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Skin Irritation Test

Extraction Method

Final Report

Article Name: Single-use medical face mask (non-sterile)

Report Number: CSTBB20030142

Method Standard: ISO10993-10:2010

Sponsor

Henan Siyuan Medical Equipment Co.,
Ltd

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Notices

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 report is only responsible for the test results of the tested samples.
5. The report shall not be reproduced except in full without the written approval of the company.



Abstract

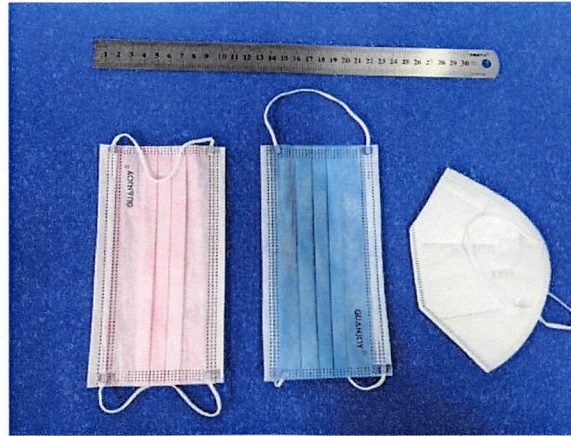
In this study, we took New Zealand white Rabbits to observe the skin irritation of the test article according to ISO10993-10:2010.

The test article were extracted in Constant Temperature Vibrator at 50 °C, 60 rpm for 72 h by 0.9 % Sodium Chloride Injection and Sesame Oil. Apply 0.5 ml extracts of test article or control to 2.5 cm×2.5 cm absorbent gauze patches, and then apply the patch soaked with the extract of test article or control directly to the skin on each side of each rabbit, and then wrap the application sites with a bandage for a minimum of 4 h. At the end of the contact time, remove the dressing. The describe and score the skin reaction for erythema and oedema for each application site at each time interval. Record the appearance of each application site at (1±0.1) h, (24±2) h, (48±2) h and (72±2) h following removal of the patches.

The results showed that the rabbits in the negative control group (0.9 % Sodium Chloride Injection, Sesame Oil) retained a normal appearance throughout the test and showed no skin irritants. A severe skin reactions for erythema and oedema were shown in the positive control group (SDS). While in test article group, the response of skin on testing side did not exceed that on the control side. The skin reactions for erythema and oedema were not observed in test article group. The data of each group met the acceptance criteria, and the results of this test were considered valid.

Based on the above results, it can be concluded that under the experimental conditions, the test article Single-use medical face mask (non-sterile) has no potential skin irritation on rabbit in the extraction method.

Study Verification and Signature



Protocol Number	SST2003009103BB
Protocol Effective Date	2020-02-20
Technical Initiation Date	2020-02-21
Technical Completion Date	2020-03-20
Final Report Completion Date	2020-03-20

Personnel	<u>Chunlei Ye</u>	<u>2020-03-20</u> Date Completed
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Approved	<u>Xiaoxin Li</u> Study Director	<u>2020-03-20</u> Date Completed
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Supervisory	<u>[Signature]</u> Test Facility Manager	<u>2020-03-20</u> Date Completed
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Huatongwei international inspection (Suzhou) Co., Ltd.

Quality Assurance Statement and GLP Statement

Quality Assurance Statement

The Quality Assurance Unit conducted inspections on the following dates. The findings were reported to the Study Director and to the HTW's Management.

The final report was reviewed to assure that the report accurately describes the methods and standard operating procedures. The reported results accurately reflect the raw data of the nonclinical study conducted per the protocol.

Phase Inspected	Date	Study Director	Management
Experiment	2020-02-21	2020-02-21	2020-02-21
Raw Data	2020-03-20	2020-03-20	2020-03-20
Final Report	2020-03-20	2020-03-20	2020-03-20

The findings of these inspections have been reported to Management and the Study Director.

HWI Jiang
Quality Assurance

2020-03-20
Date

GLP Statement

This study was conducted in compliance with current U.S. Food and Drug Administration regulations set forth in 21 CFR, Part 58.

The sections of the regulations not performed by or under the direction of HTW, exempt from this Good Laboratory Practice Statement, included characterization and stability of the test article and its mixture with carriers, 21 CFR, Part 58.105 and 58.113.

Xiang Li
Study Director

2020-03-20
Date

1.0 Purpose

To evaluate the potential skin irritation caused by test article contact with the skin surface of rabbits and extrapolating the results to humans, but it does not establish the actual risk of irritation.

