TEST FACILITY

NAMSA 9 Morgan Irvine, CA 92618 949.951.3110

SPONSOR

Mike Stewart IMBiotechnologies LTD Suite 113 – Advanced 9650 20th Avenue Edmonton, Alberta T6N 1G1 Canada

STUDY TITLE

USP Pyrogen Study - Material Mediated

TEST ARTICLE NAME

Occlusin 505 Artificial Embolization Device

TEST ARTICLE IDENTIFICATION

FL288

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The test article, Occlusin 505 Artificial Embolization Device, FL288, was extracted in sterile, nonpyrogenic 0.9% sodium chloride solution. The test solution was evaluated in the rabbit for material mediated pyrogenicity. The test was conducted based on USP General Chapter <151> Pyrogen Test. The procedure is recommended in ISO 10993-11, Biological Evaluation of Medical Devices - Part 11: Tests for Systemic Toxicity.

A single dose of 10 mL/kg was intravenously injected via the marginal ear vein into each of three rabbits. Rectal temperatures were measured and recorded prior to injection and at 30 minute intervals between 1 and 3 hours after injection.

Under the conditions of this study, the total rise of rabbit temperatures during the 3 hour observation period was within acceptable USP limits. The test article was judged as nonpyrogenic.

Study and Supervisory Personnel:

John A. Muraski, Ph.D. Manager, In Vitro & Toxicology

Approved by:

Marcia Mestre, B.S. Study Director

Date Completed

Authorization for duplication of this report, except in whole, is reserved pending NAMSA's written approval.

pm

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).

There were no deviations from the protocol, standard operating procedures or the GLP Regulations which were judged to have had any significant impact on the validity or interpretation of the data.

All laboratory data has been accurately recorded and verified, as indicated by the signature below.

Study Director:

Marcia Mestre, B.S.

Date

1. Introduction

Purpose

The test article identified below was prepared and evaluated for material mediated pyrogenicity. The purpose of this study was to determine whether an extract of the test article induced a pyrogenic response following intravenous injection in rabbits. *In vivo* biological reactivity was evaluated following a single injection of the extract.

Testing Guidelines

The study was conducted based on the United States Pharmacopeia, National Formulary, General Chapter <151>, Pyrogen Test. The procedure is recommended in International Organization for Standardization 10993-11, Biological Evaluation of Medical Devices - Part 11: Tests for Systemic Toxicity.

Dates

Test Article Receipt: October 16, 2009
Test Conducted Date: October 26, 2009

GLP Compliance

The study initiated by protocol signature on October 16, 2009, 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 the 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:

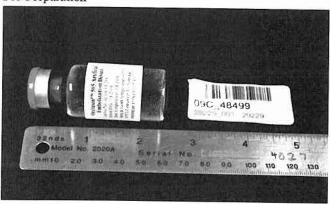
Test Article Name:

Occlusin 505 Artificial Embolization Device

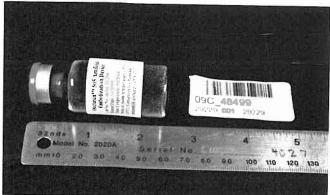
Test Article Identification:

FL288

Pre-Preparation



Post-Preparation



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:

polyactide - co-glycolide and bovine collagen.

Physical Description of the

Test Article:

Microspheres supplied as a dry powder in sterile sealed glass vials, 400 mg/vial

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Lab Number 09C 48499 02 TU010_807 GLP Report

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Storage Conditions:

Refrigerate

Sham Solution:

Sterile, nonpyrogenic 0.9% sodium chloride solution (SNPS), warmed to 37°C

Vehicle:

Sterile, nonpyrogenic 0.9% sodium chloride solution (SNPS)

SNPS Stability:

Marketed product stability characterized by its labeling

SNPS Strength,

Purity and Composition:

Strength:

Not applicable; no active components in the formulation

Purity:

Meets requirements of USP Sodium Chloride for Injection and is certified

as USP Grade. 0.9% NaCl ± 5.0% of label claim, balance is water

Composition:

CAS #: 7647-14-5, sodium chloride/water CAS #: 7732-18-5

Preparation:

Based on a ratio of 120 cm²: 20 mL, a 901.3 cm² portion of the test article was covered with 150 mL of SNPS and extracted with continuous agitation at 37°C for 72 hours. The test extract was warmed in a 37°C water bath for a minimum of 10 minutes prior to injection.

