GLP REPORT

TEST FACILITY

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SPONSOR

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STUDY TITLE

ISO Skin Irritation Study in Rabbits

TEST ARTICLE NAME

Viberect Pad Overmold

TEST ARTICLE IDENTIFICATION

Pad Overmold

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Summary

The test article, Viberect Pad Overmold, was evaluated for primary skin irritation in accordance with the guidelines of ISO 10993-10, Biological Evaluation of Medical Devices - Part 10: Tests for Irritation and Skin Sensitization. Two approximate 25 mm x 25 mm sections of the test article and control article were topically applied to the skin of each of three rabbits and left in place for 24 hours. The sites were graded for erythema and edema at 1, 24, 48 and 72 hours after removal of the single sample application.

There was no erythema and no edema observed on the skin of the animals treated with the test article. The Primary Irritation Index for the test article was calculated to be 0.0. The response of the test article was categorized as negligible.

Supervisory Personnel:

Melissa A. Cadaret, B.A., M.S.
Manager, Toxicology

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Approved by:

Jennifer N. Moritz, B.S.
Study Director

5/4/11
Date Completed

Statement of GLP Compliance

This study was conducted in accordance with the provisions of the FDA Good Laboratory Practice (GLP) Regulations (21 CFR, Part 58).

Study Director: Jennifer N. Moritz, B.S. 5-4-11 Date

1. Introduction

Purpose
The purpose of this study was to evaluate the test article for the potential to cause skin irritation in the rabbit.

Testing Guidelines
This study was conducted based on the International Organization for Standardization 10993-10, Biological Evaluation of Medical Devices, Part 10: Tests for Irritation and Skin Sensitization.

Dates

Test Article Received:	March 23, 2011
Treatment Started:	April 26, 2011
Observations Concluded:	April 30, 2011

GLP Compliance
The study initiated by protocol signature on April 14, 2011 was conducted in accordance with the provisions of the FDA Good Laboratory Practice (GLP) Regulations, 21 CFR 58. A Statement of Quality Assurance Activities was issued with this report.

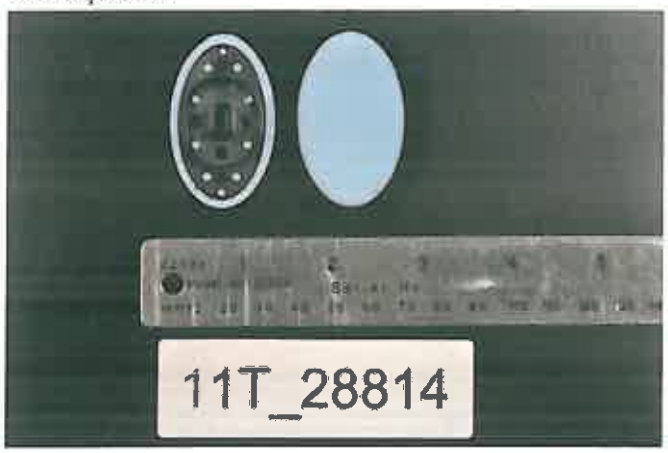
Duplication of Experimental Work
By signature on the protocol, the sponsor confirmed that the conduct of this study did not unnecessarily duplicate previous experiments.

2. Materials

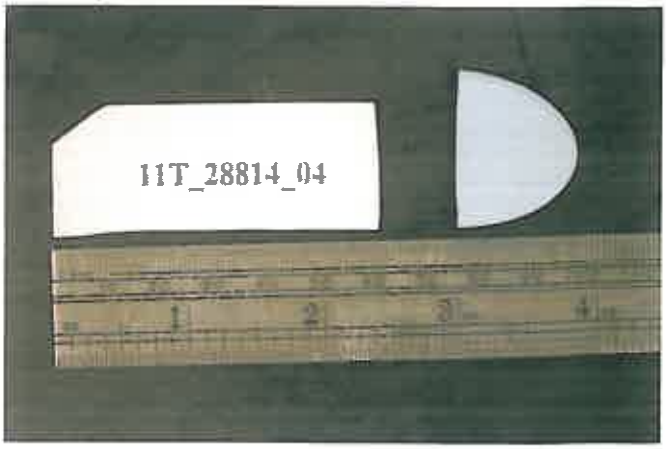
The test article provided by the sponsor was identified and handled as follows:

Test Article Name:	Viberect Pad Overmold
Identification:	Pad Overmold
Stability Testing:	In progress (per sponsor)
Expiration Date:	Stable for duration of intended testing (per sponsor)
Strength, Purity and Composition:	Strength: not applicable because no active ingredients are used to formulate a concentration Purity: not applicable because the test article is a multi-component device
	Composition: Irogran A85P4394 thrermoplastic polyurethane elastomer
Physical Description of the Test Article:	Pad overmold (blue) thermoplastic polyurethane for skin contact (penis) for vibratory nerve stimulation. Black is to be removed and discarded.
Storage Conditions:	Room Temperature

