Latex Polymer Powder Free

UNIVERSITI KEBANGSAAN MALAYSIA
*The National University of Malaysia*

# FINAL REPORT

## Primary Skin Irritation Test

Submitted by

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# FINAL REPORT

## IDENTIFICATION OF STUDY

| | |
|---|---|
| **STUDY TITLE** | PRIMARY SKIN IRRITATION TEST |
| **STUDY REQUIREMENT** | ISO 10993-10:2010 (E) |
| **TEST MATERIAL** | Latex Polymer Powder Free |
| **SPONSOR NAME AND ADDRESS** | |
| **STUDY DIRECTOR** | |
| **STUDY REFERENCE NUMBER** | PSI-03-10-12 |
| **STUDY REPORT NUMBER** | MB-PSI-03-E-32-12 |
| **JOB NUMBER** | E-32-12 |
| **REPORT ISSUED** | 12 November 2013 |

**FINAL REPORT** – Primary Skin Irritation Test

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## COMPLIANCE STATEMENT

This study was performed in compliance with the appropriate provision of the ISO10993- Part 10: 2010(E). Biological evaluation of medical devices – Part 10: Test for irritation and skin sensitization.

Pre-study procedures including animal husbandry, acclimation and health screening of animals were undertaken before finalization of the study protocol.

The management of study including quality assurance procedures was conducted in compliance with MS ISO/IEC 17025 accreditation, STR 1.2 and adhering to the principles of good laboratory practice.

Signature .....

Date 12 NOV 2013

Md Anuar Osman, DVM, M. Sc., Ph.D
Study Director

Signature .....

Date 12 NOV 2013

Nurhafizah Zam, B. Sc. (Hons)
Quality Assurance Personnel

# SUMMARY

The purpose of this study was to evaluate the potential of a test material to cause skin irritation effects following exposure on the intact skin of rabbits. The study was performed on the dorsal surface of three healthy young adult albino rabbits. The test material *Latex Polymer Powder Free* was applied (both inner and outer surface) in direct contact with the intact skin at a minimum of 4-hour exposure. Effects of erythema and oedema were evaluated according to the provisions established in the ISO 10993-10:2010(E) "Biological evaluation of medical devices – Part 10: Tests for irritation and skin sensitization.

The results show that all three rabbits appeared active and healthy with no sign of gross toxicity, adverse pharmacological effects and abnormal behavior. No irreversible alterations were observed on the skin treated with both the inner and outer surface of the test material throughout the 72-hour period. The Primary Irritation Index (PII) of the test material and negative control was '0'.

The test material ***Latex Polymer Powder Free*** did not cause an irritant response. The Primary Irritation Response Category is deemed 'Negligible'.

Signature .....

12 NOV 2013

Date .....

Md Anuar Osman, DVM, M. Sc., Ph.D
Study Director

Signature .....

12 NOV 2013

Date .....

Mimi Norhilda Mohd Hatta, B. Sc. (Hons)
Head Investigator

# TEST MATERIAL CHARACTERISTICS

| | |
|---|---|
| **Name** | Latex Polymer Powder Free |
| **Intended Use of Test Material** | Not indicated |
| **Lot/Batch Number** | 200422691201 |
| **Date Received** | 27 September 2012 |
| **Expiry date** | September 2017 |
| **Physical Appearance** | Solid |
| **Type and Material of Packaging** | Not indicated |
| **Colour** | Natural |
| **Quantity Received** | 20 pieces |
| **Storage** | Temperature of 10 °C to 30 °C |
| **Solubility** | Water |
| **Sterility** | Non-sterile |
| **Sterilization Method** | Not applicable |
| **Condition of use** | Neat |
| **Date of Study Initiation** | 22 October 2013 |
| **Date of Study Completion** | 25 October 2013 |

# TEST FACILITY AND KEY PERSONNEL

## Test Facility

Makmal Bioserasi
Centre for Research and Instrumentation Management (CRIM)
Universiti Kebangsaan Malaysia
43600 UKM Bangi
Selangor, Malaysia.

