REPORT

Quantum Medium 3.0:
Acute Dermal Irritation in the Rabbit

Study Director:	P Brunt
Test Facility:	**Harlan Laboratories Ltd.** Shardlow Business Park Shardlow Derbyshire DE72 2GD UK
Sponsor:	**Quantum Technology Group Limited** Units 606-609 6F, Biotech Centre One No. 9 Science Park West Avenue Hong Kong Science Park Shatin, New Territories HONG KONG
Study Monitor:	**SGS Institute Fresenius GmbH** Im Maisel 14 D-65232 Taunusstein GERMANY
Harlan Study Number:	**41206537**
Study Completion Date:	10 April 2013

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STUDY DIRECTOR STATEMENT OF GLP COMPLIANCE

Harlan Laboratories Ltd., Shardlow Business Park, Shardlow, Derbyshire, DE72 2GD, UK

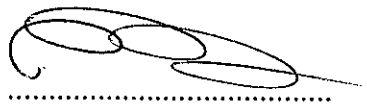
Harlan Study Number: 41206537
Study Title: Quantum Medium 3.0: Acute Dermal Irritation in the Rabbit

This study was performed in compliance with UK GLP standards (Schedule 1, Good Laboratory Practice Regulations 1999 (SI 1999/3106 as amended by SI 2004/0994)). These Regulations are in accordance with GLP standards published as OECD Principles on Good Laboratory Practice (revised 1997, ENV/MC/CHEM(98)17); and are in accordance with, and implement, the requirements of Directives 2004/9/EC and 2004/10/EC.

These principles are compatible with Good Laboratory Practice regulations specified by regulatory authorities throughout the European Community, the United States (EPA and FDA), and Japan (MHLW, MAFF and METI).

This report fully and accurately reflects the procedures used and data generated. There were no circumstances considered to have affected the integrity of the study or the validity of the data.

Study Director: P Brunt



Date: 10 APR 2013

QUALITY ASSURANCE STATEMENT

Harlan Study Number: 41206537
Study Title: Quantum Medium 3.0: Acute Dermal Irritation in the Rabbit

The general facilities and activities are inspected at least once a year and the results are reported to the relevant responsible person and management.

Study-related procedures conducted at the test facility were audited and inspected. The details of these audits and inspections are given below.

Dates and Types of QA Inspections			**Reported to the relevant Study Director and Test Facility Management**
Date of Inspection	Type of Inspection	Phase Inspected	Report Date
12 December 2012	Study Plan Verification	N/A	12 December 2012
08, 22 January 2013	Process – based	Test Item Preparation	08, 22 January 2013
22 January 2013	Process – based	Animal Preparation	22 January 2013
08 January 2013	Process – based	Dosing	08 January 2013
17 January 2013	Process – based	Assessment of Response	17 January 2013
22 March 2013	Report Audit	N/A	22 March 2013

This statement confirms that this report reflects the raw data and the procedures followed.

Quality Assurance:

L. BLANEY

Date:

11 APR 2013

SUMMARY

Introduction

The study was performed to assess the irritancy potential of the test item following single, 3-Minute, 1 and 4-Hour, semi-occluded applications to the intact rabbit skin.

Results

3-Minute and 1-Hour semi-occluded applications of the test item to the intact skin of one rabbit produced no evidence of skin irritation.

A single 4-Hour, semi occluded application of the test item to the intact skin of three rabbits produced very slight erythema and very slight edema. Slight desquamation was noted at one treated skin site at the 7-Day observation. No evidence of skin irritation was noted at two treated skin sites at the 24-Hour observation. No corrosive effects were noted.

Conclusion

The test item produced a primary irritation index of 0.7 and was classified as a mild irritant to rabbit skin according to the Draize classification scheme. No corrosive effects were noted.

