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Sanitation & Environment Technology Institute, Soochow University, Amendment Report

Report Number: SDWH-M201801675-4Amd01

(Replace SDWH-M201801675-4(E))

Skin Irritation Test of
Liquid silicone rubber
using ISO 10993-10:2010 Test Methods
Topical Application Directly

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CONTENTS

CONTENTS....2
SUPPLEMENTARY EXPLANATION....3
STUDY VERIFICATION AND SIGNATURE....4
QUALITY ASSURANCE STATEMENT....5
1.0 Summary....6
2.0 Purpose....6
3.0 Reference....6
4.0 Compliance....6
5.0 Identification of test and control articles....6
6.0 Identification of test system....7
7.0 Animal Care and Maintenance....7
8.0 Justification of the test system....7
9.0 Route of administration....8
10.0Experiment design....8
10.1Sample and Control Preparation....8
10.2 Equipment....8
10.3 Reagents....8
10.4 Experimental Procedure....8
10.5 Observation of animal....8
10.6 Evaluation of results....9
10.7 Results....9
10.8 Conclusion....9
11.0 Record Storage....9
12.0 Confidentiality Agreement....9
13.0 Deviation statement....9

SUPPLEMENTARY EXPLANATION

1. Please apply for rechecking within 15 days of receiving the report if there are any objections.
2. Any erasure or without special inspection and 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. SDWH-M201801675-4(E)Amd01 replaced the original report SDWH-M201801675-4(E);

   SDWH will not bear any corresponding responsibilities about the reference of the original report.

   Amendment description as follows:

Other were amended due to the sponsor's demand

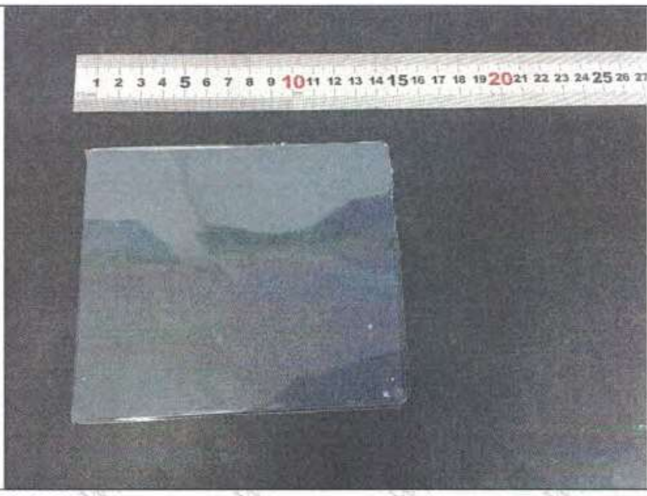
Original Statement:

Other: Applicable to Model: MCH-30XY、MCH-31XY、MCH-39XY

Amended Statment:

Other: Applicable to Model: MCS-3010-XY, LGS-9520-XY,PRS--9651-XY

STUDY VERIFICATION AND SIGNATURE

Test Article	
Test Article Receipt:	2018- 06-05
Protocol No.:	SDWH- PROTOCOL- GLP- M201801675-4
Protocol Effective Date:	2018- 06-19
Technical Initiation Date:	2018- 06-26
Technical Completion Date:	2018- 06-29
Amendment Report Completion Date	2019- 03-14

Edited by : ______________________ 2019-03-14
Date

Checked by : ______________________ 2019-03-14
Study Director Date

Approved by : ______________________ 2019-03-14
Authorized signatory Date

苏州大学卫生与环境技术研究所
检验检测专用章
(3)

Sanitation & Environment Technology Institute, Soochow University

QUALITY ASSURANCE STATEMENT

This study was conducted in compliance with 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 SDWH, 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.

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

INSPECTIONS	DATE OF INSPECTION	DATE REPORTED STUDY DIRECTOR	DATE REPORTED MANAGEMENT
EXPERIMENTAL PROCEDURE	2018-06-26	2018-06-26	2018-07-09
RAW DATA	2018-07-09	2018-07-09	2018-07-09
FINAL REPORT	2019-03-14	2019-03-14	2019-03-14

Quality Assurance Unit: Zhang Yan — 2019-03-14

QA — Date

1.0 Summary

The test article Liquid silicone rubber was evaluated for skin irritation by contact with the test system directly. The test and control articles were applied to the skin of rabbit, the skin responses on application sites were observed and recorded in (1±0.1) h, (24±2) h, (48±2) h and (72±2) h respectively after removal of the patches.
According to what was observed, the skin reaction on test sites did not exceed that on the control sites. The primary irritation index for the test article was calculated to be 0.
The test result showed that the response of the test article was categorized as negligible under the test condition.

2.0 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.

