Test Report

TEST ITEMS

Test for skin sensitization (Maximization test)

TEST ARTICLE

Non-absorbable Surgical Suture (model: PTFE)
<Specification: Z21302-60 (USP2-0/EP2.5)>

IDENTIFICATION №

150642

MANUFACTURER

Foosin Medical Supplies Inc., Ltd.

SPONSOR

TÜV SÜD Certification and Testing (China) Co., Ltd.
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SUMMARY

A guinea pig maximization test of the test article, Non-absorbable Surgical Suture (model: PTFE), was conducted to evaluate the skin sensitizing potential. This study was based on the International Organization for Standardization ISO 10993-10:2010: Biological evaluation of medical devices Part 10: Tests for irritation and skin sensitization; ISO 10993-12:2012: Biological evaluation of medical devices Part 12: Sample preparation and reference materials.

30 healthy young adult albino guinea pigs with body weight range from 300.1 g to 369.4 g were utilized. The test article was extracted in 0.9% sodium chloride injection (SC) and cotton seed oil (CSO) respectively. The test included intradermal induction phase, topical induction phase and challenge phase. In these phase, each extract was injected intradermally and patched occlusively to ten test guinea pigs (per extract) in an attempt to induce sensitization. The vehicle was similarly injected and patched occlusively to five reagent control guinea pigs (per vehicle). Following a recovery period, the test and reagent control animals were received a challenge patch of the appropriated test article extract and the reagent control. All sites were scored and the skin reactions for erythema and swelling were described and graded from 0-3 scale at 24h and 48h after patch removal. If the grades of less than 1 are seen in reagent control animals, grades of 1 or greater in the test group were generally indicated sensitization.

Under the conditions of this study, at 24h and 48h after the challenge phase, the skin sites of the test and reagent control animals had no visible changes. It can be concluded that neither SC extracts nor CSO extracts of the test article had evidence of causing sensitization in the guinea pig.

Study and Supervisory

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SUN Jiao, Ph.D. Date Completed

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INTRODUCTION

A guinea pig maximization study of the test article identified below was conducted to evaluate the potential to cause contact sensitization. This test was conducted based on the requirements of ISO 10993-10:2010: Biological evaluation of medical devices Part 10: Tests for irritation and skin sensitization. The test article was received on Jun. 16, 2015. Treatment began on Sep. 22, 2015, and the final observations were concluded on Oct. 20, 2015.

This study, initiated by protocol signature on Aug. 11, 2015, was completed in the Lab of Shanghai Biomaterials Research & Test Center (SBRTC) and was conducted in accordance with the provisions of the ISO/IEC 17025-2005.

MATERIALS

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

Test Article:	Non-absorbable Surgical Suture (model: PTFE) <Specification: Z21302-60 (USP2-0/EP2.5)>
Identification No:	150642
Sterilization Status:	Sterilized
Temperature Tolerance:	-25~+55℃(declaration from the sponsor)
Extraction Vehicle:	0.9% sodium chloride injection (SC) <K15062018> Cotton seed oil (CSO) <MKBS9702V>
Test Article Preparation:	Based on the ISO ratio of 6cm^2/ml [Surface area of the test sample to volume of extraction vehicle], 91.3cm^2 of the test samples were covered 15.2 ml of extraction vehicle under sterile conditions for preparing the SC or CSO test extract at 37℃ for 72 hours respectively in each phase. The extracts were used within 1 hour after extraction.
Reagent Control:	The vehicles (without test article) were similarly prepared to serve as the reagent control.
Condition of extracts:	All the extracts of the test and control were clear.
Additional materials:	Freund's Complete Adjuvant (FCA) was mixed 50:50 (v/v) with the vehicle. A 10% (w/w) sodium dodecyl sulfate suspension in paraffin.

In addition according ISO 10993-10 requirement, 5% mercaptobenzothiazole (dissolved in DMSO) as a positive control was used previously for another study last month. See the appendix Ⅰ. Complete data is traceable in laboratory records.

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METHODS

Test System:

Species:	Albino guinea pig
Source:	SHANGHAI SONGLIAN LAB ANIMAL-FEILD
Sex:	Male
Body Weight Range:	300.1 g to 369.4 g
Age:	Young adult
Number of animals:	Thirty

Animal Management:

Husbandry:	Conditions conformed to "Laboratory animal-Requirements of environment and housing facilities"; "ISO 10993-2:2006: Biological evaluation of medical devices Part 2: Animal welfare requirements".
Food:	Diet was provided from SHANGHAI SLAC LABORATORY ANIMAL CO. LTD.
Housing:	Healthy animals were acclimatized to the laboratory conditions for 5 days before the treatment, and then they were randomized and assigned to groups in stainless steel suspended cages identified by a card indicating the Identification № of the test article and first treatment date.
Environmental:	The room temperature and humidity were monitored daily. The room temperature range was from 22℃ to 25℃. The room humidity range was from 57 % to 62 %.
Personnel:	Associates involved were appropriately qualified and trained.
Selection:	Only healthy, unused animals were selected.

