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Test Report

Report Number: SSMT-R-2020-03009-03B

Sample Name: Menstrual cup

Study Title: Skin Sensitization Test

Standard: GB/T 16886.10-2017

ISO 10993-10:2010

Test facility

Jiangsu Science Standard Medical Testing Co., Ltd.

C4 Building, No.9 Changyang Road, Wujin District, Changzhou, Jiangsu, China

Sponsor

Xi'an Furuize Biotechnology Co., Ltd.

Room 11131, Building 3, i Duhui, No.11, Tangyan South Road, Zhangba Street Office, High-tech Zone, Xi'an City, Shaanxi, China.

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Explanation

1. Please apply for rechecking within 15 days of receiving the report if there is any objection.
2. Any erasure or without special testing seal renders the report null and void.
3. The report is only valid when signed by the persons who edited, checked and approved it.
4. The result relate only to the articles tested.
5. The report shall not be reproduced except in full without the written approval of the institute.
6. This experiment was carried out in the sub-site and the address is: No. 68, Yaoluo Road, Wujin District, Changzhou City.

Conclusion

The extract of the test article was evaluated for its potential skin sensitization in the Guinea Pig Maximization Test.

The test articles were extracted with 0.9% sodium chloride injection and sesame oil respectively. The test article extract was intradermally injected into guinea pigs and applied topically for induction. Control animals were treated accordingly but with the solvent alone.

The topical challenge with the test article elicited no skin reaction in the test or the control animals. The skin sensitization rates of polar and non-polar group were both determined with 0%.

Study verification and signature

The study was carried out in accordance with the standard operating procedure. The test process was conducted in compliance with the requirements of CNAS-CL01:2018 (ISO/IEC17025:2017, IDT) and RB/T214-2017.

Date Received	2020-10-15
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Edited by Molly Liu 2020.11.19
Date

Checked by Suri Han 2020.11.19
Date

Approved by Daisy Zhang 2020.11.20
Authorized signatory Date

Jiangsu Science Standard Medical Testing Co., Ltd.

1.0 Purpose

The test was designed to evaluate the potential of a test article to cause skin sensitization using Guinea Pig Maximization Test.

2.0 Reference

Biological evaluation of medical devices-Part 10:Tests for irritation and skin sensitization(GB/T 16886.10-2017)

Biological evaluation of medical devices-Part 12:Sample preparation and reference materials(GB/T 16886.12-2017)

Biological evaluation of medical devices-Part 2: Animal welfare requirements (GB/T 16886.2-2011)

Biological evaluation of medical devices-Part 10:Tests for irritation and skin sensitization(ISO 10993-10:2010)

Biological evaluation of medical devices-Part 12:Sample preparation and reference materials(ISO 10993-12:2012)

Biological evaluation of medical devices-Part 2: Animal welfare requirements (ISO 10993-2:2006)

3.0 Test and control articles

3.1 Test article (The information about the test article was supplied by the sponsor wherever applicable.)

Test article name: Menstrual cup

Sterilization state: Unsterilized

Model/Size: N/S

Lot/ Batch#: N/S

Physical State: Solid

Color: See the photo

Density: N/S

Stability: N/S

Solubility: N/S

Test Article Material: Silica gel

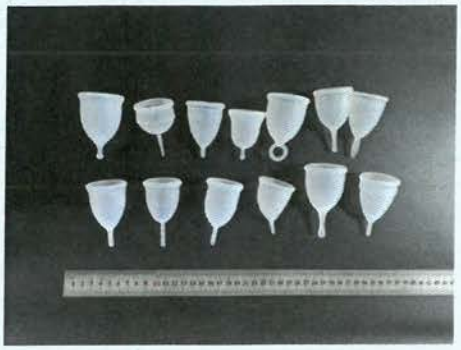
Packing Material: N/S

Storage Condition: Room temperature

Manufacturer: Xi'an Furuize Biotechnology Co., Ltd.

Manufacturer address: Room 11131, Building 3, i Duhui, No.11, Tangyan South Road, Zhangba Street Office, High-tech Zone, Xi' an City, Shaanxi, China.

Sample photograph:



3.2 Control Articles

3.2.1 Polar Negative Control

Name: 0.9% Sodium chloride injection (SC)

Manufacturer: Chenxin Pharmaceutical Co., Ltd.

Size: 250 ml

Physical State: Liquid

Color: Colourless

Lot/ Batch#: 1906112830

Storage Condition: Room Temperature

3.2.2 Non-polar Negative Control

Name: Sesame Oil (SO)

Manufacturer: Ji'an Ivyuanxiangliao. Co., Ltd.

