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CNAS L3940

Final Report

Skin sensitization test

Guinea pig maximization test with polar/non-polar extraction vehicle

B-S2025-090528E-103

Test sample: **Light-curing resin (surgical guides, trays)**

Sponsor:

Name: Shenzhen Zhongchuang Medical Group Co., Ltd

Address: Room 204, Administration Building, Jia Tai Pharmaceutical, No.1 Industrial Zone, Tangwei Community, Fuhai Street, Bao'an District, Shenzhen City

Manufacturer:

Name: Shenzhen Zhongchuang Medical Group Co., Ltd

Address: Room 204, Administration Building, Jia Tai Pharmaceutical, No. 1 Industrial Zone, Tangwei Community, Fuhai Street, Bao'an District, Shenzhen City

四川医疗器械生物材料和制品检查中心有限公司 检验专用章

Sichuan Testing Center for Biomaterials and Medical Devices Co., Ltd.

Supplementary Explanation

1. The report is invalid without the special inspection seal of inspection body and laboratory and the signature of the approving person.
2. The report that has been altered, added or deleted is invalid. The copies of the report without the special seal for inspection are invalid.
3. If there is any objection to the report, it shall be submitted to inspection body and laboratory in writing within 15 days from the date of receiving the report.
4. The data and conclusions in this report are the inspection results of the items tested in the sample.
5. The results and name of the institution of the report shall not be used for advertising, evaluation and commercial publicity without the written approval.

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Statement of Quality Assurance Activities

This study has been reviewed in accordance with the provisions of the ISO/IEC 17025:2017. 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 report results accurately reflect the raw data of the study.

Phase Inspected	Date inspected	Auditor	Date reported to Management
Test	2025-09-19	Tun Yuan	2025-09-19
Report generation	2025-10-20	Lifang Jia	2025-10-20

Wen Zou

QA Representative: Wen Zou

2025-11-07

Date:

1. Summary

A skin sensitization study was designed to assess the possible contact hazards from chemicals released that may cause skin sensitization. The study was conducted in accordance with the requirements of ISO 10993-10: 2021 Biological evaluation of medical devices Part 10: Tests for skin sensitization.

The test sample extract liquids, 0.9% sodium chloride injection, cottonseed oil were injected into intradermal of each animal at the injection sites for respective group. 6 days after the intradermal injection stage, the topical induction phase was carried out. 15 days after topical induction phase, challenge phase was performed on the upper flank unused sites of the animal.

For the test groups (polar and non-polar extraction vehicle), no visible change was observed on the skin of guinea pigs. The scales of dermal erythema of the animals were 0. The skin sensitization frequency for test groups was 0%.

For the vehicle control groups (polar and non-polar extraction vehicle), no visible change was observed on the skin of guinea pigs, the scales of dermal erythema of the guinea pig were 0. The skin sensitization frequency for vehicle control groups was 0%.

Under the conditions of this study, no visible change was observed in the test groups. The results showed that there was no skin sensitization response for the test sample extracts.

Study and Supervisory

Personnel: **Ming Yang**
Hua Zhang
Yi Wei
Qing Chang

Study supervisor: lifang Jia
Lifang Jia

Director: Jie Liang — 2025-11-07
Jie Liang — **Date Completed**

This report is authorized by signatures above.

Sichuan Testing Center for Biomaterials and Medical Devices Co., Ltd.

2. Introduction

2.1 Purpose

The test sample described below was evaluated for the potential to cause skin sensitization in the guinea pig.

2.2 Testing Guidelines

Biological evaluation of medical devices Part 10: Tests for skin sensitization. (ISO 10993-10: 2021)
Biological evaluation of medical devices Part 12: Sample preparation and reference materials. (ISO 10993-12: 2021)
Biological evaluation of medical devices part 2: Animal welfare requirements. (ISO 10993-2: 2022)

2.3 Dates

Test sample Received:	2025-09-15
Animal Purchased:	2025-09-16
Intradermal Injection:	2025-09-22
Testing Ended:	2025-10-16

3. Compliance

Sichuan Testing Center for Biomaterials and Medical Devices Co., Ltd. has been accredited by China National Accreditation Service for Conformity Assessment (CNAS L3940). Our inspection body and laboratory is also a testing institution licensed by the Sichuan Provincial Department of Science and Technology for the use of experimental animals（SYXK（川）2023-0017）.

4. Materials

4.1 Test sample

Test sample:	Light-curing resin (surgical guides, trays) (Fig.1)
Sample Serial No:	S2025-090528
Specification:	2.5*2.5*0.2cm/unit
Model:	transparent；blue
Batch:	/
Physical State:	See test sample image
Storage Condition:	Room temperature

The above test sample information is provided by the sponsor. The sponsor is responsible for all test sample characterization data.