Condition of Extract:

Clear

3. Test System

Test System

Species:

Rabbit (Oryctolagus cuniculus)

Breed: Source: New Zealand White Myrtle's Rabbitry Inc.

Sex:

Male

Body Weight Range:

3.2 kg to 3.5 kg

Age:

No particular age was prescribed for this test

Acclimation Period:

Minimum 5 days

Number of Animals:

Three

Identification Method:

Ear tag

Justification of Test System

The pyrogen test is specified in the current USP and ISO 10993, Part 11 guidelines. No in vitro alternative exists for detecting material mediated pyrogens.

4. Animal Management

Conditions conformed to NAMSA Standard Operating Procedures that are based on the "Guide for the Husbandry:

Care and Use of Laboratory Animals."

Food: Food was withheld from the animals used during the period of the test.

Potable water was provided ad libitum through species appropriate water containers or delivered through Water:

an automatic watering system.

Contaminants reasonably expected in feed or water supplies were not believed to have influenced the Contaminants:

outcome of this test.

Animals were individually housed in stainless steel suspended cages identified by a card indicating the Housing:

animal number, test code, and sex. Noise level will be maintained to avoid exciting the animals.

Environment: The room temperature and relative humidity were monitored daily. The temperature for the room was

20°C-23°C (68.0°F-73.4°F) and the relative humidity was 30-70%. The room was also free from

disturbances likely to excite 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: Rabbits used in this study were used previously for another pyrogen study. The establishment and

maintenance of a pyrogen colony is defined in the current USP. Complete history of animal usage is traceable in laboratory records. The reuse criteria are described in NAMSA Standard Operating

Procedures.

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. Any significant changes to this procedure were

approved by the IACUC prior to conduct.

5. Method

Animals were placed in a restrainer and allowed to acclimate for a minimum of 2 hours.

Preliminary Test - Sham

Animals were placed in a restrainer and a rectal probe was inserted in the rectum of each animal. The animals were allowed to acclimate to their restrainer position at least 1 hour prior to initiating temperature collection. Four temperature readings were conducted at 30 minute intervals beginning 90 minutes prior to injection. The mean temperature of the last two readings was considered the initial temperature.

Each of the rabbits was injected intravenously via the marginal ear vein with SNPS at a dose of 10 mL/kg. The solution was injected within a 4 minute period. For all rabbits, temperatures were recorded at 30 minute intervals for 3 hours after injection. Animals with a temperature rise of greater than 0.6°C, animals with temperatures outside of the 38.0°C to 39.8°C range or animals with a temperature variation greater than 0.2°C between the 0.5 and 0.0 hour pre-injection temperatures were excluded from the main test.

Main Test

Three animals were placed in a restrainer and a rectal probe was inserted in the rectum of each animal. The animals were allowed to acclimate to their restrainer position at least 15 minutes prior to initiating temperature collection. Two control temperatures were taken at least 30 minutes apart. The second temperature was recorded no more than 30 minutes prior to the injection; this temperature became the baseline temperature for the study.

Each of the rabbits was injected intravenously via the marginal ear vein with the test extract at 10 mL/kg of body weight. The test extract was injected within a 10 minute period. For all rabbits, temperatures were recorded at 30 minute intervals between 1 and 3 hours after injection.

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

No statistical analysis of the data was performed. Once the temperature readings had been recorded, the maximum rise in temperature for each rabbit was determined. A decrease in temperature was recorded as a 0.0°C change.—If no single animal showed an increase of 0.5°C or more above its baseline temperature, then the extract was judged nonpyrogenic. If the total maximum temperature of all three rabbits exceeded 3.3°C the extract was judged pyrogenic.

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7. Results

Main Test

No single animal showed a temperature increase of 0.5°C or more above its baseline temperature. Individual temperatures are presented below.

