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CNAS L10066

Test Report

Report Number: SSMT-R-2022-04964-02B

Sample Name: PLA

Study Title: Skin Sensitization Test - 0.9% Sodium Chloride Injection Extract

Standard: ISO 10993-10:2021

Test facility

Jiangsu Science Standard Medical Testing Co., Ltd.

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

Sponsor

Shenzhen Esun Industrial Co.,Ltd.

Wuhan University Building A403-I and A901, No.6 Yuexing 2 Road, Nanshan District, Shenzhen, China

Contents

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: E3 Building, No.9 Changyang Road, Wujin District, Changzhou, Jiangsu, China.

Conclusion

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

The test article were extracted with 0.9% sodium chloride injection. The test article extract was intradermally injected and applied topically for induction to ten guinea pigs. Five control animals were treated accordingly but with the solvent alone.

The topical challenge with the extract of test article elicited no skin reaction in the test and the control animals. The skin sensitization rate was 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	2022-08-24
Technical Initiation Date	2022-09-02
Technical Completion Date	2022-10-02
Final Report Completion Date	2022-10-08

Edited by Alex tang 2022.10.08
Date

Checked by Molly Liu 2022.10.08
Date

Approved by Daisy Zhang 2022.10.17
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 skin sensitization(ISO 10993-10:2021)

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: PLA

Initial State: Non-sterile

Model: N/S

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: N/S

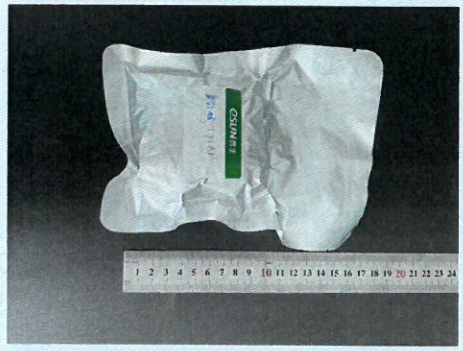
Packing Material: N/S

Storage Condition: Room temperature

Manufacturer: Shenzhen eSunMed Biotechnology Co.,Ltd.

Manufacturer Address: Floor 3, No. 9, Yifenghua Innovation Industrial Park, Xinshi community, Dalang Street, Longhua district, Shenzhen City

Sample photograph:



3.2 Control Article

Name: 0.9% Sodium chloride injection (SC)

Manufacturer: Anhui Shuanghe Pharmaceutical Co. , Ltd .

Size: 500 ml

Physical State: Liquid

Color: Colourless

Lot/ Batch#: 200714 2C

Storage Condition: Room Temperature

4.0 Identification of test system

Species: White guinea pig

Number: 15 (10 for test group and 5 for control group)

Sex: Males

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: Animal marker pen

The quarantine period: 3 days

5.0 Animal Care and Maintenance

Animal purchase: Provided by Danyang Changyi experimental animal breeding Co., Ltd <Permit Code: SCXK (SU) 2021-0002>

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(Intradermal induction phase I: 0.1%; Topical induction phase II : 0.5%; Challenge phase: 0.1%).

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

Electronic balance (SSMT-494)

Electronic balance (SSMT-147)

Electronic balance (SSMT-532)

Thermostatic oscillation incubator (SSMT-564)

Clean bench (SSMT-501)

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
Random sampling	Intradermal induction phase I	2.33 g	0.9% sodium chloride injection	0.2 g : 1 ml	11.6 ml	37 °C, 72 h	Clear
	Topical induction phase II	2.37 g			11.8 ml	37 °C, 72 h	Clear
	Challenge phase	1.90 g			9.5 ml	37 °C, 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.

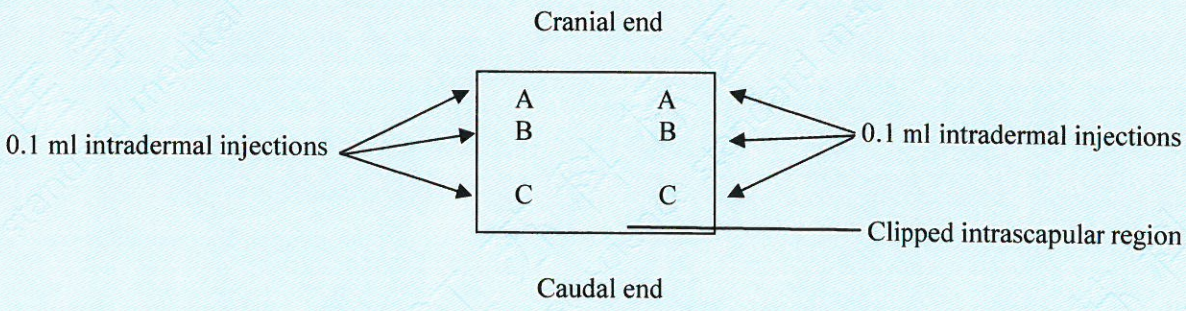


Figure 1 Location of intradermal injection sites

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 8 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 14 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 is shown in Table 3. The positive control test results are in shown Table 4.

Table 3 Guinea pig Sensitization Dermal Reactions

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
Control	2022-04964-02-J1001	0	0	0%	323.5-356.0	478.7-504.2	None
	2022-04964-02-J1002	0	0				None
	2022-04964-02-J1003	0	0				None
	2022-04964-02-J1004	0	0				None
	2022-04964-02-J1005	0	0				None
Test	2022-04964-02-J2001	0	0	0%	330.5-358.4	479.8-511.9	None
	2022-04964-02-J2002	0	0				None
	2022-04964-02-J2003	0	0				None
	2022-04964-02-J2004	0	0				None
	2022-04964-02-J2005	0	0				None
	2022-04964-02-J2006	0	0				None
	2022-04964-02-J2007	0	0				None
	2022-04964-02-J2008	0	0				None
	2022-04964-02-J2009	0	0				None
	2022-04964-02-J2010	0	0				None

Table 4 Results of positive control test

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
Control	X1001	0	0	0%	329.8-367.0	476.4-516.7	None
	X1002	0	0				None
	X1003	0	0				None
	X1004	0	0				None
	X1005	0	0				None
Test	X2001	3	2	100%	324.2-353.7	468.9-492.3	None
	X2002	3	3				None
	X2003	2	1				None
	X2004	3	2				None
	X2005	2	2				None

Note: The skin sensitized positive control test is conducted every three months. The data was from the report SSMT-R-2022-01071-05 (Complete Date: 2022.07.10) and the allergenic rate is 100%. (Intradermal induction phase I: 0.1%; Topical induction phase II : 0.5%; Challenge phase: 0.1%)

Under the conditions of this study, the test article did not show significant evidence of causing skin sensitization in the guinea pig. The skin sensitization rate was 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.