S2025-090528

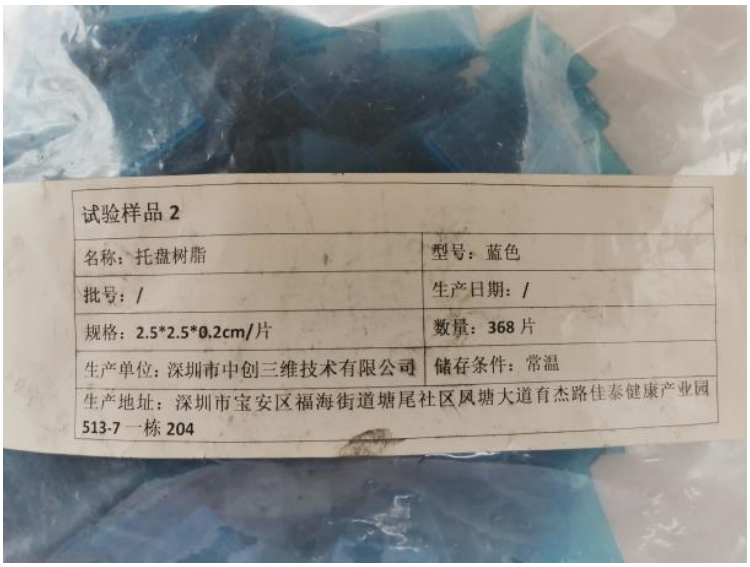
A


试验样品 1
名称：手术导板树脂
型号：透明
批号：/
生产日期：/
规格：2.5*2.5*0.2cm/片
数量：505 片
生产单位：深圳市中创三维技术有限公司
储存条件：常温
生产地址：深圳市宝安区福海街道塘尾社区凤塘大道育杰路佳泰健康产业园 513-7 一栋 204

B


S2025-090528

C



D

Fig.1. Photograph of the sample. A. The test sample for use 1; B. Sample label 1; C. The test sample for use 2; D. Sample label 2.

4.2 Polar extract vehicle

Name:	0.9% sodium chloride injection
Manufacturer:	Sichuan Medcalo pharmaceutical Ltd.
Model:	500mL
Batch:	24120313
Color:	Colorless
Physical State:	Liquid
Storage Conditions:	Room temperature

4.3 Non-polar extract vehicle

Name:	Cottonseed oil
Manufacturer:	Hebei J&K superfine materials Co., Ltd.
Model:	2.5L
Batch:	LI60Z03
CAS:	8001-29-4
Color:	Yellow
Physical State:	Liquid
Storage Conditions:	Room temperature.

5. Identification of test system

Species:	Guinea pig (Cavia parcellus).
Strain:	Dunkin-Hartely (Outbred).
Source:	Sichuan Vital River Laboratory Animal Technology Co., Ltd..
	Permit code: SCXK（川）2023-0040.
Body Weight Range:	317.7g-427.6g.
Selection:	Only healthy, previously unused and female nulliparous and not pregnant

	animals were selected.
Acclimation Period:	At least 7 days.
Number of Animals:	30.
Identification Method:	Label.
IACUC:	This procedure has been approved by the Sichuan Testing Center for Biomaterials and Medical Devices Co., Ltd. Institutional Animal Care and Use Committee, and is reviewed at least annually by the same committee.

6. Justification of test system

The guinea pig (Dunkin-Hartely) is widely used for tests for skin sensitization. The current ISO standards recommend guinea pig as test animals to evaluate skin sensitization of medical devices and biomaterials. Positive-control substance 2, 4-dinitrochlorobenzene (DNCB) is used in this laboratory and its reproducibility and sensitivity has been confirmed, see appendix for details.

7. Test system management

Husbandry:	Conditions conformed to the standard of ISO10993-2: 2022 Biological evaluation of medical devices part 2: Animal welfare requirements.
Feed:	Guinea pig diet. Pengzhou Kangda Feed Co., Ltd. Permit Code: 川（2019）01074.
Water:	Sufficient tap water was provided daily.
Contamination:	Reasonably expected contaminations in feeding stuffs or water supply did not have the potential to influence the outcome of this test.
Housing:	Animals were housed in groups in stainless steel suspended cages identified by a card, indicating the lab number, animal numbers, test code, sex, animal code, date and dosed.
Environmental:	The room temperature was monitored daily. The room temperature range for the guinea pig was 18℃-22℃. The room humidity was monitored daily. The humidity range for the guinea pig was 42%-51%. The light cycle was controlled using an automatic timer (12 hours light, 12 hours dark).
Personnel:	Associates involved were appropriately qualified and trained.