Size: 20 kg

Physical State: Liquid

Color: Pale yellow

Lot/ Batch#: 20190516

Storage Condition: Room Temperature

4.0 Identification of test system

Species: Hartley Guinea Pig (Cavia Porcellus)

Number: 15 for polar group and 15 for non-polar group (10 for test and 5 for control in each group)

Sex: Male

Health status: Healthy, not previously used in other experimental procedures

Housing: Animals were housed in groups in cages identified by a card indicating the lab number and test code.

Animal identification: Stain with picric acid

The quarantine period: 5 days

5.0 Animal Care and Maintenance

Animal purchase: Provided by Suzhou Genesc Biotechnolongy Co .,Ltd <Permit Code: SCXK (SU) 2020-0001>

Bedding: NA

Feed: Guinea Pig Diet, Beijing Keao Xieli Feed Co., Ltd.

Water: Drinking water met the Standards for Drinking Water Quality GB 5749-2006

Cages: Plastic cage, Suzhou Fengqiao purification equipment Co.,Ltd.

Environment: Temperature 18-29℃, Relative humidity 40%-70%, Lights 12 hours light/dark cycle

Personnel: Associates involved were appropriately qualified and trained

Selection: Only healthy, previously unused animals were selected

Veterinarian: Vet takes care of the whole course

Ethics: Test methods of operation were reviewed and approved by the Commission on Science Standard animal ethics

There were no known contaminants present in the feed, water, or bedding expected to interfere with the test data.

6.0 Justification of the test system

6.1 The guinea pig is believed to be the most sensitive animal model for this type of study. The susceptibility of the guinea pig to a known sensitizing agent, dinitrochlorobenzene (DNCB) has been substantiated at SSMT. The skin sensitized positive control test is conducted every six months. The last allergenic rate is 100%. The data was from the report SSMT-R-2020-00198-03 (Date: 2020-09-27) .

6.2 The test article was extracted and administered in vivo through a medium compatible with the test system, which is considered as the best route of administration.

7.0 Instruments and reagents

7.1 Instruments

Digital oscillation incubator (SSMT-300)

Electronic balance (SSMT-075)

Electronic balance (SSMT-147)

Clean bench (SSMT-187)

7.2 Reagents

Sodium dodecyl sulfate (SDS)

Freund's Adjuvant, Complete liquid

8.0 Experiment design and dose

8.1 Sample preparation

The test article was extracted as Table 1. Extract was checked and used immediately after extraction without the process of filtering, centrifugation, dilution, etc. The pH of the extract was not adjusted prior to testing. The preparation process was aseptic. The control article was prepared under the same condition.

Table 1 Sample Preparation

Aseptic Sampling			Aseptic Agitation Extraction In Inert Container				Final Extract
Sampling Manner	Test phase	Actually Sampling	Extraction solvent	Extraction ratio	Solvent volume	Condition	Clear or Not
Take the whole. One test sample was used in every test phase.	Intradermal induction phase I	14.18 g	0.9% sodium chloride injection	0.2 g : 1 ml	70.9 ml	50 ℃, 72 h	Clear
	Topical induction phase II	12.13 g			60.6 ml	50 ℃, 72 h	Clear
	Challenge phase	16.90 g			84.5 ml	50 ℃, 72 h	Clear
	Intradermal induction phase I	9.60 g	Sesame oil	0.2 g : 1 ml	48.0 ml	50 ℃, 72 h	Clear
	Topical induction phase II	10.88 g			54.4 ml	50 ℃, 72 h	Clear
	Challenge phase	17.07 g			85.3 ml	50 ℃, 72 h	Clear

8.2 Test method

8.2.1 Intradermal induction phase I

A pair of 0.1 ml intradermal injections was made for each animal, at the sites (A, B and C) in the clipped intrascapular region as shown in the following Figure 1.

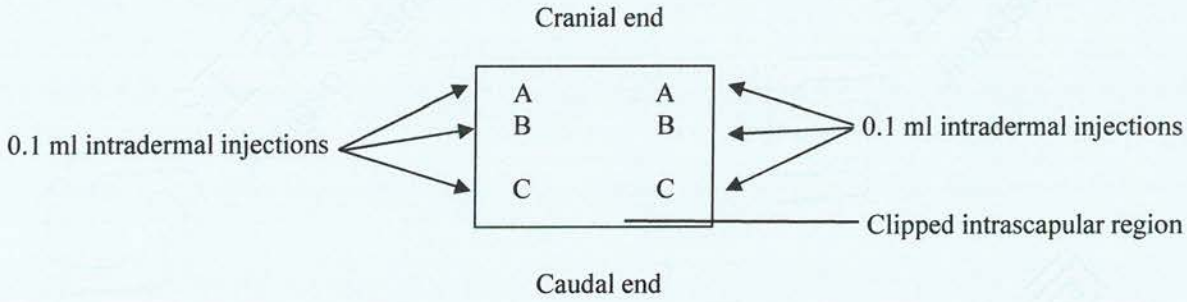


Figure 1 Location of intradermal injection sites

Site A: A 50:50 volume ratio stable emulsion of Freund's complete adjuvant mixed with the solvent.

