Huntingdon

{redacted}

SKIN IRRITATION TO THE RABBIT

Report

Company Sanitized. Does not contain TSCA CBI

CONFIDENTIAL

DPT 430/984441/SE

[redacted]

SKIN IRRITATION TO THE RABBIT

Sponsor

DuPont Speciality Chemicals
Jackson Laboratory
Chambers Works
Deepwater
NJ 08023
USA

Research Laboratory

Huntingdon Life Sciences Ltd
P.O. Box 2
Huntingdon
Cambridgeshire
PE18 6ES
ENGLAND

Report issued 9 December 1998

CONTENTS

COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

The study described in this report was conducted in compliance with the following Good Laboratory Practice standards and I consider the data generated to be valid.

The UK Good Laboratory Practice Regulations 1997 (Statutory Instrument No 654).

OECD Principles of Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM(98)17.

EC Council Directive 87/18/EEC of 18 December 1986 (Official Journal No L 15/29).

B Parcell

9.12.98

Brenda I. Parcell, M.I.A.T.,
Study Director,
Huntingdon Life Sciences Ltd.

Date

QUALITY ASSURANCE STATEMENT

The following have been inspected or audited in relation to this study

Study Phases Inspected	Date of Inspection	Date of Reporting
Protocol Review	22 September 1998	22 September 1998
Process Based Inspections		
Husbandry	10 July 1998	13 July 1998
Housing/Environment	10 July 1998	13 July 1998
Weighing of animals	10 July 1998	13 July 1998
Test material:-	10 July 1998	13 July 1998
Control/Administration	10 July 1998	13 July 1998
Treatment Procedure	10 July 1998	13 July 1998
Scoring	10 July 1998	13 July 1998
Records Audit	10 July 1998	13 July 1998
Training Records	10 July 1998	13 July 1998
Report	11 November 1998	11 November 1998

Protocol: An audit of the protocol for this study was conducted and reported to the Study Director and Company Management as indicated above.

Process based inspections: At or about the time this study was in progress inspections and audits of routine and repetitive procedures employed on this type of study were carried out. These were conducted and reported to appropriate Company Management as indicated above.

Report Audit: This report has been audited by the Quality Assurance Department. This audit was conducted and reported to the Study Director and Company Management as indicated above.

The methods, procedures and observations were found to be accurately described and the reported results to reflect the raw data.

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Kevin P. de-Salis, B.A. (Hons.), C.Biol., M.I.Biol., Dip.R.Q.A.,
Quality Assurance Unit Head,
Department of Quality Assurance,
Huntingdon Life Sciences Ltd.

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Date

RESPONSIBLE PERSONNEL

Brenda I. Parcell, M.I.A.T.,
Study Director,
Department of Acute Toxicology.

SUMMARY

A study was performed to assess the skin irritation potential of [redacted] to the rabbit. The method followed was that described in:

EEC Methods for the determination of toxicity, Annex to Directive 92/69/EEC (Official Journal No. L383A, 29.12.92), Part B, Method B.4. Acute toxicity (Skin Irritation).

OECD Guideline for Testing of Chemicals No. 404 "Acute Dermal Irritation/Corrosion". Adopted 17 July 1992.

Three rabbits were each administered a single dermal dose of 0.5 ml of the test substance and observed for 4 days.

No dermal irritation was observed following a single semi-occlusive application of [redacted] to intact rabbit skin for up to four hours.

[redacted] will not require labelling with the risk phrase R38, "Irritating to skin", in accordance with Commission Directive 93/21/EEC.

INTRODUCTION

The study was designed to assess skin irritation potential of [redacted] following a single dermal application to rabbits. The test substance may come into contact with skin during handling or use.

The study was conducted in compliance with the following guidelines:

EEC Methods for the determination of toxicity, Annex to Directive 92/69/EEC (Official Journal No. L383A, 29.12.92), Part B, Method B.4. Acute toxicity (Skin Irritation).

OECD Guideline for Testing of Chemicals No. 404 "Acute Dermal Irritation/Corrosion". Adopted 17 July 1992.

The albino rabbit was chosen as it has been shown to be a suitable model for skin irritation studies and is the animal recommended in the test guidelines.

The amount of test substance administered was chosen in compliance with the guidelines.

The protocol was approved by Huntingdon Life Sciences Management on 7 July 1998, by the Sponsor on 17 July 1998 and by the Study Director on 11 September 1998.

The experimental phase of the study was undertaken between the 15 and 19 September 1998.

TEST SUBSTANCE

Identity:	[redacted]
Chemical name:	[redacted]
Intended use:	[redacted]
Appearance:	[redacted]
Storage conditions:	Room temperature
Lot number:	[redacted]
Expiry:	Two years from date of receipt
Purity:	[redacted]
Sample received:	23 June 1998

EXPERIMENTAL PROCEDURE

ANIMAL MANAGEMENT

Animals for this study were selected from a stock supply of healthy adult rabbits of the New Zealand White strain, obtained from Harlan UK Ltd, Bicester, Oxon, England.

They were in the weight range of 2.1 to 2.6 kg and at least 11 weeks of age, prior to treatment (Day 1). All rabbits were acclimatised to the experimental environment for a minimum period of five days prior to the start of the study.

The rabbits were selected without conscious bias for the study. They were housed individually in stainless steel cages with perforated floors in Building R14 Room 5.