GENERAL INFORMATION

Schedule

Experimental Starting Date:	22 January 2013
Experimental Completion Date:	15 February 2013

Animal Welfare

The study was designed and conducted to cause the minimum suffering or distress to the animals consistent with the scientific objectives and in accordance with the Harlan Laboratories Ltd, Shardlow, UK policy on animal welfare and the requirements of the United Kingdom's Animals (Scientific Procedures) Act 1986. The conduct of the study may be reviewed, as part of the Harlan Laboratories Ltd, Shardlow, UK Ethical Review Process.

The study was conducted in accordance with the UK Home Office Guidance document on Regulatory Toxicology and Safety Evaluation Studies and the OECD guidance document on recognition, assessment and use of clinical signs as humane endpoints for experimental animals used in safety evaluation.

Deviations from Study Plan

There were no deviations (unplanned changes) from the study plan.

Archiving

Unless instructed otherwise by the Sponsor, the study plan (general study plan and study specific supplement), all raw data (paper and electronic) and the final report will be retained in the Harlan Laboratories Ltd, Shardlow, UK archives for five years after which instructions will be sought as to further retention or disposal. Further retention or return of the data will be chargeable to the Sponsor.

No data will be discarded without contacting the Sponsor to obtain their written consent.

1 INTRODUCTION AND PURPOSE

The study was performed to assess the irritancy potential of the test item following single, 3-Minute, 1 and 4-Hour, semi-occluded applications to the intact rabbit skin.

1.1 Guidelines / Regulations

This study was designed to be compatible with the procedures indicated by the following internationally accepted guidelines and recommendations:

- OECD Guidelines for the Testing of Chemicals No. 404 "Acute Dermal Irritation/Corrosion" (adopted 24 April 2002)
- Method B4 Acute Toxicity (Skin Irritation) of Commission Regulation (EC) No. 440/2008

2 TEST ITEM

Information as provided by the Sponsor.

Identification:	Quantum Medium 3.0
Batch:	Qtg20121004-03
Purity:	not supplied
Expiry date:	04 October 2015
Storage Conditions:	room temperature in the dark

3 MATERIALS AND METHODS

3.1 Test System

3.1.1 Animals and Animal Husbandry

Three New Zealand White (Hsdlf:NZW) strain rabbits were supplied by Harlan Laboratories UK Ltd., Leicestershire, UK. At the start of the study the animals weighed 2.15 to 2.53 kg and were twelve to twenty weeks old. After an acclimatization period of at least five days each animal was given a number unique within the study which was written with a black indelible marker-pen on the inner surface of the ear and on the cage label.

The animals were individually housed in suspended cages. Free access to mains drinking water and food (2930C Teklad Global Rabbit diet supplied by Harlan Laboratories UK Ltd., Oxon, UK) was allowed throughout the study. The diet and drinking water were considered not to contain any contaminant of a level that might have affected the purpose or integrity of the study.

The temperature and relative humidity were set to achieve limits of 17 to 23 °C and 30 to 70% respectively. Any occasional deviations from these targets were considered not to have affected the purpose or integrity of the study. The rate of air exchange was at least fifteen changes per hour and the lighting was controlled by a time switch to give twelve hours continuous light (06:00 to 18:00) and twelve hours darkness.

The animals were provided with environmental enrichment items which were considered not to contain any contaminant of a level that might have affected the purpose or integrity of the study.

3.1.2 Justification

The rabbit is the preferred species of choice as historically used for irritation studies and is specified in the appropriate test guidelines.

3.2 Test Item Formulation and Experimental Preparation

For the purpose of the study the test item was used as supplied.

The absorption of the test item was not determined.

3.3 Measurement of pH

The pH of the test item was determined prior to commencement of the study and found to be as follows:

Preparation	pH Measurement	
	immediately	after 10 minutes
Undiluted as Supplied	5.2	not applicable
90% v/v aqueous preparation of the test item	5.2	5.2

3.4 Procedure

On the day before the test each of a group of three rabbits was clipped free of fur from the dorsal/flank area using veterinary clippers. Only animals with a healthy intact epidermis by gross observation were selected for the study.