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## Key Personnel

**Study Director**
Md Anuar Osman, DVM, M. Sc., Ph.D

**Head Investigator**
Mimi Norhilda Mohd Hatta, B. Sc. (Hons)

**Investigators**
Nur Faeza Mohd Nor, DVM
Nurhardyawati Ismail, B. Sc. (Hons)
Nur Zahira Kasmini, B. Sc. (Hons)

**Animal Care**
Suhairi Che Ismail
Suhana Shaian

**Quality Assurance Personnel**
Nurhafizah Zam, B. Sc. (Hons)

## STUDY DESIGN

**Purpose**
To provide information on the potential irritation effects likely to arise from a single exposure of a test material on the intact skin of rabbits.

**Animal Strain and Species**
New Zealand white rabbits.

**Number of animal**
Three rabbits (all females)

**Animal Source**
A Sapphire Enterprise, Seri Kembangan, Selangor.

**Authorization**
Approval from Universiti Kebangsaan Malaysia's Animal Ethics Committee (UKMAEC) for study entitled: Safety assessment of cosmetics, traditional preparations, plastics, gloves, rubber fibres and medical devices.

**Body Weight at initiation of study**
Minimum : 2.89 kg
Maximum: 3.20 kg

**Housing**
Rabbits were housed individually in suspended stainless steel cages with mesh floors of internal dimension: 40 cm by 40 cm by 60 cm. The animals were selected randomly prior to acclimation.

**Caging and Identification**
One animal per cage. Each cage attached with an identification card labeled with animal number, gender, and job number.

**Acclimation**
6 days (16 October – 22 October 2013)

**Diet**
Standard rabbit pellet (Grower Pellet)

**Room Environment**
Temperature: 20.0 °C to 23.4 °C
Lighting: 12-hour light/dark cycles

**Type and Frequency of Observations**
Once daily up to 72 hours post-treatment

**Control item**
Normal saline as negative control, and SDS in petroleum jelly as the positive control.

## STUDY TIMETABLE

| | |
|---|---|
| Acclimation period | 16 October – 22 October 2013 |
| Date of initiation | 22 October 2013 |
| Dates of observation | 22 October – 25 October 2013 |
| End of test | 25 October 2013 |

# PROCEDURES

## Pre-Dosing Procedures

### Check for ill health
On arrival and just before dosing, only healthy animals were selected and used in the study.

### Body weight
All animals were weighed prior to treatment.

### Preparation of Application Site
Only animals without pre-existing skin irritation were selected for the study. The dorsal surface of each side of the rabbit was clipped free of hair with a clipper to expose a surface of approximately 10 cm by 15 cm. Care was taken to avoid abrading the skin and trauma. After exposing the skin and prior to treatment, animals were again examined for any abnormalities and ill health. Four test sites were delineated; two sites for test material application (inner and outer surface), a third site for negative control, and the fourth site for positive control.

### Preparation of Test Material
The test material was cut to a dimension of 2.5 cm by 2.5 cm and applied neat on the test site. Absorbent gauze (2.5 cm by 2.5 cm) soaked in normal saline was used as negative control. Positive control SDS in petroleum jelly was prepared by spreading 0.5 g on a filter paper at corresponding control site.

### Application of Test Material
The test material and control items were applied to each designated site of the prepared skin. Sites were individually covered with double layered surgical gauze and wrapped with a non-reactive adhesive tape to minimize evaporation and to avoid dislocation of test patches. The entire trunk was further wrapped with an elastic bandage and following which rabbits were returned to their individual cages.

Patches including bandages were removed after 6 hours of exposure. The applied sites were gently wiped with a moist clean towel to remove any residues. Individual sites were then scored according to the scoring system for skin reaction (Table 1a) at 1 ±0.1, 24 ±2, 48 ±2 and 72 ±2 hours after removal of test patches.

