CIBA–GEIGY

Report

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A Division of Ciba-Geigy (ADP) Company.

CIBA-GEIGY Pharmaceuticals Division
STAMFORD LODGE, UK
PHARMA TOXICOLOGY

42/83/SL
CONFIDENTIAL

Triphenyl Phosphate

Eye Irritation Test in New Zealand White Rabbits

15th July 1983

Toxicology Department,
Geigy Pharmaceuticals,
Stamford Lodge,
Wilmslow

FROM:

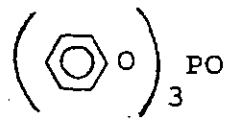
Dr P Miles
Industrial Chemicals Division
CIBA-GEIGY P&A Company
Trafford Park

icology tests
hired and
cies of animals
be used

Skin and eye irritation tests (rabbits)

nical name
formula

Triphenyl phosphate



ended use

Plasticiser for use in photographic film

er relevant information
. possible hazards,
icity of similar
micals if known,etc.

. Notebook No.
Plant batch No.

General bulk production

whom report is to
sent

Dr P Miles

e chemical to be sent to
mford Lodge and amount

3rd June 1983 100g

e: 3/6/83

Signed: P. Miles

. REQUESTS FOR TOXICOLOGY STUDIES SHOULD BE SENT TO HEAD OF TOXICOLOGY DEPARTMENT AT
AMFORD LODGE

Test Substance	:	Triphenyl Phosphate
Description of Study	:	Eye Irritation Test in New Zealand White Rabbits
Study Sponsor	:	Industrial Chemicals Division CIBA-GEIGY P & A Company Trafford Park Manchester M17 1WT
Testing Facility	:	CIBA-GEIGY Pharmaceuticals Division Stamford Lodge Wilmslow Cheshire UK Pharma Toxicology
Experimental No.	:	83L008
Starting Date	:	21.06.83
Finishing Date	:	27.06.83
Location of Raw Data	:	As for testing facility
Study Director	:	..... (K. Lloyd, Bsc) 14.7.83
Responsible for conduct of animals studies	:	..... (K. O'Brien, AIAT) 14.7.83
Head of Toxicology CIBA-GEIGY Pharmaceuticals Division Stamford Lodge Wilmslow Cheshire UK	:	..... (W.A. Bradley, BVSc, MRCVS) 14.7.83

ASSESSMENT

Triphenyl Phosphate is a minimal eye irritant in the New Zealand White rabbit.

EXPERIMENTAL RESULTS

Conjunctiva

Very slight reactions were seen in 2/3 washed and 3/3 unwashed eyes 1 hour after compound application. The reactions were less severe at 24 hours although all washed and unwashed eyes were affected. 3/3 washed eyes and 1/3 unwashed eyes were normal at 48 hours, 1 unwashed eye at 72 hours and the remaining unwashed eye at 6 days.

Cornea

Slight opacity and damage to the surface epithelium was seen in 1 unwashed eye at 24 hours. This was no longer apparent at 48 hours.

The reactions seen in unwashed eyes were more severe than those in washed eyes.

The grades of reaction are shown on page 4.

EXPERIMENTAL PROCEDURE

Animals

Healthy New Zealand White rabbits were used. These were aged 14 - 18 weeks with average body weights of 2.57 kgs. (♂♂) and 2.68 kgs. (♀♀) and were obtained from a commercial supplier (Froxfield Rabbits). Six rabbits (3 ♂♂ and 3 ♀♀) were acclimatized in the test area for one week prior to the start of the trial.

Husbandry

The rabbits were caged singly in an experimental room maintained at a temperature of 16°C (± 1°) and a relative humidity of 50 - 70%. Animals were exposed to artificial light for 10 hours daily from 08.00 - 18.00 hours. A commercial diet (Labsure, Christopher Hill Group) was fed ad lib. Sterile filtered water was available at all times.

Test Compound

White flakes labelled TPP.

Method

The test was carried out in accordance with the procedure set out in the "Hazardous Substances Regulations" under the U.S.A. Federal Hazardous Substances Labelling Act Sect. 191.12 (February 1965), with slight modification.

The eyes of the experimental animals were examined and found normal prior to the test. 100mg of the test compound were instilled into the conjunctival sac of the left eye. The eyelids were then held closed for 1 second. The right eye served as a control. After 30 seconds the compound was, as far as possible, flushed out of the eyes of three of the rabbits with approximately 200 ml. of warm water.

The rabbits were examined 1, 24, 48 and 72 hours after application of the test compound and for any further period that was considered necessary. The ocular reactions were scored by the method described in "Appraisal of the Safety of Chemicals in Food Drugs and Cosmetics" page 51, published by the Association of Food and Drug Officials of the U.S.A. (see appendix 1). Fluorescein (Fluorets - Smith and Nephew Pharmaceuticals Limited) was used as an aid in assessing corneal damage.

The eye reactions were assessed as follows:-

Score	Assessment
0	Non irritant
>0 - 10	Minimally irritant
11 - 25	Slightly irritant
26 - 56	Moderately irritant
57 - 84	Marked irritant
> 84	Extremely irritant

NOTE: WHERE THE SCORING PROCEDURE AND THE CLINICAL JUDGEMENT ARE NOT IN AGREEMENT, THE ASSESSMENT OF IRRITANCY IS BASED ON THE LATTER.