2.0 Reference

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

Groups	Test article	Negative Control Article(Polar)	Negative Article(Non-Polar)	Positive Control
Name	Single-use medical face mask (non-sterile)	0.9% Sodium Chloride Injection (SC)	Sesame Oil (SO)	10 % sodium dodecyl sulfate (SDS)
Manufacture	Henan Siyuan Medical Equipment Co., Ltd	Sichuan Kelun Pharmaceutical Co., Ltd.	Jiangxi xinsen natural vegetable oil co., Ltd.	SIGMA
Sterilization state	Not provided	/	/	/
Size	Not provided	500 ml	25 kg	25 g
Model	Flat Type(red) Flat Type(blue) Folded Type	/	/	/
Lot Batch#	20200218	B190105051	181120	SLBL2304V
Test Article Material	Not provided	/	/	/
Physical State	Solid	Liquid	Liquid	Solid
Color	White, blue, red	Colorless	Light yellow	Colorless
Package material	Not provided	/	/	/
Concentration	/	/	/	10 %
Total Surface/Weight	Not provided	/	/	/
Storage Condition	Room Tep.	Room Tep.	Room Tep.	Room Tep.
The information about the test article was supplied by the sponsor wherever applicable.				

4.0 Identification of test system

4.1 Test animal

Species: New Zealand white Rabbit

Number: 6

Sex: 3 ♀, 3 ♂

Weight: 2.11~2.26 kg

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

Animal identification: Ear tattoo

Cages: Stainless steel cage

Acclimation Period: 7 days under the same conditions as for the actual test

4.2 Justification of test system

The rabbit is specified as an appropriate animal model for evaluating potential skin irritants by the current testing standards. Positive control 10% sodium dodecyl sulfate has been substantiated at HTW with this method.

5.0 Animal Management

Animal purchase: Wuxi hengtai experimental animal breeding co. LTD SCXK (SU) 2015-0004

Bedding: /

Feed: Experimental rabbits were fed a maintenance diet, Wuxi hengtai experimental animal breeding co. LTD

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

Animal room temperature: 18-26 °C

Animal room relative humidity: 30 %-70 %

Lights: 12 hours light/dark cycle, full-spectrum lighting

Personnel: Associates involved were appropriately qualified and trained

Selection: Only healthy, previously unused animals were selected

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

6.0 Equipment and reagents

6.1 Instruments

Constant Temperature Vibrator (SHB007, 2019/3/15), Autoclave (SHB026, 2019/3/15), Electronic scale (SHB017, 2019/3/7)

7.0 Experiment design

7.1 Sample preparation

The extracts of test article will be prepared according to the following steps:

Aseptic Sampling			Extraction in sterile vessels				
Sampling Manner	Actually sampling	Ratio	Reagent		Temperature	Time	pH
Whole	1518.8 cm ²	6 cm ² : 1 ml	SC	253.1 ml	50 °C	72 h	5.5
	SO		253.1 ml	5.5			

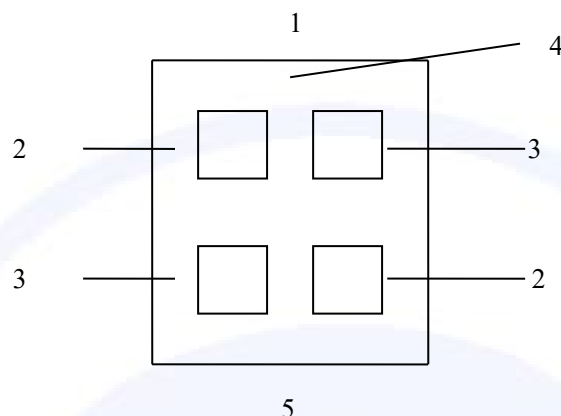
The state of the leaching solution did not change visually after the leaching was advanced. The extractions were clear, and the pH value has not been adjusted, filtered, centrifuged, diluted and other processes, before dosing stored at room temperature no more than 24 h. The control solution was prepared under the same conditions

7.2 Test method

Use the rabbits with healthy intact skin. Fur was generally clipped within 24 h period before testing on the

backs of the rabbits, a sufficient distance on both sides of the spine for application and observation of all test sites (approximately 10×15 cm).

Apply 0.5 ml extract (s) of test article or control to 2.5 cm×2.5 cm absorbent gauze patches, and then apply the patch soaked with the extract of test article or control directly to the skin on each side of each rabbit as shown in Figure 1, and then wrap the application sites with a bandage (semi-occlusive or occlusive) for a minimum of 4h. At the end of the contact time, remove the dressing.



1- Cranial end, 2- Test site, 3- Control site, 4- Clipped dorsal region, 5- Caudal end

Figure1 Location of skin application sites

8.0 The results observed

The Describe and score the skin reaction for erythema and oedema according to the scoring system given in Table 1 for each application site at each time interval. Record the appearance of each application site at (1±0.1) h, (24±2) h, (48±2) h and (72±2) h following removal of the patches.

