GLP Final Report

Report No.: T51512019(E)

Exclusively prepared for:

SPONSOR
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TESTING FACILITY
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STUDY TITLE
Rabbit Pyrogen Study, Material Mediated

TEST ARTICLE
hemostatic xerogel sponge
Model: XLJ-I

ilac-MRA
ANAB ACCREDITED ISO/IEC 17025 TESTING LABORATORY AT-2046

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Summary

The test article, hemostatic xerogel sponge, XLJ-I, was evaluated for its material-mediated pyrogenicity. The test article was extracted in 0.9% sodium chloride solution (SC). A single dose of 10ml/kg was intravenously injected via the marginal ear vein into each of three animals. Rectal temperatures were measured and recorded prior to injection and 30 minutes intervals between 1 and 3 hours after injection.

Under the conditions of this study, the temperature rise of each animal during the 3 hours observation period meet the acceptable USP limits.

Approved by: 傅立 11/12/2019

Lee Fu, Authorized Signatory
Study Director

Date

GLP STATEMENT

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

There was no deviation to the protocol or provisions of GLP Regulation noted during the course of the study.

Approved by: 傅立

Lee Fu, Authorized Signatory
Study Director

11/12/2019
Date

1. Generals

1.1 Purpose

The purpose of this study was to evaluate for it material-mediated pyrogenicity.

1.2 Guidelines

1) ISO 10993-11:2017 Biological evaluation of medical devices – Part 11: Tests for systemic toxicity;
2) USP 42 NF 37 <151> Pyrogen Test.

1.3 Dates

Test Article Received:	08/19/2019
Initiated:	09/26/2019
Completed:	09/30/2019

2. Materials

Test Article	hemostatic xerogel sponge
Model	XLJ-I
Manufacturer	Same as sponsor
Identification Number	201904001
Status	Radiation sterilization
Physical Description	Solid
Composition	chitosan; Sodium polyacrylate; Polyethylene glycol
Stability	Stability was determined by and on file with the sponsor.
Strength	Not applicable, no active ingredient
Purity	Not applicable, no active ingredient
Storage Condition	Room Temperature
Note	Information regarding the test article was provided by sponsor in the Sample Submission Form.
Extraction Vehicle (Control)	0.9% sodium chloride
Polar	
Manufacturer	China Otsuka Pharmaceutical Co.,Ltd.
Lot Number	9A86G2
Physical Description	Clear, Colourless, Liquid
Composition	NaCl
Strength	500ml
Purity	Conforms to China Pharmacopoeia (2015)
Stability	Marketed product, stability is characterized by its labelling
Storage Condition	Room Temperature
Sample Preparation	Prior to the extraction, test article was removed from the package and absorb corresponding extract vehicle (SC: 420 ml) to saturation and then covered in the extraction vehicle.

Extraction Procedure

The test article was subjected to the extraction conditions as described below. The extract was continuously agitated during extraction.
Extraction Ratio: 0.1g:1ml
Sample Amount: 15.42g
Extraction Vehicle Volume: 154 ml
Extraction Condition: 50℃ 72 hours
Condition of Extract: Clear, no particulates
Note: The extract was not centrifuged, filtered or otherwise altered prior to dosing. Before dosed, it was stored at 4℃ for no more than 24h after extraction.

3. Test Systems and Justification

Species:	Rabbit
Breed:	Japanese White
Source:	Tianjin Yuda Laboratory Animal Breeding Co., Ltd.
Body Weight Range:	2.00 kg above
Sex:	Female, Females were nulliparous and non-pregnant.
Age:	Young adults
Acclimation Period:	Minimum 5 days
Number of Animals:	Three (3)
Identification Method:	Ear tag
Justification:	The current Pharmacopeia suggests rabbit as the test system. No in vitro alternative exists for detecting material mediated pyrogens. Three healthy albino rabbits, previously sham tested were used for the study.

4. Animal Management

Husbandry, Housing and Environment	Conditions conform to MID-LINK Standard Operating Procedures. Animals were individually housed in a cage with an identification card indicating the animal number, test code.
Food, Water and Contaminants	A commercially available rabbit feed was provided daily. Potable water was provided ad libitum through species appropriate water containers. No contaminant present in the feed and water was expected to impact the results of this study.
Personnel	Associates involved in this study were appropriately qualified and trained.
Veterinary Care	Standard veterinary medical care was provided during the study, if applicable.
Selection	Only healthy, previously unused animals will be selected.

5. Methods

Three animals were placed in a restrainer and a rectal probe was inserted in the rectum of each animal. 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 control temperature for the study. Use only those rabbits whose control temperatures do not vary by more than 1℃ from each other, and any rabbit with a temperature exceeding 39.8℃ shall not be used. Test extract was warmed to 37±2℃ prior to injection. Each of the animals was injected intravenously via the marginal ear vein with the test extract at 10mL/kg of body weight. The test extract was injected within a 10 minute period. For all animals, temperatures were recorded at 30 minute intervals between 1 and 3 hours after injection.

6. Evaluation

Consider any temperature decreases as zero rise. If no rabbit shows an individual rise in temperature of 0.5℃ or more above its respective baseline temperature, the product meets the requirements for the absence of pyrogens.

7. Results

See Attachment: Results

8. Conclusion

Under the conditions of this study, the temperature rise of each animal during the 3 hours observation period meet the acceptable USP limits.

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

9. Deviation

There was no deviation during the study.

10. Records

All raw data pertaining to this study and a copy of final report are retained in designated Mid-Link's archive files in accordance with Mid-Link SOP.

STATEMENT OF QUALITY ASSURANCE ACTIVITIES

Phase Inspected	Date Inspected
Extraction	09/26/2019
Study Data Review	09/30/2019
Final Report Review	10/12/2019

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). Results are included in the Periodic Status Report to Management and Study Director.

QA Representative _____ 11/12/2019
Authorized Signature Date

Attachment 1: Results

Animal Number		#1 A057	#2 A216	#3 A078
Sex		Female	Female	Female
Weight (kg)		2.58	2.59	2.62
Dose Volume (ml)		25.8	25.9	26.2
Temperature (℃)	Before Injection			
	Control 1	39.4	39.6	39.7
	Baseline	39.2	39.5	39.6
	After Injection			
	1.0 Hour	39.6	39.2	39.5
	1.5 Hours	39.5	39.4	39.6
	2.0 Hours	39.5	39.3	39.6
	2.5 Hours	39.4	39.1	39.6
	3.0 Hours	39.4	38.9	39.6
	Maximum Rise	0.4	0.0	0.0

Attachment 2: Illustration of Test Article