Experimental Procedure:

1. Intradermal induction phase (Induction I):

The day prior to treatment, the fur was clipped on all treatment sites with an electric clipper. The 1st day, the test animals were injected with the fresh extracts of test article and the reagent control animals were injected with the reagent control. Three rows of intradermal injections (two per row) were given to each animal within an approximate 2cm×4cm boundary of the fur clipped area as illustrated below:

Cranial

a	a
b	b
c	c

Caudal

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Test Animals:

a) 0.1ml of 50:50(v/v) mixture of FCA and the chosen vehicle

b) 0.1ml of test extract

c) 0.1ml of 50:50(v/v) mixture of a and b

Reagent Control Animals:

a) 0.1ml of 50:50(v/v) mixture of FCA and the vehicle

b) 0.1ml of vehicle

c) 0.1ml of 50:50(v/v) mixture of a and b

2. Topical induction phase (Induction II):

At 7th day after completion of the intradermal induction phase, the same area was clipped free of fur and treat with 10% sodium dodecyl sulfate suspension in paraffin. The suspension was massaged into the skin over the injection site to provoke a mild acute inflammation. The area was left uncovered.

At 8th day, a 20mm×40mm section of absorbent gauze patch, saturated with freshly prepared the extract of the test article, and then was topically applied to the previously injected sites of the test animals. The reagent control animals were similarly patched with the appropriate reagent control. Each patch was secured with an occlusive dressing. The dressings and patches were removed after 48h.

3. Challenge phase

At 22nd day, the fur was clipped and shaved from the left flank areas. At 23rd day, absorbent gauze patches were soaked with the corresponding solution at the concentration of site C, and patched on the left upper flank of each animal in test and reagent control group. Then the animals were secured with an occlusive dressing. The dressings and patches were removed after 24h.

4. Observation of animals

The appearance of the challenge skin sites of the test and reagent control animals was observed respectively at 24h and 48h after removal of the dressing. The skin reactions for erythema and swelling were described and graded in according with the criteria shown below:

Patch test reaction	Grading scale
No visible change	0
Discrete or patchy erythema	1
Moderate and confluent erythema	2
Intense erythema and swelling	3

If the grades of less than 1 are seen in reagent control animals, grades of 1 or greater in the test group were generally indicated sensitization.

DEVIATIONS

There were no deviations from the ISO 10993-10:2010 and SBRTC-PROTOCOL-2-261.

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RESULTS

Clinical Observation:

All animals appeared clinically normal throughout the study. Individual body weights and clinical observations was given in APPENDIX II.

Dermal Observations:

No evidence of sensitization was observed. Individual results of dermal scoring for the challenge phase were shown as below. The detail data was given in the APPENDIX III.

	Hours following patch removal			
Time	24h		48h	
Vehicle	SC	CSO	SC	CSO
Test article	0	0	0	0
Reagent Control	0	0	0	0

The result showed the skin sites of the test and reagent control animals had no visible changes at 24h and 48h after the challenge phase.

Results and conclusions apply only to the test article tested. No further evaluation of these results is made by Shanghai Biomaterials Research & Test Center.

CONCLUSION

Under the conditions of this study, neither SC extracts nor CSO extracts of the test article had evidence of causing sensitization in the guinea pig.

RECORD STORAGE

All raw data pertaining to this study and a copy of the final report are to be stored in the designated archive files at Shanghai Biomaterials Research & Test Center.