A standard laboratory rabbit diet (Special Diet Services STANRAB (P) SQC pellet) and drinking water were provided *ad libitum*. The batch of diet used for the study was analysed by the supplier for nutrients, possible contaminants and micro-organisms likely to be present in the diet and which, if in excess of specified amounts, might have an undesirable effect on the test system. The animals were fed hay on arrival and subsequently three times a week.

The water supplied to Huntingdon Life Sciences by Anglian Water was potable water for human consumption. Anglian Water takes its guidelines on water quality from the EEC directive relating to water for human consumption (80/778/EEC) and conforms to the United Kingdom Water Act 1989 and subsequent amendments. Results of routine physical and chemical examination of drinking water at Consumers' taps, as conducted by the supplier, are made available to Huntingdon Life Sciences Ltd as quarterly summaries.

Animal room temperature was maintained at 17 to 20°C and relative humidity at 50 - 72%. These environmental parameters were recorded daily. Lighting was controlled by means of a time switch to give 12 hours of artificial light (0700 - 1900 hours) in each 24 hours period.

Each animal was identified by animal stock number and an ear tattoo. This identification will be unique within the Department throughout the duration of the study. Each cage, was identified by a coloured label displaying the study number, animal number and initials of the Study Director and Home Office licensee.

TEST SUBSTANCE PREPARATION

[redacted] was administered as supplied by the Sponsor.

The absorption of the test substance was not determined.

The homogeneity, stability and purity of the test substance were the responsibility of the Sponsor.

TREATMENT PROCEDURE

Approximately 24 hours prior to application of the test substance, hair was removed with electric clippers from the dorso-lumbar region of each rabbit exposing an area of skin approximately 100 mm x 100 mm.

Approximately 0.5 ml of the test substance was applied under a 25 mm x 25 mm gauze pad, to intact skin on each animal.

To help clarify the irritant potential of the test substance, initially only one animal was treated. With this animal, the test substance was applied to three treatment sites and the exposure period was varied between treatment sites (ie three minutes, 60 minutes and four hours).

The exposure periods were initiated in a step-wise manner with the 60 minute and four hour exposures only initiated after consideration of results from the earlier exposure periods.

On the basis of results from this phase of the study, the four hour exposure period was selected for use in the remaining two animals, when the test substance was applied to one intact skin site on each animal.

Each treatment site was covered with "Elastoplast" elastic adhesive dressing. Only during the three and 60 minute exposure periods was the initial animal restrained. For the four hour exposure, none of the animals were restrained but were returned to their cages immediately after treatment.

At the end of the exposure period(s), the semi-occlusive dressing and gauze pad were removed and the treatment sites washed with warm (33 to 36°C) water to remove any residual test substance. The treated area was blotted dry with absorbent paper.

OBSERVATIONS

Clinical signs

All animals were observed daily for signs of ill health or toxicity.

Dermal responses

Examination of the treated skin was made on Day 1 (immediately after removal of the patches following 3 minute and 60 minute exposure and approximately 60 minutes after the four hour exposure) and on Days 2, 3 and 4 (equivalent to 24, 48 and 72 hours after exposure).

Local dermal irritation was assessed using the prescribed numerical system:

Erythema and eschar formation:

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to eschar formation (injuries in depth) preventing erythema reading	4

Oedema formation:

No oedema	0
Very slight oedema (barely perceptible)	1
Slight oedema (edges of area well-defined by definite raising)	2
Moderate oedema (raised approximately 1 millimetre)	3
Severe oedema (raised more than 1 millimetre and extending beyond the area of exposure)	4

ARCHIVES

All raw data and study related documents generated during the course of the study at Huntingdon together with a copy of the final report will be lodged in the Huntingdon Life Sciences Ltd Archive, Huntingdon.

Such records will be retained for a minimum period of five years from the date of issue of the final report. At the end of the five year retention period the client will be contacted and advice sought on the future requirements. Under no circumstances will any item be discarded without the client's knowledge.

DEVIATIONS FROM PROTOCOL

There were no deviations that were considered to have affected the integrity or validity of the study. However, the following were noted:

Each animal was identified by animal stock number and an ear tattoo.

The higher value recorded for relative humidity was 72%. This exceeded the 30 - 70% range stated in the protocol.

There were no other deviations from the protocol.

RESULTS

CLINICAL SIGNS

There were no signs of toxicity or ill health in any rabbit during the observation period.

DERMAL RESPONSES

The numerical values given to the dermal reactions elicited by [redacted] are shown in Table 1.

No dermal response to treatment was observed following a three minute, 1 hour or 4 hour exposure.

CONCLUSION

A single semi-occlusive application of [redacted] to intact rabbit skin for up to four hours elicited no dermal irritation.

TABLE 1

Dermal reactions observed after application of [redacted]

Animal No. & Sex	Exposure Time	E=Erythema O=Oedema	Day 1	2	3	4
1319 Male*	3 Minutes	E	0	0	0	0
		O	0	0	0	0
	1 Hour	E	0	0	0	0
		O	0	0	0	0
	4 Hours	E	0	0	0	0
		O	0	0	0	0
1320 Male	4 Hours	E	0	0	0	0
		O	0	0	0	0
1321 Male	4 Hours	E	0	0	0	0
		O	0	0	0	0

* Screen animal