		I : :				Te	emperati	ıre - °C			
Rabbit Number	Sex	Weight (kg)	Dose Volume	Before I	njection		Hour	s after In	jection		Maximum Rise
			(mL)	Control 1	Baseline	1.0	1.5	2.0	2.5	3.0	1
94592*	Male	3.5	35	39.2	39.2	39.1	39.1	39.2	39.1	39.1	0.0
94593*	Male	3.2	32	39.4	39.3	39.3	39.3	39.4	39.3	39.3	0.1
94594*	Male	3.3	33	39.6	39.7	39.6	39.5	39.6	39.5	39.8	0.1
									TOTA	L RISE:	0.2

^{*}Previous use history traceable in laboratory records.

8. Conclusion

Under the conditions of this study, the total rise of rabbit temperatures during the 3 hour observation period was within acceptable USP limits. The test article was judged as nonpyrogenic.

Results and conclusions apply only to the test article tested. Any extrapolation of these data to other samples is the sponsor's responsibility. All procedures were conducted in conformance with good manufacturing practices and certified to ISO 13485:2003.

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 to be retained in designated NAMSA archive files.

11. References

21 CFR 58 (GLP Regulations).

Code of Federal Regulations (CFR), Title 9, Parts 1-199, Animal Welfare Act (2008).

National Research Council, Guide for the Care and Use of Laboratory Animals, Washington, DC: National Academy Press, 1996.

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

International Organization for Standardization (ISO) 10993-11, Biological Evaluation of Medical Devices - Part 11: Tests for Systemic Toxicity (2006).

International Organization for Standardization (ISO) 10993-2, Biological Evaluation of Medical Devices - Part 2: Animal Welfare Requirements (2006).

United States Pharmacopeia 32, National Formulary 27 (USP), General Chapter 151, Pyrogen Test (2009).

Statement of Quality Assurance Activities

Phase Inspected	Date Inspected	Date Reported to Study Director	Date Reported to Management
Injections	October 26, 2009	October 26, 2009	October 26, 2009
Study Data Review	October 27, 2009	October 27, 2009	October 27, 2009
Final Report Review	October 30, 2009	October 30, 2009	October 30, 2009

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:		
	William Wooten, ASQ-CQA Ouality Assurance	Date



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GLP SAMPLE SUBMISSION FORM

PEOPLE > SCIENCE > SOLUTIONS

096-48499

www.namsa.com

Testing: Biocompatibility/Chemistry (con't)	NAMSA recommends the highest temperature that will not degrade the test article unless other limits apply. *For tests that require extraction only,	1 CAME ODG

Special Instructions:

Product is biodegradable. Extraction temperature should be no more than 37 °C, where required.

Product is microspheres packaged as a dry sterile powder in sealed sterile glass vials. Each vial contains 400 mg of microspheres with an approximate product surface area of 2575 cm²; or 6436 cm² per gram of per gram of the contains are contained by the con

TEST	FACI	ידו וו	v.
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NAMSA 9 Morgan Irvine, OH 92618

SPONSOF	?
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Mike Stewart
Suite 113 – Advanced 9650 20th Avenue
Edmonton, Alberta T6N 1G1
Canada

STUDY TITLE:

USP Pyrogen Study, Material Mediated

NAMSA

090-48499 02

PEOPLE > SCIENCE > SOLUTIONS

NAMSA Use Only (11)

Lab No.:

TU010_807 GLP PROTOCOL

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090-4849902

Approvals

Sponsor Representative (Sponsor):	M.W. Fewart
Date Approved:	September 28, 2009
Study Director (NAMSA):	Cu le
Date Initiated:	10-110-09

09C-4849902

1. Introduction

Purpose

The purpose of the study is to determine if a test solution (TS) induces a pyrogenic response following intravenous injection in rabbits. The test article will be extracted in sterile, nonpyrogenic 0.9% sodium chloride solution (SNPS). This study will be conducted based on the methods described in USP General Chapter <151> PYROGEN TEST. The USP method is recommended by ISO 10993-11 (2006) Biological Evaluation of Medical Devices - Part 11: Tests for Systemic Toxicity.

GLP Compliance

Good Laboratory Practice - This nonclinical laboratory study will be conducted in accordance with the United States Food and Drug Administration Good Laboratory Practice Regulations, 21 CFR Part 58.

Duplication of Experimental Work

By signature on this protocol, the sponsor confirms that the conduct of this study does not unnecessarily duplicate previous experiments.