One rabbit was initially treated. Three suitable sites were selected on the back of the rabbit. A quantity of 0.5 mL of the test item was applied directly to the skin under a 2.5 cm x 2.5 cm cotton gauze patch. Each patch was secured in position with a strip of surgical adhesive tape.

To prevent the animal interfering with the patches, the trunk of the rabbit was wrapped in an elasticated corset for the duration of the exposure period.

One patch was removed at each of three time points: 3 minutes, 1 hour and 4 hours after application. Any residual test item was removed by gentle swabbing with cotton wool soaked in distilled water.

After consideration of the skin reactions produced in the first animal, an additional two animals were treated with 0.5 mL of test item. One patch was applied to the back of each rabbit and was allowed to remain in contact with the skin for a period of four hours.

Immediately following removal of the patches and approximately 1, 24, 48 and 72 hours later, the test sites were examined for evidence of primary irritation and scored according to the following scale:

EVALUATION OF SKIN REACTIONS

Erythema and Eschar Formation	**Value**
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beef redness) to eschar formation preventing grading of erythema	4
Edema Formation	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1 millimeter)	3
Severe edema (raised more than 1 millimeter and extending beyond the area of exposure)	4

Any other skin reactions and clinical signs of toxicity, if present, were also recorded.

An additional observation was made in the first treated animal on Day 7 to assess the reversibility of skin reactions.

Individual body weights were recorded on Day 0 (the day of dosing) and at the end of the observation period.

3.5 Interpretation of Results

Calculation of Primary Irritation Index and Grading of Irritancy Potential Using the Draize Scheme

The scores for erythema and edema at the 24 and 72-Hour readings were totaled for the three test rabbits (12 values) and this total was divided by six to give the primary irritation index of the test item. The test item was classified according to the following scheme devised by Draize, J.H. (1959):

Primary Irritation Index	Classification of Irritancy
0	Non-irritant
> 0 to 2	Mild irritant
> 2 to 5	Moderate irritant
> 5 to 8	Severe irritant

If irreversible alteration of the dermal tissue is noted in any rabbit, as judged by the Study Director, which include ulceration and clear necrosis or signs of scar tissue, the test item is classified as corrosive to rabbit skin. Classification according to Draize may, therefore, not be applicable.

4 RESULTS

4.1 Skin Reactions

4.1.1 3-Minute Exposure Period

The individual scores for erythema/eschar and edema are given in Table 1.

Yellow coloured staining, not preventing evaluation of skin responses, was noted at the treated skin site at all observations.

No evidence of skin irritation was noted during the study.

4.1.2 1-Hour Exposure Period

The individual scores for erythema/eschar and edema are given in Table 1.

Yellow coloured staining, not preventing evaluation of skin responses, was noted at the treated skin site at all observations.

No evidence of skin irritation was noted during the study.

4.1.3 4-Hour Exposure Period

The individual scores for erythema/eschar and edema are given in Table 2.

Yellow coloured staining, not preventing evaluation of skin responses, was noted at all treated skin sites at all observations.

Very slight erythema was noted at two treated skin sites one hour after patch removal. No other evidence of skin irritation was noted at these two treated skin sites.

Very slight erythema and very slight edema were noted at the other treated skin site at the 24, 48 and 72-Hour observations. Slight desquamation was noted at this treated skin site at the 7-Day observation.

4.2 Body Weight

Individual body weights and body weight change are given in Table 3.

All animals showed expected gain in body weight during the study.

5 CONCLUSION

The test item produced a primary irritation index of 0.7 and was classified as a mild irritant to rabbit skin according to the Draize classification scheme. No corrosive effects were noted.

6 REFERENCES

DRAIZE, J.H., (1959) "Dermal Toxicity" In: Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics. *Association of Food and Drug Officials of the United States*, Austin, Texas, p. 46 59.

ORGANISATION FOR ECONOMIC COOPERATION AND DEVELOPMENT (2000). *Series on Testing and Assessment No. 19. Guidance document on the recognition, assessment and use of clinical signs as humane endpoints for experimental animals used in safety evaluation.* ENV/JM/MONO 7.