8. Test design

8.1 Sample Preparation

According to requirements of the sponsor, Sample 1 (transparent sample) and Sample 2 (blue sample) were used in a 1:1 ratio for the test. The total surface area of each sample (2.5cm × 2.5cm × 0.2cm) was 14.5 cm² by calculation.

Polar extraction:

Test Phase	Extraction Ratio	Amount	Volume of Vehicle	Extraction Condition
Intradermal induction		58cm^2	19.3mL	
Topical induction	3cm^2/mL	87cm^2	29mL	37℃, 72h, 60rpm
Challenge		87cm^2	29mL	

Non-polar extraction:

Test Phase	Extraction Ratio	Amount	Volume of Vehicle	Extraction Conditions
Intradermal induction	3cm²/mL	58cm²	19.3mL	37℃, 72h, 60rpm
Topical induction		87cm²	29mL	
Challenge		87cm²	29mL	

Vehicle control: The extract vehicle was prepared in the same way.

The condition of extracts:

Test phase	Vehicle	Extract	Condition of Extracts		
			Color	Clarity	Particulates
Intradermal induction	Polar	Test	Colorless	Clear	None
		Vehicle control	Colorless	Clear	None
	Non-polar	Test	Yellow	Clear	None
		Vehicle control	Yellow	Clear	None
Topical induction	Polar	Test	Colorless	Clear	None
		Vehicle control	Colorless	Clear	None
	Non-polar	Test	Yellow	Clear	None
		Vehicle control	Yellow	Clear	None
Challenge	Polar	Test	Colorless	Clear	None
		Vehicle control	Colorless	Clear	None
	Non-polar	Test	Yellow	Clear	None
		Vehicle control	Yellow	Clear	None

The extracts were tested immediately following extraction. The extracts were not centrifuged, filtered, or otherwise altered prior to using.

8.2 Test Procedure

8.2.1 Intradermal induction phase

Make a pair of 0.1mL intradermal injections of each of the following, into each animal, at the injection sites (A, B and C), as shown in Fig. 2, in the clipped intrascapular region.

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

Site B: The test sample (undiluted extract); inject the control animals with the extraction vehicle 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 extraction vehicle; inject the control animals with an emulsion of the vehicle control with adjuvant.

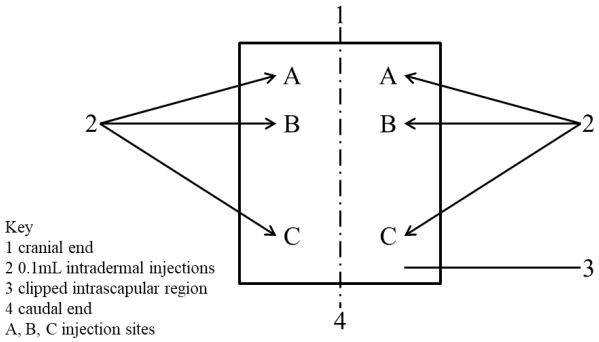


Fig.2. Location of intradermal injection sites.

8.2.2 Topical induction phase

6 days after intradermal induction phase, a 9cm^2 patch (absorbent pad) saturated in the test sample was applied to cover the intradermal injection sites. If the maximum concentration that could be achieved in 8.2.1 did not produce irritation, pretreat the area with 10 % sodium dodecyl sulfate (SDS) massaged into the skin 24h±2h before the patch was applied. Any remaining SDS should be removed prior to application of the patches for the topical induction phase. Secure the patches with an occlusive dressing. Remove the dressings and patches after 48h ±2h.
Treat the control animals similarly, using the vehicle control alone.

8.2.3 Challenge phase

15 days after completion of the topical induction phase. The extracts should be administered by topical application to shaved sites that were not treated during the induction stage, such as the upper flank of each animal, using appropriate patches soaked in the test sample at the concentration selected in 8.2.1 for site B.
Control animals shall be dosed with undiluted vehicle.
All wraps and patches were removed after 24h±2h.

8.2.4 Observation of animal

Observe the appearance of the challenge skin sites of the test and control animals 24h±2h and 48h±2h after removal of the dressings. Describe and grade the skin reactions for erythema and oedema according to the Magnusson and Kligman grading scale given in Tab.1 for each challenge site and at each time interval.

Tab.1. 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. Evaluation of results

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. A rechallenge shall be carried out 1 week to 2 weeks after the first challenge. The outcome of the test is presented as the frequency of positive challenge results in test and control animals.