2. Materials

Test Article

The sponsor will submit the test article to be evaluated. Detailed information about the test article was provided to NAMSA by the sponsor and is listed below:

Test Article Name:	Occlusin 505 Artificial Embolization Device
Test Article Identification:	FL288
Test Article Physical Description:	Microspheres supplied as a dry powder in sterile sealed glass vials/ 400mg/vial
Test Article Intended Clinical Use:	Embolotherapy
Test Article Stability:	Stability testing is in progress and sponsor affirms that test article is stable for duration of intended testing.
Test Article Strength:	Strength is not applicable because no active ingredients are used to formulate a concentration.
Test Article Purity:	Purity is not applicable because the test article is a multi-component device.
Test Article Composition:	The test article is composed of the following materials: polylactide – co-glycolide and bovine collagen
Test Article Mixture Analysis:	Analysis is not necessary because test article is a solid, powder, gel, or liquid being extracted or being tested as received (will not be mixed with a carrier).
Test Article Disposition:	Discard unused test article.

Preparation

The following information was completed based on the sponsor providing the information to NAMSA. Further instructions may be attached to the protocol. It is recommended that a minimum 150 mL extract of the material in SNPS be prepared as follows:

Ratio of Test Article to Extraction Vehicle

Material thickness less than 0.5 mm - 900 cm²:150 mL (ratio of 120 cm²:20 mL)

Test Article Preparation Instructions

Prepare based on the following: Use 0.14g of sample. 0.14g of sample has a surface area of 901.25cm².

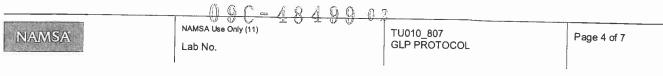
Extraction Conditions

37°C, 72 hours

Does the test article contain a protein component?

Yes

The test solution will be warmed in a 37°C water bath or incubator for a minimum of 10 minutes prior to dosing.



Special Laboratory Instructions

Following the extraction procedure, it is acceptable to centrifuge the extract with the sample in it to be able to remove enough extract for testing.

Control Article

No control article will be needed in the study.

3. Test System

Test System

Species:

Breed: Source:

Rabbit (Oryctolagus cuniculus) New Zealand White USDA licensed supplier

Sex:

No particular sex is prescribed for this test

Body Weight Range:

Not less than 1.5 kg at injection

Age: Acclimation Period:

No particular age is prescribed for this test Minimum 5 days

Number of Animals: Identification Method: Three Ear tag

Justification of Test System

The pyrogen test is specified in USP General Chapter <151> Pyrogen Test and ISO 10993-11 (2006) Biological Evaluation of Medical Devices - Part 11: Tests for Systemic Toxicity. No in vitro alternative exists for detecting material mediated pyrogens. Three healthy albino rabbits, previously sham tested will be used for the study. Five additional rabbits may be required for retest in the event of a high temperature rise in the three rabbit test.

4. Animal Management

Husbandry:

Conditions will conform to NAMSA Standard Operating Procedures that are based on the "Guide for the

Care and Use of Laboratory Animals."

Food:

Food will be withheld from the animals used during the period of the test.

Water:

Potable water will be provided ad libitum through species appropriate water containers or delivered

through an automatic watering system.

Contaminants:

Contaminants reasonably expected in feed or water supplies should not have the potential to influence the

outcome of this test.

Housing:

Animals will be individually housed in stainless steel suspended cages identified by a card indicating the animal number, test code and sex. Noise level will be maintained to avoid exciting the animals.

Environment:

The room temperature will be monitored daily. The temperature range for the room is 20°C and 23°C

(68.0°F and 73.4°F) and free from disturbances likely to excite the animals.

The room humidity will be monitored daily. The humidity range for the room is 30-70%. 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 will be appropriately qualified and trained.

Selection:

Rabbits used in this study may have been used previously for another pyrogen study. The establishment and maintenance of a pyrogen colony is defined in the current USP. Complete history of animal usage will be traceable in laboratory records. The reuse criteria are described in NAMSA Standard Operating Procedures.

Sedation, Analgesia or

Anesthesia:

It has been determined that the use of sedation, analgesia or anesthesia will not be necessary during the routine course of this procedure.

NAMSA

NAMSA Use Only (11) Lab No.

