opacity and degree of density (most dense area scored)	
-	No opacity.....	0
	Scattered or diffuse area, 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	Area of cornea involved	
-	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
A x B x 5	Maximum possible score.....	80

IRIS

A	Values	
-	Normal.....	0
-	Folds above normal, congestion, swelling, circumcornea injection (any or all of these or combination of any thereof) iris still reaction to light (sluggish reaction is positive).....	1
-	No reaction to light, hemorrhage, gross destruction (any or all of these).....	2
A x 5	Maximum possible score.....	10

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CONJUNCTIVAE

- A Redness (refers to palapebral and bulbar conjunctiva excluding cornea and iris)
 - Vessels normal..... 0
 - Vessels definitely injected above normal..... 1
 - More diffuse, deeper 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 about half closed to completely 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 the eye..... 3

- (A + B + C) x 2 Maximum possible score..... 20

4.4 Calculation of the Primary Eye Irritation Index

The mean reaction scores for cornea, iris and conjunctiva observed after 1, 2, 3, 4 and 7 days were summed up and the sum divided by 5.

Index

0	= none
0.1 - 10.9	= minimal
11.0 - 25.9	= slight
26.0 - 55.9	= moderate
56.0 - 84.0	= marked
above 84.0	= extreme

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4.5 Procedure

Starting date of the experiment

12.07.82

End date of the experiment

19.07.82

5. RESULTS

The results of the primary eye irritation test are reported in tables 2-4 .

(b) (4) was found to cause moderate irritation when applied to the rabbit eye mucosa.

6. ARCHIVES

Final Report

WST 454

Copy of the Final report

WST 452

Raw Data

WST 454

7. DISTRIBUTION

Sponsor

Archives

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TABLE 2 - CALCULATION OF THE PRIMARY EYE IRRITATION INDEX

TIME AFTER EXPOSURE	MEAN REACTION SCORE					
	UNRINSED EYES (A)			RINSED EYES (B)		
	CORNEA	IRIS	CONJUNC- TIVA	CORNEA	IRIS	CONJUNC- TIVA
24 HOURS	33.3	5.0	13.3	11.7	3.3	6.7
48 HOURS	33.3	5.0	14.0	10.0	3.3	5.3
72 HOURS	26.7	5.0	12.0	8.3	3.3	6.0
4 DAYS	23.3	5.0	10.0	6.7	3.3	4.0
7 DAYS	16.7	1.7	3.3	5.0	0.0	1.3
SUBTOTAL	133.3	21.7	52.6	41.7	13.2	23.3
TOTAL	207.6			87.2		

PRIMARY IRRITATION INDEX IN UNRINSED EYES

$$A = 207.6 : 5 = 41.5$$

PRIMARY IRRITATION INDEX IN RINSED EYES

$$B = 87.2 : 5 = 17.4$$

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TEST No. : (b) (4)
 SUBSTANCE :
 TEST PERIOD: 12.7.11 - 17.1.12

RABBIT EYE IRRITATION SCORES - REFERENCE PROCEDURE

EYE TREATMENT	24 HOURS/DAYS						48 HOURS/DAYS						72 HOURS/DAYS					
	not fixed			fixed			not fixed			fixed			not fixed			fixed		
Animal No.	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33
1. CORNEA																		
A Opacity	2	2	1	1	0	1	2	2	1	1	0	1	2	1	1	1	0	1
B Area Involved	4	4	4	4	0	3	4	4	4	4	0	2	4	4	4	3	0	2
a = A+B+C (Max. 80)	98	40	10	10	0	15	40	40	20	20	0	10	40	10	10	15	0	10
MEAN SCORE CORNEA	33.3						11.7						26.7					
2. IRIS																		
b = Score x 5 (Max. 10)	1	1	1	1	0	1	1	1	1	1	0	1	1	1	1	1	0	1
MEAN SCORE IRIS	5						3.3						5					
3. CONJUNCTIVA																		
A Redness	2	2	2	2	1	1	3	3	3	2	1	1	2	2	2	2	1	2
B Chemosis	2	2	2	2	0	1	2	2	2	2	0	0	2	2	2	1	0	1
C Discharge	2	2	2	2	0	0	2	2	2	1	0	0	2	1	1	1	0	0
c = 2A+2B+C (Max. 20)	14	14	14	14	2	4	14	14	14	11	2	2	14	10	11	10	2	6
MEAN SCORE CONJUNCTIVA	12.3						6.7						12					
TOTAL REACTION SCORE	57	57	37	37	2	26	57	57	37	31	2	17	57	25	37	30	2	21
GROUP MEAN	51.7						21.2						43.7					

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TEST No. : (b) (4)
 SUBSTANCE :
 TEST PERIOD: 12.7.12 - 19.7.12

RABBIT EYE IRRITATION SCORES - REFERENCE PROCEDURE

EYE TREATMENT	4 HOURS/DAYS						7 HOURS/DAYS						10 HOURS/DAYS					
	not fixed			fixed			not fixed			fixed			not fixed			fixed		
Animal No.	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33
1. CORNEA																		
A Opacity	2	1	1	1	0	1	2	1	1	1	0	1						
B Area Involved	4	3	3	2	0	2	4	1	1	1	0	2						
a = A+B+C (Max. 80)	40	15	15	15	0	10	40	5	5	5	0	10						
MEAN SCORE CORNEA	23.3						6.7											
2. IRIS																		
b = Score x 5 (Max. 10)	1	1	1	1	0	1	1	0	0	0	0	0						
MEAN SCORE IRIS	5						3.3											
3. CONJUNCTIVA																		
A Redness	3	2	2	2	1	1	1	1	1	1	0	1						
B Chemosis	2	1	2	1	0	0	1	0	1	0	0	0						
C Discharge	1	1	1	1	0	0	0	0	0	0	0	0						
c = 2A+2B+C (Max. 20)	11	7	10	7	2	2	4	2	4	2	0	2						
MEAN SCORE CONJUNCTIVA	10						4											
TOTAL REACTION SCORE	57	28	30	23	2	17	49	7	9	7	0	12						
GROUP MEAN	38.3						11.7											

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