# OBSERVATIONS

## Method of Scoring

Evaluation of skin lesions on each application site at 1 ±0.1 hour, 24 ±2 hours, 48 ±2 hours and 72 ±2 hours following patch removal was graded and scored as follows:

Table 1a: Scoring system for skin reaction.

| Reactions | Description | Score |
|---|---|---|
| Erythema (E) | Erythema and eschar formation | |
| | No erythema | 0 |
| | Very slight erythema (barely perceptible) | 1 |
| | Well-defined erythema | 2 |
| | Moderate erythema | 3 |
| | Severe erythema (beet redness) to eschar formation preventing grading of erythema | 4 |
| Oedema (O) | Oedema formation | |
| | No oedema | 0 |
| | Very slight oedema (barely perceptible) | 1 |
| | Well-defined oedema (edges of the area well defined by definite raising) | 2 |
| | Moderate oedema (raised approximately 1mm) | 3 |
| | Severe oedema (raised more than 1mm and extending beyond exposure area) | 4 |
| Maximal possible score for irritation | | 8 |
| Other adverse changes at the skin sites shall be recorded and reported | | |

Table 1b: Irritation Response categories in rabbit

| Mean score | Response category |
|---|---|
| 0 to 0.4 | Negligible |
| 0.5 to 1.9 | Slight |
| 2 to 4.9 | Moderate |
| 5 to 8 | Severe |

## INTERPRETATION OF RESULTS

Only observations at 24 ±2 hours, 48 ±2 hours and 72 ±2 hours were used for calculations. The Primary Irritation Scores (PIS) for erythema and oedema at each time point per animal were combined and the summation of the combined scores was divided by six. The irritation scores (PIS) for each animal are totaled and divided by the total number of animals to give the Primary Irritation Index (Table 1 b).

## RESULTS AND DISCUSSION

The three rabbits appeared active and healthy with no sign of gross toxicity, adverse pharmacological effects and abnormal behavior. No irreversible alterations were observed on the skin treated with both the inner and outer surface of the test material throughout the 72-hour period. The Primary Irritation Index (PII) of the test material and negative control was '0' (Appendix 1).

Cutaneous reactions at the sites of contact with positive control article (SDS in petroleum jelly) produced erythema and oedema at 1 ±0.1 hour, 24 ±2 hours, 48 ±2 hours and 72 ±2 hours post treatment. The Primary Irritation Index (PII) for positive control was '3.17'.

Cutaneous reaction scores of the test material and controls are presented in Appendix 1 and Appendix 2.

## CONCLUSION

The test material ***Latex Polymer Powder Free*** did not cause an irritant response. The Primary Irritation Response Category is deemed 'Negligible'.

## REFERENCES

1. ISO 10993-10:2010(E). Biological evaluation of medical devices – Part 10: Tests for irritation and skin sensitization.
2. ISO 10993-12:2012 (E). Biological evaluation of medical devices – Part 12: Sample preparation and reference materials.
3. Medical Glove Guidance Manual
4. Consumer Product Safety Commission, Title 16, Chapter II, Part 1500.

## AMENDMENTS AND DEVIATIONS

The amendments and deviations made are recorded in the Protocol Amendment/Deviation form (ADF01) with the approval of the Study Director.

## QUALITY ASSURANCE STATEMENT

This final report was audited in agreement with the raw data records and for compliance with the protocol and Standard Operating Procedures of Makmal Bioserasi. Dates of inspections and audits performed during the study and the dates of reporting of the inspection and audit findings to the Study Director are presented.

This study has been inspected by the Quality Assurance Personnel, and the findings have been reported to Study Director and Head Investigator on the following dates:

| Inspection Dates | Phase | Date reported to Study Director and Head Investigator |
|---|---|---|
| 6 November 2013 | Data | 7 November 2013 |
| 7 November 2013 | Report | 7 November 2013 |
| 12 November 2013 | Report | 12 November 2013 |

Nurhafizah Zam
Quality Assurance Personnel

12 NOV 2013
Date

## ARCHIVING

A copy of this signed report including all raw data generated during the course of study are retained in Makmal Bioserasi's archive for at least 6 years.