TU010 807 GLP PROTOCOL

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Veterinary

Care: All anesthetics, analgesics, and other medications may be given or altered at the discretion of the attending

veterinarian in accordance with standard veterinary practice and the study objectives. This applies to specific medication, dose, and dosing intervals. In the unlikely event that an animal should become injured, ill, or moribund, care will be conducted in accordance with current veterinary medical practice. If warranted for humane reasons, euthanasia will be conducted in accordance with the current report of the American Veterinary Medical Association's Guidelines on Euthanasia. The objective of the study will be

given due consideration in any decision and the study sponsor will be advised.

IACUC:

This protocol has been approved by NAMSA Institutional Animal Care and Use Committees (IACUC), and is reviewed at least annually by the same committees. Any significant changes to this protocol must

be approved by the IACUC prior to conduct.

5. Method

Three animals will be placed in a restrainer and a rectal probe will be inserted in the rectum of each animal. The animals will be allowed to acclimate to their restrainer position at least 15 minutes prior to initiating temperature collection. Two control temperatures will be taken at least 30 minutes apart. The second temperature will be recorded no more than 30 minutes prior to the injection; this will become the baseline temperature for the study.

Each of the rabbits will be injected intravenously via the marginal ear vein with the test extract at 10 mL/kg of body weight. The TS will be injected within a 10 minute period. For all rabbits, temperatures will be recorded at 30 minute intervals between 1 and 3 hours after injection. After the test is completed, all animals will be handled in accordance with IACUC approved NAMSA procedures.

6. Evaluation and Statistical Analysis

No statistical analysis of the data will be performed. Once the temperature readings have been recorded, the maximum rise in temperature for each rabbit will be determined. If no single animal shows an increase of 0.5°C or more above its baseline temperature, then the extract will be judged nonpyrogenic. If the total maximum temperature of all three rabbits exceeds 3.3°C, the extract will be judged pyrogenic. If one or more rabbits show an increase of 0.5°C or more above its baseline temperature then the extract will be injected in five additional rabbits. In this case, if the total temperature increase of the eight rabbits does not exceed 3.3°C and if no more than three of the eight rabbits attain an individual temperature increase of 0.5°C or more, the extract will be judged nonpyrogenic. A decrease in temperature will be recorded as a 0.0°C change. In the case of a retest a fresh extract will be prepared or the refrigerated extract can be used, provided it does not exceed 24 hours after decanting.

If the test solution is judged pyrogenic, an *in vitro* endotoxin specific assay may be conducted to confirm that the response is due to a non-endotoxin (chemical). Approval by the sponsor will be obtained prior to the conduct of the *in vitro* assay.

7. Report

The final report will include a description of the methods employed, baseline and temperature recordings at 30 minute intervals and maximum temperature rises for the test animals.

8. Quality Assurance

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

9. Proposed Dates

The study dates will be finalized by the study director following receipt of the sponsor-approved protocol and appropriate material for the study. Initiation of the study will be the date on which the study director signs the GLP protocol. Projected dates for starting the study (first treatment) and for the completion of the study (final report release) will be provided to the sponsor (or representative of the sponsor).

10. Records

Test article preparation, body weights, rabbit temperatures and maximum rises will be recorded.

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



NAMSA US 0 10 1 C = 4 8 4 9 9 0 TU010_807
Lab No. TU010_807

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11. References

Code of Federal Regulations (CFR), Title 21, Part 58, Good Laboratory Practice for Nonclinical Studies (2008).

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12. Protocol Changes

Any necessary changes to the protocol after sponsor approval or study initiation will be documented and approved by the study director as protocol amendments. Copies will be distributed to the sponsor, the raw data file, and the NAMSA Quality Assurance department.

> TU010 807 GLP PROTOCOL Lab No.



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October 19, 2009

Michael Stewart
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Edmonton Research Park 9650 20th AvenueSuite 113 Advanved Technology Centre
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Canada

PROTOCOL AMENDMENT I

Test Article:

Occlusin 505 Artificial Embolization Device

Identification:

FL288

NAMSA Submission ID.: 09C_48499

We have received appropriate test article and approved protocol(s) for the program to be conducted in accordance with the Good Laboratory Practice (GLP) Regulations on the material described above. Below is a projected schedule for the work to be performed.