Site B: The test sample (undiluted extract); inject the control animals with the control articles alone.

Site C: The test sample at the concentration used at site B, emulsified in a 50:50 volume ratio stable emulsion of Freund's complete adjuvant and the solvent (50%); inject the control animals with an emulsion of the blank liquid with adjuvant.

8.2.2 Topical induction phase II

At 6 d after completion of the intradermal induction phase, administer the test sample by topical application to the intrascapular region of each animal, using a patch of area approximately 8 cm^2 (absorbent gauze) soaked with 0.5 ml extract, so as to cover the intradermal injection sites. Use the concentration selected in the intradermal induction phase for site B. If the maximum concentration that can be achieved in Intradermal induction phase I did not produce irritation, animals were pretreated with 10% sodium dodecyl sulfate 24 hours before the topical induction application. Secure the patches with an occlusive dressing. Remove the dressings and patches after 48 h.

Treat the control animals similarly, using the blank liquid alone.

8.2.3 Challenge phase

At 13 d after completion of the topical induction phase, challenge all test and control animals with the test sample. Administer the test sample and a blank by topical application to left and right abdomen of animals respectively, using absorbent gauze (about 8 cm^2) soaked with 0.5ml extracts or solvent control. Secure with an occlusive dressing. Remove the dressings and patches after 24 h.

8.3 Observation of animal

Observe the appearance of the challenge skin sites of the test and control animals 24 h and 48 h after removal of the dressings. Full-spectrum lighting was used to visualize the skin reactions. Describe and grade the skin reactions for erythema and oedema according to the Magnusson and Kligman grading given in Table 2 for each challenge site and at each time interval.

Table 2 Magnusson and Kligman scale

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

9.0 Evaluation criteria

Magnusson and Kligman grades of 1 or greater in the test group generally indicate sensitization, provided grades of less than 1 are seen in control animals.

If grades of 1 or greater are noted in control animals, then the reactions of test animals which exceed the most severe reaction in control animals are presumed to be due to sensitization.

If the response is equivocal, rechallenge is recommended to confirm the results from the first challenge.

10.0 Results of the test

The skin response of guinea pigs and body weight change are shown in Table 3.

Table 3 Guinea pig Sensitization Dermal Reactions

Extraction solvent	Group	Animal Number	Excitation patch removed 24 h	Excitation patch removed 48 h	Positive rate after challenge phase	Weight range before injection (g)	Weight range after experiment (g)	Abnormal appearance except dermal reactions
0.9% sodium chloride injection	Control	J1001	0	0	0%	315.4-349.2	462.9-485.4	None
		J1002	0	0				None
		J1003	0	0				None
		J1004	0	0				None
		J1005	0	0				None
	Test	J2001	0	0	0%	310.2-365.1	465.6-528.4	None
		J2002	0	0				None
		J2003	0	0				None
		J2004	0	0				None

		J2005	0	0				None
		J2006	0	0				None
		J2007	0	0				None
		J2008	0	0				None
		J2009	0	0				None
		J2010	0	0				None
Sesame oil	Control	F1001	0	0	0%	309.1-349.2	451.2-490.8	None
		F1002	0	0				None
		F1003	0	0				None
		F1004	0	0				None
		F1005	0	0				None
	Test	F2001	0	0	0%	314.9-373.6	465.4-526.2	None
		F2002	0	0				None
		F2003	0	0				None
		F2004	0	0				None
		F2005	0	0				None
		F2006	0	0				None
		F2007	0	0				None
		F2008	0	0				None
		F2009	0	0				None
		F2010	0	0				None

Under the condition of this study, the test article did not show significant evidence of causing skin sensitization in the guinea pigs. The skin sensitization rates of polar and non-polar test group were both determined with 0%.

11.0 Deviation statement

There was no deviation from the standard operating procedure which were judged to have any impact on the validity of the data.

12.0 Record

All the original data and records related to this test and copies of the final report are retained in the archives of Science Standard Medical Testing.

13.0 Confidentiality agreement

Statements of confidentiality were as agreed upon prior to study initiation.