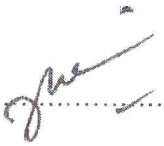
## VERIFICATION

We the undersigned declare that the methods, results and data contained in this report faithfully reflect the procedures used and the raw data collected during the course of this study.

12 NOV 2013

Md Anuar Osman, DVM, M. Sc., Ph.D
Study Director

Date



12 NOV 2013

Mimi Norhilda Mohd Hatta, B. Sc. (Hons)
Head Investigator

Date

12 NOV 2013

Nurhafizah Zam, B. Sc. (Hons)
Quality Assurance Personnel

Date

# Appendix 1

Cutaneous reaction scores of ***Latex Polymer Powder Free (inner surface)***

| No | Animal Number/ Sex | 1 hour (Post removal) | | 24 hours (Post removal) | | 48 hours (Post removal) | | 72 hours (Post removal) | | Primary Irritation Score (Mean) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Score | | Score | | Score | | Score | | |
| | | Erythema | Oedema | Erythema | Oedema | Erythema | Oedema | Erythema | Oedema | |
| 1 | r016D Female | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | r017D Female | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | r018D Female | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Cutaneous reaction scores of ***Latex Polymer Powder Free (outer surface)***

| No | Animal Number/ Sex | 1 hour (Post removal) | | 24 hours (Post removal) | | 48 hours (Post removal) | | 72 hours (Post removal) | | Primary Irritation Score (Mean) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Score | | Score | | Score | | Score | | |
| | | Erythema | Oedema | Erythema | Oedema | Erythema | Oedema | Erythema | Oedema | |
| 1 | r016D Female | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | r017D Female | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | r018D Female | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Cutaneous reaction scores for negative control (normal saline)

| No | Animal Number/ Sex | 1 hour (Post removal) | | 24 hours (Post removal) | | 48 hours (Post removal) | | 72 hours (Post removal) | | Primary Irritation Score (Mean) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Score | | Score | | Score | | Score | | |
| | | Erythema | Oedema | Erythema | Oedema | Erythema | Oedema | Erythema | Oedema | |
| 1 | r016D Female | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | r017D Female | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | r018D Female | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Cutaneous reaction scores for positive control (SDS in petroleum jelly)

| No | Animal Number/ Sex | 1 hour (Post removal) | | 24 hours (Post removal) | | 48 hours (Post removal) | | 72 hours (Post removal) | | Primary Irritation Score (Mean) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Score | | Score | | Score | | Score | | |
| | | Erythema | Oedema | Erythema | Oedema | Erythema | Oedema | Erythema | Oedema | |
| 1 | r016D Female | 4 | 3 | 4 | 2 | 3 | 2 | 3 | 1 | 2.5 |
| 2 | r017D Female | 4 | 4 | 4 | 4 | 4 | 4 | 3 | 2 | 3.5 |
| 3 | r018D Female | 4 | 4 | 4 | 4 | 4 | 3 | 4 | 2 | 3.5 |

# Appendix 2

Primary Irritation Indices of ***Latex Polymer Powder Free*** (inner and outer surface), normal saline, and SDS in petroleum jelly observed during the 72-hour period.

| | Primary Irritation Score (Mean) | | | |
|---|---|---|---|---|
| **Animal Number** | **Test Material (Inner surface)** | **Test Material (Outer surface)** | **Negative Control (Normal saline)** | **Positive Control (SDS in petroleum jelly)** |
| r016D | 0 | 0 | 0 | 2.5 |
| r017D | 0 | 0 | 0 | 3.5 |
| r018D | 0 | 0 | 0 | 3.5 |
| **Primary Irritation Index** | **0** | **0** | **0** | **3.17** |