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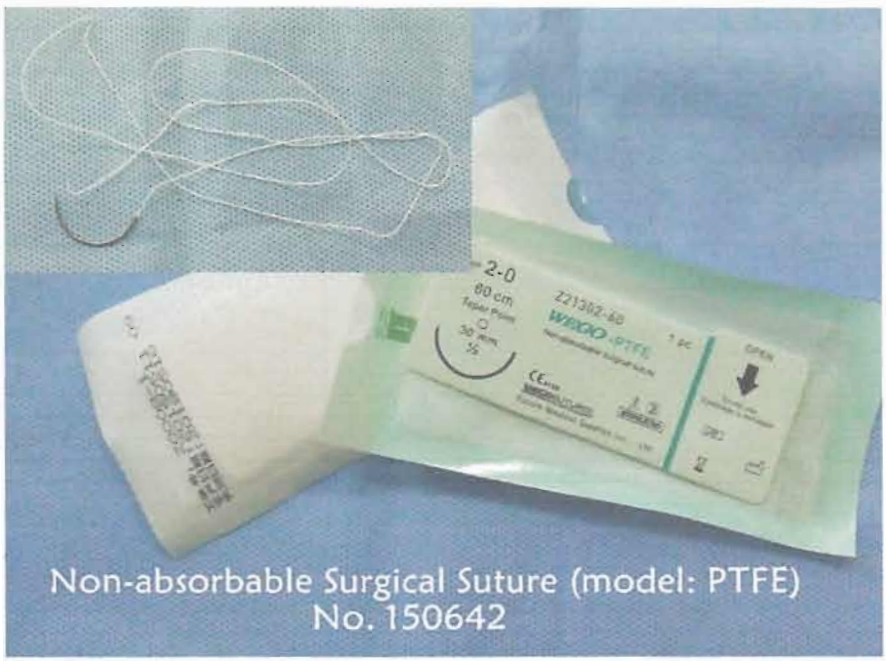
PHOTOGRAPH OF THE TEST ARTICLE



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APPENDIX I

The result of controls in the guinea pig from the historical data in our center was showed as below:

Date: 2015.8.20~2015.9.14	Hours following patch removal (Hours)		
	Positive Control: 5% mercaptobenzothiazole		
Animal №	Pretreatment Body Weight (g)	24	48
1	342.3	2	3
2	361.2	2	3
3	342.9	3	3
4	330.8	3	3
5	351.4	2	2
	Negative Control: SC		
Animal №	Pretreatment Body Weight (g)	24	48
1	319.5	0	0
2	328.4	0	0
3	351.0	0	0
4	358.4	0	0
5	347.9	0	0
	Negative Control: CSO		
Animal №	Pretreatment Body Weight (g)	24	48
1	322.1	0	0
2	310.5	0	0
3	312.5	0	0
4	355.9	0	0
5	340.1	0	0

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APPENDIX II

Individual body weights and clinical observations were given as below:

SC GROUP Individual Observation			CSO GROUP Individual Observation		
Animal Number	Pretreatment Body Weight (g)	Clinical Observations	Animal Number	Pretreatment Body Weight (g)	Clinical Observations
1 Test	347.5	Appeared normal	1 Test	362.1	Appeared normal
2 Test	348.2	Appeared normal	2 Test	364.7	Appeared normal
3 Test	362.4	Appeared normal	3 Test	369.4	Appeared normal
4 Test	357.2	Appeared normal	4 Test	343.4	Appeared normal
5 Test	338.0	Appeared normal	5 Test	342.0	Appeared normal
6 Test	342.6	Appeared normal	6 Test	349.3	Appeared normal
7 Test	319.7	Appeared normal	7 Test	357.2	Appeared normal
8 Test	306.9	Appeared normal	8 Test	355.4	Appeared normal
9 Test	348.2	Appeared normal	9 Test	362.1	Appeared normal
10 Test	349.7	Appeared normal	10 Test	364.9	Appeared normal
1 Control	304.2	Appeared normal	1 Control	327.6	Appeared normal
2 Control	300.1	Appeared normal	2 Control	322.4	Appeared normal
3 Control	350.9	Appeared normal	3 Control	318.9	Appeared normal
4 Control	348.2	Appeared normal	4 Control	320.0	Appeared normal
5 Control	333.3	Appeared normal	5 Control	315.2	Appeared normal

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APPENDIX III

Dermal observations were given as below:

SC GROUP Interval (hours)			CSO GROUP Interval (hours)		
Animal Number	24	48	Animal Number	24	48
1 Test	0	0	1 Test	0	0
2 Test	0	0	2 Test	0	0
3 Test	0	0	3 Test	0	0
4 Test	0	0	4 Test	0	0
5 Test	0	0	5 Test	0	0
6 Test	0	0	6 Test	0	0
7 Test	0	0	7 Test	0	0
8 Test	0	0	8 Test	0	0
9 Test	0	0	9 Test	0	0
10 Test	0	0	10 Test	0	0
1 Control	0	0	1 Control	0	0
2 Control	0	0	2 Control	0	0
3 Control	0	0	3 Control	0	0
4 Control	0	0	4 Control	0	0
5 Control	0	0	5 Control	0	0

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