Pre-Preparation



Post-Preparation



Control Article:	Four-ply gauze supplied by the test facility was cut into 25 mm x 25 mm sections and moistened with 0.5 mL of saline per section.
Stability Testing:	Marketed product; stability characterized by its labeling
Strength, Purity, Composition or Other Characteristics:	Purity: FDA Quality System Requirements (QSR) as stipulated in 21 CFR Part 820; Composition: 20% rayon, 80% polyester blend
Preparation:	The test article was cut into approximate 25 mm x 25 mm sections. The smooth side of the test article was moistened with 0.5 mL of saline, backed with four-ply gauze, and applied to the skin of the rabbit. The black portion was not used.

3. Test System

Test System

Species:	Rabbit (*Oryctolagus cuniculus*)
Breed:	New Zealand White
Source:	Myrtle's Rabbitry, Inc.
Sex:	Male
Body Weight Range:	2.4 kg to 2.3 kg at selection
Age:	Young adult
Acclimation Period:	Minimum 5 days
Number of Animals:	Three
Identification Method:	Ear tag

Justification of Test System

The rabbit (animal) is specified as an appropriate animal model for evaluating potential skin irritants by the current ANSI/AAMI/ISO testing standards. The rabbit is widely used for this purpose and relative ranking of irritant scores can be determined.

4. Animal Management

Husbandry:	Conditions conformed to NAMSA Standard Operating Procedures that are based on the "*Guide for the Care and Use of Laboratory Animals*."
Food:	A commercially available rabbit feed, PROLAB Hi-Fiber Rabbit - 5P25, was provided daily.
Water:	Potable water was provided *ad libitum* through species appropriate water containers or delivered through an automatic watering system.
Contaminants:	Contaminants reasonably expected in feed or water supplies were not believed to have influenced the outcome of this test.
Housing:	Animals were individually housed in stainless steel or plastic suspended cages identified by a card indicating the lab number, animal number, test code, sex, and date dosed.
Environment:	The animal housing room temperature and relative humidity were monitored daily. The recommended temperature for the room was 61-72°F and the recommended relative humidity was 30-70%. There were no significant temperature or relative humidity excursions that adversely affected the health of the animals.
	The light cycle was controlled using an automatic timer (12 hours light, 12 hours dark).
Accreditation:	NAMSA is an AAALAC International accredited facility and is registered with the United States Department of Agriculture. Additionally, NAMSA maintains an approved Animal Welfare Assurance on file with the National Institutes of Health, Office for Laboratory Animal Welfare.
Personnel:	Associates involved were appropriately qualified and trained.
Selection:	Only healthy, previously unused, animals free from irritation or other dermatological lesions that could interfere with the test were selected.
Veterinary Care:	Standard veterinary medical care was provided in this study.

IACUC: This procedure has been approved by NAMSA Institutional Animal Care and Use Committees (IACUC), and is reviewed at least annually by the same committees.

5. Method

The animals were weighed and the fur on the back of each animal was clipped with an electric clipper 4 to 24 hours prior to treatment. On the day of treatment, four sites, two on each side of the back and positioned cranially and caudally, were designated on each animal. The sites were free of blemishes that could interfere with the interpretation of results.

An approximate 25 mm x 25 mm section of the test article was moistened with 0.5 mL of saline and applied to one cranial site and one caudal site (two sites per animal) by introduction under a 4 ply gauze layer to an area of skin approximately 25 mm x 25 mm square. The patches were covered with a nonreactive tape. The control was similarly applied to the opposite cranial and caudal sites. The trunk of each animal was wrapped with an elastic binder to maintain the test patches in position. Animals were returned to their cages after treatment.

After the 24 hour exposure, the binders, tape, and patches were removed. The sites were gently wiped with a gauze sponge dampened with deionized water in an attempt to remove any remaining residue.

Laboratory Observations

1. Animals were observed daily for general health.
2. Body weights were recorded for each animal at pretreatment.
3. Dermal observations for erythema and edema were recorded at 1, 24, 48 and 72 hours after patch removal in accordance with the criteria in Appendix 1.

All times and temperatures reported herein are approximate and are within ranges established by the external standards described in the References section of this report and/or NAMSA standard operating procedures.

6. Evaluation and Statistical Analysis

The Primary Irritation Index of the test was calculated following test completion for each animal. The erythema and edema scores obtained at the 24, 48 and 72 hour intervals were added together and divided by the total number of observations. This calculation was conducted separately for the test and control article for each animal. The score for the control was subtracted from the score for the test article to obtain the Primary Irritation Score. The Primary Irritation Score for each animal was added together and divided by the number of animals to obtain the Primary Irritation Index. The Primary Irritation Index was characterized based on the definitions outlined in Appendix 1.