ORGANISATION FOR ECONOMIC COOPERATION AND DEVELOPMENT (2002). *OECD Guidelines for the Testing of Chemicals No. 404: Acute Dermal Irritation/Corrosion.* Paris: OECD, pp. 13.

UK Animal (Scientific Procedures) Act (1986).

UK Home Office Guidance on the conduct of Regulatory Toxicology and Safety Evaluation Studies (2005).

TABLES

Table 1 Individual Skin Reactions Following 3-Minute and 1-Hour Exposures

Skin Reaction	Observation Time (following patch removal)	Individual Scores - Rabbit Number and Sex	
		72909 Male	
		3-Minute Exposure	1-Hour Exposure
Erythema/Eschar Formation	Immediately	0 STA	0STA
	1 Hour	0 STA	0STA
	24 Hours	0 STA	0STA
	48 Hours	0 STA	0 STA
	72 Hours	0 STA	0STA
	7 Days	0 STA	0STA
Oedema Formation	Immediately	0	0
	1 Hour	0	0
	24 Hours	0	0
	48 Hours	0	0
	72 Hours	0	0
	7 Days	0	0

STA = Yellow coloured staining

Table 2 Individual Skin Reactions Following 4-Hour Exposure

Skin Reaction	Observation Time (following patch removal)	Individual Scores – Rabbit Number and Sex			Total
		72909 Male	72968 Male	72969 Male	
Erythema/Eschar Formation	Immediately	0STA	0STA	0STA	(0)
	1 Hour	0STA	1STA	1STA	(2)
	24 Hours	1 STA	0STA	0STA	1
	48 Hours	1STA	0STA	0STA	(1)
	72 Hours	1STA	0STA	0STA	1
	7 Days	0STAD	-	-	(0)
Edema Formation	Immediately	0	0	0	(0)
	1 Hour	0	0	0	(0)
	24 Hours	1	0	0	1
	48 Hours	1	0	0	(1)
	72 Hours	1	0	0	1
	7 Days	0	-	-	(0)
Sum of 24 and 72-Hour Readings (S)	:	4			
Primary Irritation Index (S/6)	:	4/6 = 0.7			
Classification	:	MILD IRRITANT			

( ) = Total values not used for calculation of primary irritation index
STA = Yellow coloured staining
D = Slight desquamation
- = Not applicable

Table 3 Individual Body Weights and Body Weight Change

Rabbit Number and Sex	Individual Body Weight (kg)		Body Weight Change (kg)
72909 Male	Day 0	Day 7	0.21
	2.53	2.74	
72968 Male	Day 0	Day 3	0.13
	2.26	2.39	
72969 Male	Day 0	Day 3	0.09
	2.15	2.24	

APPENDIX

Monitoring Authority Statement of GLP Compliance

Department of Health

THE DEPARTMENT OF HEALTH OF THE GOVERNMENT OF THE UNITED KINGDOM

GOOD LABORATORY PRACTICE

STATEMENT OF COMPLIANCE IN ACCORDANCE WITH DIRECTIVE 2004/9/EC

TEST FACILITY

Harlan Laboratories Ltd
Shardlow Business Park
London Road
Shardlow
Derby
DE72 2GD

TEST TYPE(S)

Analytical/Clinical Chemistry
Environmental Toxicity
Environmental Fate
Mutagenicity
Phys/Chem. Tests
Toxicology

DATE OF INSPECTION
10 July 2012

An inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above test facility as part of the UK Good Laboratory Practice Compliance Monitoring Programme.

This statement confirms that, on the date of issue, the UK Good Laboratory Practice Monitoring Authority were satisfied that the above test facility was operating in compliance with the OECD Principles of Good Laboratory Practice.

This statement constitutes a Good Laboratory Practice Instrument (as defined in the UK Good Laboratory Practice Regulations 1999).

30/11/12

Dr. Andrew J. Gray
Head, UK GLP Monitoring Authority

MHRA