Rabbit eye irritation scores-reference procedure

Rabbit No.	1 hour						6 hours						1 day						2 days						3 days					
	11	13	15	12	14	16	11	13	15	12	14	16	11	13	15	12	14	16	11	13	15	12	14	16	11	13	15	12	14	16
Eye, L or R																														
I. Cornea																														
A Opacity													1																	
B Area involved													1																	
a = AxBx5 (Max. 80)													5																	
II. Iris																														
b = Score x 5 (Max.10)																														
III. Conjunctivae																														
A Redness	1	1		1	1	1							1	1	1	1	1	1	1	1					1					
B Chemosis	1			1																										
C Discharge																														
c = (A+B+C)x2 (Max.20)	4	2		4	2	2							2	2	2	2	2	2	2	2					2					
Total = a+b+c (Max.110)	4	2	–	4	2	2							7	2	2	2	2	2	2	2	–	–	–	–	2	–	–	–	–	–

Compound: Triphenyl Phosphate 4.

Eyes Washed, 14, 15 16.

Rabbit No.	6 days						10 days						14 days																	
	11	13	15	12	14	16	11	13	15	12	14	16	11	13	15	12	14	16	11	13	15	12	14	16	11	13	15	12	14	16
Eye, L or R																														
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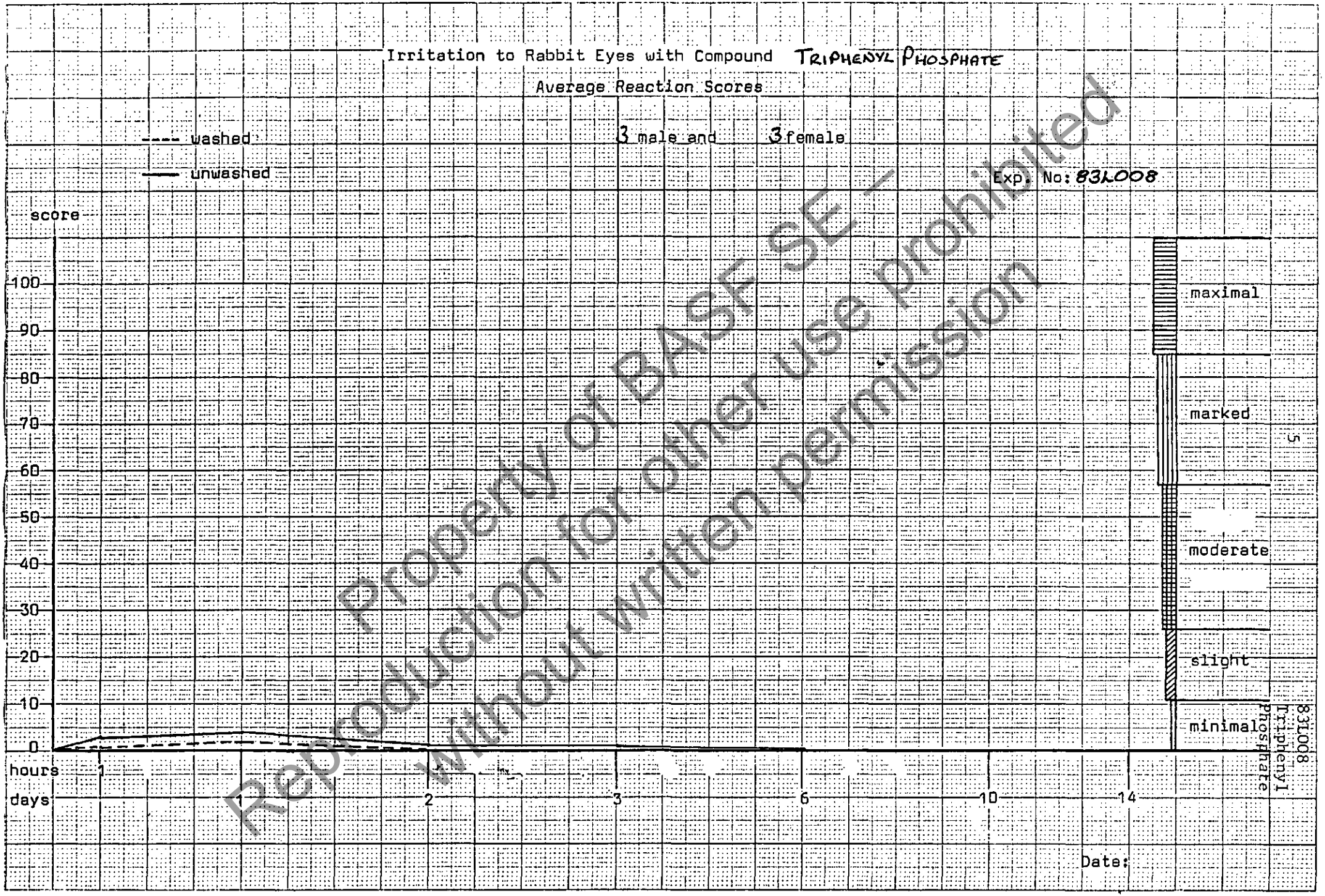
Total = a+b+c (Max.110)	–	–	–	–	–	–																								

Exp No: 83R008 Triphenyl Phosphate



APPENDIX 1

Evaluation of the Eye Reactions

rnea

Opacity-degree of density (area most dense taken for reading)

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

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

x B x 5 Total maximum = 80

is

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
No reaction to light, haemorrhage, gross destruction (any or all of these).....2

x 5 Total maximum = 10

njunctivae

Redness (refers to palpebral and bulbar conjunctivae 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

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

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