7. Results

All animals were clinically normal throughout the study. Individual results of dermal scoring appear in Appendix 2. No irritation was observed on the skin of the animals. The Primary Irritation Index of the test article was calculated to be 0.0. The irritation calculations are shown below:

Animal Number	Test Score Average	-	Control Score Average	Individual Primary Irritation Score	Combined Primary Irritation Score (CPIS)	Primary Irritation Index (CPIS ÷ 3)	Response Category
74376	0.0	-	0.0	0.0	0.0	0.0	Negligible
74385	0.0	-	0.0	0.0			
74387	0.0	-	0.0	0.0			

8. Conclusion

There was no erythema and no edema observed on the skin of the animals treated with the test article. The Primary Irritation Index for the test article was calculated to be 0.0. The response of the test article was categorized as negligible.

Results and conclusions apply only to the test article tested. Any extrapolation of these data to other articles is the sponsor's responsibility.

9. Quality Assurance

Inspections were conducted at intervals adequate to assure the integrity of the study in conformance with 21 CFR 58.35(b)(3). The final report was reviewed for conformance to Section 58.185, Subpart J, of the GLP Regulations. A Statement of Quality Assurance Activities was issued with the report.

10. Records

All raw data pertaining to this study and a copy of the final report are retained in designated NAMSA archive files.

11. ISO Compliance

All procedures were certified to ISO 13485:2003 and accredited to ISO 17025:2005.

12. References

Code of Federal Regulations (CFR), Title 21, Part 58, Good Laboratory Practice for Nonclinical Laboratory Studies.

Code of Federal Regulations (CFR), Title 9, Parts 1-199, Animal Welfare Act.

National Research Council, *Guide for the Care and Use of Laboratory Animals*, Washington, DC: National Academy Press, 2011.

Office of Laboratory Animal Welfare (OLAW), Public Health Service Policy on Humane Care and Use of Laboratory Animals.

Code of Federal Regulations (CFR), Title 16, Part 1500, Federal Hazardous Substances Act (FHSA) Regulations (2008).

International Organization for Standardization (ISO) 10993-2, Biological Evaluation of Medical Devices - Part 2: Animal Welfare Requirements (2008).

International Organization for Standardization (ISO) 10993-10, Biological Evaluation of Medical Devices - Part 10: Tests for Irritation and Skin Sensitization (2010).

International Organization for Standardization (ISO) 13485, Medical Devices - Quality Management Systems - Requirements for Regulatory Purposes (2003).

International Organization for Standardization (ISO) 17025, General Requirements for the Competence of Testing and Calibration Laboratories (2005).

Appendix 1 - Classification System For Skin Reaction

Reaction	Numerical Grading
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
Edema Formation	
No edema	0
Very slight edema (barely perceptible)	1
Well-defined edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond exposure area)	4
Total possible score for irritation	8

NOTE: Other adverse changes at the skin sites shall be recorded and reported

Irritation Response Categories in the Rabbit

Response Category	Mean Score
Negligible	0.0 to 0.4
Slight	0.5 to 1.9
Moderate	2.0 to 4.9
Severe	5.0 to 8.0

Appendix 2 - Dermal Observations

Animal Number/ Sex	Weight (kg)	Group	Observation	Interval (hours)							
				1		24		48		72	
				Left	Right	Left	Right	Left	Right	Left	Right
74376 Male	2.4	Test	Erythema	0	0	0	0	0	0	0	0
			Edema	0	0	0	0	0	0	0	0
		Control	Erythema	0	0	0	0	0	0	0	0
			Edema	0	0	0	0	0	0	0	0
74385 Male	2.4	Test	Erythema	0	0	0	0	0	0	0	0
			Edema	0	0	0	0	0	0	0	0
		Control	Erythema	0	0	0	0	0	0	0	0
			Edema	0	0	0	0	0	0	0	0
74387 Male	2.3	Test	Erythema	0	0	0	0	0	0	0	0
			Edema	0	0	0	0	0	0	0	0
		Control	Erythema	0	0	0	0	0	0	0	0
			Edema	0	0	0	0	0	0	0	0

Statement of Quality Assurance Activities

Phase Inspected	Date Inspected	Date Reported to Study Director	Date Reported to Management
Scoring	April 29, 2011	April 29, 2011	April 29, 2011
Study Data Review	May 2, 2011	May 2, 2011	May 2, 2011
Final Report Review	May 3, 2011	May 3, 2011	May 3, 2011

Based on a review of this study, it has been concluded that this report accurately describes the methods and standard operating procedures, and that the reported results accurately reflect the raw data of the study. This study has been reviewed in accordance with the provisions of the FDA Good Laboratory Practice Regulations (21 CFR, Part 58).

QA Representative: _____ 5-4-11

Marie Glodowski, B.S.
Auditor, Quality Assurance

Date