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Test Report

TEST ITEMS

Test for skin sensitization (Maximization test)

TEST ARTICLE

silicone rubber
<Specification: ZT-9773; LOT: 202305150451>

IDENTIFICATION №

230554

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SUMMARY

A guinea pig maximization test of the test article, **silicone rubber**, was conducted to evaluate the skin sensitizing potential. This study was based on the International Organization for Standardization ISO 10993-10:2021 Biological evaluation of medical devices Part 10: Tests for skin sensitization; ISO 10993-12:2021 Biological evaluation of medical devices Part 12: Sample preparation and reference materials.

The test sample was extracted in 0.9% sodium chloride injection (SC) and cotton seed oil (CSO). 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 sample extract and the reagent control. All sites were scored at 24h and 48h after patch removal.

Under the conditions of this study, the SC and CSO extracts of the test samples showed no evidence of causing sensitization in the guinea pigs.

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Aug 24. 2023 — Date Completed

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 10993-10:2021 Biological evaluation of medical devices Part 10: Tests for skin sensitization. The test article was received on May 24, 2023. Treatment began on Jul. 11, 2023, and the final observations were concluded on Aug.8, 2023.

This study was completed in the lab of Shanghai Biomaterials Research & Test Center (SBRTC). SBRTC was conducted in accordance with the provisions of the ISO/IEC 17025: 2017.

MATERIALS

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

Test Article:	silicone rubber <Specification: ZT-9773; LOT: 202305150451>
Identification №:	230554
Sterilization Status:	Non STERILE
Storage Conditions:	Room Temperature
Extraction Vehicles:	0.9% Sodium Chloride Injection (SC) Cotton seed oil (CSO)
Test Extract Preparation:	According to the requirement of the sponsor, the test sample was sterilized at 121℃ for 30min (110KPa) before testing. Based on the ISO 10993-12: 2021, the ratio of $3cm^2/ml$ [Surface area of the test sample to volume of extraction vehicle], $45cm^2$ of the test samples (Sampling randomly according to the statement of the sponsor) were cut and covered with 15ml of extraction vehicles separately to enhance submersion in the extract medias under aseptic conditions for preparing the SC and CSO test extracts at 37℃ for 72h respectively with continuously agitation during extraction. The extracts were used after extraction. The extracts were freshly prepared for 3 times in the process of the whole experiment.
Reagent Controls:	Two extraction vehicles without the test sample were similarly prepared respectively.
Condition of Extracts:	All the extracts of the test samples and controls were clear, no suspended particulates and without any special treatments.
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 to the requirement of ISO 10993-10:2021, 5% mercaptobenzothiazole (dissolved in DMSO) as a positive control was used previously for another study last month. The method used in the positive control group was the same as the negative control group and test group. Complete data was traceable in laboratory records.

METHODS

Test System:

Species:	Albino guinea pig
Source:	Shanghai Jiagan Biotechnology Corporation
Sex:	Half males and half females (females were nulliparous and nonpregnant)
Body Weight Range:	309.5 g to 325.4 g
Age:	Young adult
Number of animals:	Thirty

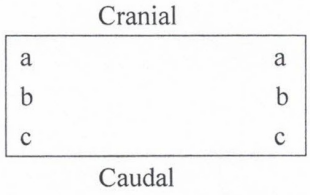
Animal Management:

Husbandry:	Conditions conformed to "Laboratory animal-Requirements of environment and housing facilities"; "ISO 10993-2:2022: Biological evaluation of medical devices Part 2: Animal welfare requirements".
Food:	Diet was provided from DOUBLE LION EXPERIMENTAL ANIMAL FEED TECHNOLOGY 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 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 20℃ to 26℃. The room humidity range was from 50% to 70 %.
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 sample and the 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:



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

Control Animals:

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

Positive Control Animals:

a) 0.1ml of 50:50(v/v) mixture of FCA and the vehicle
b) 5% mercaptobenzothiazole (dissolved in DMSO)
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 the freshly prepared corresponding solution at the concentration of site b, and then was topically applied to the previously injected sites of the test animals. The 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 b, 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 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.

RESULTS

Clinical Observation:

All animals appeared clinically normal throughout the study.

Dermal Observations:

No evidence of sensitization was observed. Individual results of dermal scoring for the challenge phase shown below:

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

CONCLUSION

Under the conditions of this study, the SC and CSO extracts of the test samples showed no evidence of causing sensitization in the guinea pigs.

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

RECORD STORAGE

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

PHOTOGRAPH OF THE TEST ARTICLE