10. Results

The scale of the animals for three groups was showed in Tab.2.
For the test sample group (polar extract), no visible change was observed on the skin of guinea pigs. The scales of dermal erythema of the guinea pig were 0 (Fig.3, A).
For the vehicle control group (polar extraction vehicle), no visible change was observed on the skin of guinea pigs. The scales of dermal erythema of the guinea pig were 0 (Fig.3, B).
For the test sample group (non-polar extract), no visible change was observed on the skin of guinea pigs. The scales of dermal erythema of the guinea pig were 0 (Fig.4, A).
For the vehicle control group (non-polar extraction vehicle), no visible change was observed on the skin of guinea pigs. The scales of dermal erythema of the guinea pig were 0 (Fig.4, B).

Results apply only to the test sample tested. No further evaluation of these results is made by. Any extrapolation of these data to other samples is the responsibility of the sponsor.

11. Conclusion

Under the conditions of this study, there was no skin sensitization response for the test sample extracts.

12. Quality assurance

The study has been performed according to standard operating procedures and standard protocols. Inspections were conducted at intervals adequate to assure the integrity of the study in compliance with ISO/IEC 17025:2017 General requirements for the competence of testing and calibration laboratories. The final report was reviewed for conformance to the section 7.8 of ISO/IEC 17025: 2017.

13. Deviation

This experiment was conducted according to ISO 10993-10:2021 Biological evaluation of medical devices Part 10: Tests for skin sensitization without deviation.

14. Record Storage

All raw data pertaining to this study and a copy of the final report are to be retained in designated archive files in our inspection body and laboratory.

A B

Fig.3. The result of polar extraction. A. No visible change was observed on the animal skin of the test group (48h after challenge). B. No visible change was observed on the animal skin of the vehicle control group (48h after challenge).

A B

Fig.4. The result of non-polar extraction. A. No visible change was observed on the animal skin of the test group (48h after challenge). B. No visible change was observed on the animal skin of the vehicle control group (48h after challenge).

Tab.2. The Magnusson and Kligman scale of the test groups and control groups animals at 24h and 48h after challenging.

Group	Animal No.	Scale		Frequency
		24h	48h	
Test group (polar extraction liquid)	1	0	0	0%
	2	0	0	
	3	0	0	
	4	0	0	
	5	0	0	
	6	0	0	
	7	0	0	
	8	0	0	
	9	0	0	
	10	0	0	
Vehicle control group (polar extraction vehicle)	11	0	0	0%
	12	0	0	
	13	0	0	
	14	0	0	
	15	0	0	
Test group (non-polar extraction liquid)	16	0	0	0%
	17	0	0	
	18	0	0	
	19	0	0	
	20	0	0	
	21	0	0	
	22	0	0	
	23	0	0	
	24	0	0	
	25	0	0	
Vehicle control group (non-polar extraction vehicle)	26	0	0	0%
	27	0	0	
	28	0	0	
	29	0	0	
	30	0	0	

Appendix

The skin sensitization test of positive-control substance

(test date: 2025-05-06~2025-05-30)

1. Purpose

To ensure reproducibility and sensitivity, a test of a positive-control substance for skin sensitization was conducted by our laboratory in order to validate the test system and demonstrate a positive response.

2. Material

Name: 2,4-dichloronitrobenzene (DNCB)

Manufacturer: Xiya Chemical Technology (Shangdong) Co., Ltd.

Model: 10g

Batch: 20240718-10

Purity: >99.0%(GC)

Physical State: Light yellow, Crystalline powder

Storage Conditions: Room temperature.

3. Animal

15 animals (351.2g~451.6g), including 10 test group animals and 5 control group animals. They were purchased from Sichuan Vital River Laboratory Animal Technology Co., Ltd (SCXK（川）2023-0040).

4. Test Procedure

The DNCB was added to anhydrous ethanol solution at the ratio of 0.001g/mL, mixed and applied to the test. The test procedure was according to ISO 10993-10: 2021 Biological evaluation of medical devices Part 10: Tests for skin sensitization.

5. Result

The skin sensitization frequency for test group was 100%, the skin sensitization frequency for anhydrous ethanol control group was 0%, shown as Schedule 1 for details.

Schedule 1. Magnusson and Kligman scale of test and control animals

Group	Animal No.	Scale		Frequency
		24h	48h	
Test group	1	2	2	100%
	2	1	2	
	3	0	1	
	4	1	1	
	5	1	2	
	6	0	1	
	7	1	1	
	8	1	1	
	9	0	1	
	10	1	1	
anhydrous ethanol control group	11	0	0	0%
	12	0	0	
	13	0	0	
	14	0	0	
	15	0	0	