Table 1 Classification System for Skin Reaction

Erythema and Eschar Formation:	Numerical Grading
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate erythema	3
Severe erythema (beet redness) to eschar formation preventing grading of erythema	4
Edema Formation:	
No edema	0
Very slight edema (barely perceptible)	1
Well-defined edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1mm)	3
Severe edema (raised more than 1mm and extending beyond exposure area)	4
Maximal possible score for irritation	8
Irritation Response Categories in the Rabbit	
Response Category	Mean score

Negligible	0 to 0.4
Slight	0.5 to 1.9
Moderate	2 to 4.9
Severe	5 to 8

9.0 Evaluation criteria

Use only (24±2) h, (48±2) h and (72±2) h observations for calculation.

After the 72 h grading, all erythema grades plus oedema grades (24±2) h, (48±2) h and (72±2) h were totalled separately for each test article and blank for each animal. The primary irritation score for an animal was calculated by dividing the sum of all the scores by 6 (two test/observation sites, three time points).

To obtain the primary irritation index for the test article, add all the primary irritation scores of the individual animals and divide by the number of animals.

When blank or negative control was used, calculate the primary irritation score for the controls and subtract that score from the score using the test material to obtain the primary irritation score.

10.0 Results of the test

All animals were survived and no abnormal signs were observed during the study. According to what observed, the response of skin on testing side did not exceed that on the control side. Thus, the primary irritation index for the test article was calculated to be 0. See table 2.

11.0 Conclusion

The test result showed that the response of the test article extract was categorized as negligible under the test condition.

12.0 Compliance

US FDA Good Laboratory Practice Regulations 21 CFR 58, effective June 20, 1979, as amended 52 FR 33780, Sept. 4, 1987, and subsequent amendments

Standard operating procedure of CCIC Huatongwei international inspection (Suzhou) Co., Ltd.

13.0 Record

All raw data pertaining to this study and a copy of the final report are retained in designated Huatongwei archive.

14.0 Confidentiality Agreement

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

Table 2 Skin irritation response observation

Reagent	Rabbit No	Pretest weigh(g)	Finished weigh(g)	Group	Reaction	Interval (hours): score=left/right			
						1h	24h	48h	72h
SC	1	2.12	2.22	Test Article	Erythema	0/0	0/0	0/0	0/0
					Oedema	0/0	0/0	0/0	0/0
				Negative Control	Erythema	0/0	0/0	0/0	0/0
					Oedema	0/0	0/0	0/0	0/0
	2	2.13	2.20	Test Article	Erythema	0/0	0/0	0/0	0/0
					Oedema	0/0	0/0	0/0	0/0
				Negative Control	Erythema	0/0	0/0	0/0	0/0
					Oedema	0/0	0/0	0/0	0/0
	3	2.24	2.31	Test Article	Erythema	0/0	0/0	0/0	0/0
					Oedema	0/0	0/0	0/0	0/0
				Negative Control	Erythema	0/0	0/0	0/0	0/0
					Oedema	0/0	0/0	0/0	0/0
Primary irritation index						0			
SO	4	2.11	2.19	Test Article	Erythema	0/0	0/0	0/0	0/0
					Oedema	0/0	0/0	0/0	0/0
				Negative Control	Erythema	0/0	0/0	0/0	0/0
					Oedema	0/0	0/0	0/0	0/0
	5	2.26	2.32	Test Article	Erythema	0/0	0/0	0/0	0/0
					Oedema	0/0	0/0	0/0	0/0
				Negative Control	Erythema	0/0	0/0	0/0	0/0
					Oedema	0/0	0/0	0/0	0/0
	6	2.22	2.31	Test Article	Erythema	0/0	0/0	0/0	0/0
					Oedema	0/0	0/0	0/0	0/0
				Negative Control	Erythema	0/0	0/0	0/0	0/0
					Oedema	0/0	0/0	0/0	0/0
Primary irritation index						0			

Table 3 Positive control

Rabbit No	Group	Reaction	Interval (hours): score=left site/right site			
			1h	24h	48h	72h
1	Positive control	Erythema	0/0	1/2	2/3	3/3
		Oedema	0/0	2/1	2/2	3/3
	Negative Control	Erythema	0/0	0/0	0/0	0/0
		Oedema	0/0	0/0	0/0	0/0
2	Positive control	Erythema	0/1	2/1	3/3	4/3
		Oedema	1/0	2/2	3/3	3/4
	Negative Control	Erythema	0/0	0/0	0/0	0/0
		Oedema	0/0	0/0	0/0	0/0
3	Positive control	Erythema	1/0	1/2	3/3	4/3
		Oedema	0/1	2/1	3/4	3/4
	Negative Control	Erythema	0/0	0/0	0/0	0/0
		Oedema	0/0	0/0	0/0	0/0
Primary irritation index			5.2			

Positive control performed once every six months see CSTBB20020001P3(Finish date: 2020-02-21)