NAMSA

NAMSA Lab

Code

Number

Study

Estimated Start Date:

Estimated Report Release Date:

TU010_807

09C 48499 02

Pyrogen Study - Material Mediated - 0.9% SC Extract

October 19, 2009

November 09, 2009

Marcia Mestre, B.S. Study Director

Date

cc: QA (NAMSA) Sponsor



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Michael Stewart IMBiotechnologies LTD Suite 113 – Advanced 9650 20th Avenue Edmonton, Alberta T6N 1G1 Canada

REVISED** PROTOCOL AMENDMENT I

Test Article:

Occlusin 505 Artificial Embolization Device

Identification:

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09C_48499 02

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November 09, 2009

Marcia Mestre, B.S. Study Director

Date

cc: QA (NAMSA) Sponsor

^{**}This amendment has been issued to correct the Sponsor facility address.

GLP PROTOCOL

NAMSA 9 Morgan Irvine, OH 92618	NAMSA Ohio 6750 Wales Road Northwood, OH 43619
	STUDY TITLE:
	USP Pyrogen Study, Material Mediated

SPONSOR:

TEST FACILITY:

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Approvals	
Sponsor Representative (Sponsor):	
Date Approved:	
Study Director (NAMSA):	
Date Initiated:	



1. Introduction

Purpose

The purpose of the study is to determine if a test solution (TS) induces a pyrogenic response following intravenous injection in rabbits. The test article will be extracted in sterile, nonpyrogenic 0.9% sodium chloride solution (SNPS). This study will be conducted based on the methods described in USP General Chapter <151> PYROGEN TEST. The USP method is recommended by ISO 10993-11 (2006) Biological Evaluation of Medical Devices - Part 11: Tests for Systemic Toxicity.

GLP Compliance

Good Laboratory Practice – This nonclinical laboratory study will be conducted in accordance with the United States Food and Drug Administration Good Laboratory Practice Regulations, 21 CFR Part 58.

Duplication of Experimental Work

By signature on this protocol, the sponsor confirms that the conduct of this study does not unnecessarily duplicate previous experiments.

2. Materials

Test Article

The sponsor will submit the test article to be evaluated. Detailed information about the test article was provided to NAMSA by the sponsor and is listed below:

Test Article Name:	Occlusion 505 Artificial Embolization Device
Test Article Identification:	FL288
Test Article Physical Description:	Microspheres supplied as a dry powder in sterile sealed glass vials/ 400mg/vial
Test Article Intended Clinical Use:	Embolotherapy
Test Article Stability:	Stability testing is in progress and sponsor affirms that test article is stable for duration of intended testing.
Test Article Strength:	Strength is not applicable because no active ingredients are used to formulate a concentration.
Test Article Purity:	Purity is not applicable because the test article is a multi-component device.
Test Article Composition:	The test article is composed of the following materials: polylactide – co-glycolide and bovine collagen
Test Article Mixture Analysis:	Analysis is not necessary because test article is a solid, powder, gel, or liquid being extracted or being tested as received (will not be mixed with a carrier).
Test Article Disposition:	Discard unused test article.

Preparation

The following information was completed based on the sponsor providing the information to NAMSA. Further instructions may be attached to the protocol. It is recommended that a minimum 150 mL extract of the material in SNPS be prepared as follows:

Ratio of Test Article to Extraction Vehicle

Material thickness less than 0.5 mm - 900 cm²:150 mL (ratio of 120 cm²:20 mL)

Test Article Preparation Instructions

Prepare based on the following: Use 0.14g of sample. 0.14g of sample has a surface area of 901.25cm².

Extraction Conditions

37°C, 72 hours

Does the test article contain a protein component?

No

The test solution will be warmed in a 37°C water bath or incubator for a minimum of 10 minutes prior to dosing.



Special Laboratory Instructions

Following the extraction procedure, it is acceptable to centrifuge the extract with the sample in it to be able to remove enough extract for testing.

Control Article

No control article will be needed in the study.

3. Test System

Test System

Species: Rabbit (Oryctolagus cuniculus)

Breed: New Zealand White Source: USDA licensed supplier

Sex: No particular sex is prescribed for this test

Body Weight Range: Not less than 1.5 kg at injection

Age: No particular age is prescribed for this test

Acclimation Period: Minimum 5 days

Number of Animals: Three Identification Method: Ear tag

Justification of Test System

The pyrogen test is specified in USP General Chapter <151> Pyrogen Test and ISO 10993-11 (2006) Biological Evaluation of Medical Devices - Part 11: Tests for Systemic Toxicity. No *in vitro* alternative exists for detecting material mediated pyrogens. Three healthy albino rabbits, previously sham tested will be used for the study. Five additional rabbits may be required for retest in the event of a high temperature rise in the three rabbit test.

4. Animal Management

Husbandry: Conditions will conform to NAMSA Standard Operating Procedures that are based on the "Guide for the

Care and Use of Laboratory Animals."

Food: Food will be withheld from the animals used during the period of the test.

Water: Potable water will be provided *ad libitum* through species appropriate water containers or delivered

through an automatic watering system.

Contaminants: Contaminants reasonably expected in feed or water supplies should not have the potential to influence the

outcome of this test.

Housing: Animals will be individually housed in stainless steel suspended cages identified by a card indicating the

animal number, test code and sex. Noise level will be maintained to avoid exciting the animals.

Environment: The room temperature will be monitored daily. The temperature range for the room is 20°C and 23°C

(68.0°F and 73.4°F) and free from disturbances likely to excite the animals.

The room humidity will be monitored daily. The humidity range for the room is 30-70%. 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 will be appropriately qualified and trained.

Selection: Rabbits used in this study may have been used previously for another pyrogen study. The establishment

and maintenance of a pyrogen colony is defined in the current USP. Complete history of animal usage will be traceable in laboratory records. The reuse criteria are described in NAMSA Standard Operating

Procedures.

Sedation, Analgesia or

Anesthesia: It has been determined that the use of sedation, analgesia or anesthesia will not be necessary during the

routine course of this procedure.

Lab No.



Veterinary

Care: All anesthetics, analgesics, and other medications may be given or altered at the discretion of the attending

veterinarian in accordance with standard veterinary practice and the study objectives. This applies to specific medication, dose, and dosing intervals. In the unlikely event that an animal should become injured, ill, or moribund, care will be conducted in accordance with current veterinary medical practice. If warranted for humane reasons, euthanasia will be conducted in accordance with the current report of the American Veterinary Medical Association's Guidelines on Euthanasia. The objective of the study will be

given due consideration in any decision and the study sponsor will be advised.

IACUC: This protocol has been approved by NAMSA Institutional Animal Care and Use Committees (IACUC),

and is reviewed at least annually by the same committees. Any significant changes to this protocol must

be approved by the IACUC prior to conduct.

5. Method

Three animals will be placed in a restrainer and a rectal probe will be inserted in the rectum of each animal. The animals will be allowed to acclimate to their restrainer position at least 15 minutes prior to initiating temperature collection. Two control temperatures will be taken at least 30 minutes apart. The second temperature will be recorded no more than 30 minutes prior to the injection; this will become the baseline temperature for the study.

Each of the rabbits will be injected intravenously via the marginal ear vein with the test extract at 10 mL/kg of body weight. The TS will be injected within a 10 minute period. For all rabbits, temperatures will be recorded at 30 minute intervals between 1 and 3 hours after injection. After the test is completed, all animals will be handled in accordance with IACUC approved NAMSA procedures.

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No statistical analysis of the data will be performed. Once the temperature readings have been recorded, the maximum rise in temperature for each rabbit will be determined. If no single animal shows an increase of 0.5°C or more above its baseline temperature, then the extract will be judged nonpyrogenic. If the total maximum temperature of all three rabbits exceeds 3.3°C, the extract will be judged pyrogenic. If one or more rabbits show an increase of 0.5°C or more above its baseline temperature then the extract will be injected in five additional rabbits. In this case, if the total temperature increase of the eight rabbits does not exceed 3.3°C and if no more than three of the eight rabbits attain an individual temperature increase of 0.5°C or more, the extract will be judged nonpyrogenic. A decrease in temperature will be recorded as a 0.0°C change. In the case of a retest a fresh extract will be prepared or the refrigerated extract can be used, provided it does not exceed 24 hours after decanting.

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