3.0 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)

4.0 Compliance

Good Laboratory Practice Regulations, 21 CFR, Part 58
ISO/IEC 17025:2005 General requirements for the competence of testing and calibration laboratories (CNAS-CL01 Accreditation Criteria for the competence of testing and calibration laboratories)
China National Accreditation Service for Conformity Assessment
Laboratory Accreditation Certificate No.CNAS L2954
Accreditation Criteria for the competence of Inspection Body (Certification and Accreditation Administration of the People's Republic of China CMA 180015144061)

5.0 Identification of test and control articles

5.1 Test article

Name: Liquid silicone rubber
Test article initial state: Not Sterilized
CAS Code: Not supplied by sponsor (N/S)
Size: N/S
Lot/ Batch: N/S
Test Article Material: Silicone rubber
Packaging Material: N/S
Physical State: Solid
Color: see the image
Density: N/S
Stability: N/S
Solubility: N/S
Storage Condition: Room Temperature
Other: Applicable to Model: MCS-3010-XY, LGS-9520-XY,PRS--9651-XY

The information about the test article was supplied by the sponsor wherever applicable; The Sponsor was responsible for all test article characterization data as specified in the GLP regulations.

5.2 Negative Control

Name: Gauze swabs sterile
Manufacturer: Shaoxing Jiangxi Zhonggan Medical apparatus and instruments Co.,Ltd
Size: 6cm×8cm-8P
Lot/ Batch#: 20180203
Physical State: solid
Color: white
Storage Condition: Room Temperature

5.3 Positive Control

Name: 20% sodium dodecyl sulfate
Manufacturer: Sinopharm Chemical Reagent Co., Ltd.
Size: 500g
Lot/ Batch#: 20150113
Concentration: 20%
Solvent: 0.9% sodium chloride injection (SC)
Date prepared: 2018-01-03
Physical State: Liquid
Color: Colorless
Storage Condition: Room Temperature

6.0 Identification of test system

Species: New Zealand white Rabbit (single strain)
Number: 3
Sex: Female
Weight: Initial body weight not less than 2kg
Health status: Healthy, not previously used in other experimental procedures, young adult, nulliparous and not pregnant.
Housing: Animals were housed in cages identified by a card indicating the lab number, test code and first treatment date.
Animal identification: Stain with picric acid
Cages: Stainless steel cage
Acclimation Period: 7 days under the same conditions as for the actual test

7.0 Animal Care and Maintenance

Animal purchase: Provided by Suzhou Experimental Animal Sci-tech Co., Ltd. <Permit Code: SCXK (SU) 2015-0007>
Bedding: NA
Feed: Rabbit Diet, Suzhou Experimental Animal Sci-tech Co., Ltd.
Water: Drinking water met the Standards for Drinking Water Quality GB 5749-2006
Animal room temperature: 18-26℃
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 expected to interfere with the test data.

8.0 Justification of the test system

The rabbit is specified as an appropriate animal model for evaluating potential skin irritants by the current testing standards. Positive control 20% sodium dodecyl sulfate has been substantiated at SDWH with this method.

9.0 Route of administration

Apply the test article directly to the rabbit skin is considered to be the best mean of contact.

10.0Experiment design

10.1Sample and Control Preparation

Aseptically clip the test article (Remove the protective films) and control article into 2.5cm×2.5cm.

10.2 Equipment

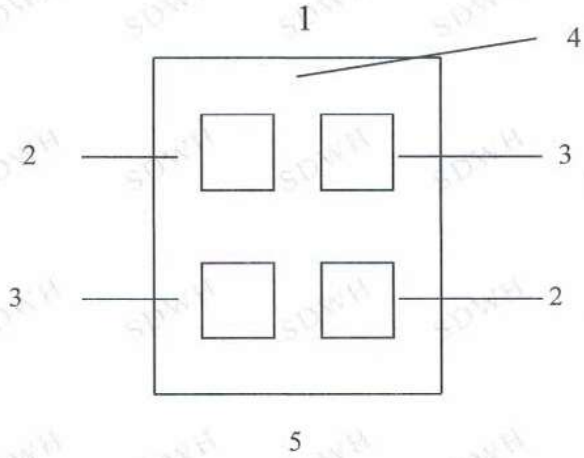
Steel Straight Scale (SDWH463), Calibration Expire (2018-09-10)
Electronic Scale (SDWH442), Calibration Expire (2018-09-03)

10.3 Reagents

NA

10.4 Experimental Procedure

Use the rabbits with healthy intact skin. Fur was generally clipped within 4-24h of 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 10×15cm).



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

Figure1 Location of skin application sites

Apply the test article (adhesive side) directly to the skin on each side of each rabbit as shown in Figure 1. Similarly, apply the control article to each rabbit, 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.

10.5 Observation of animal

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
Total 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

NOTE: Other adverse changes at the skin sites were recorded and are reported.

10.6 Evaluation of results

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 is 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.

10.7 Results

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.

10.8 Conclusion

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

11.0 Record Storage

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

12.0 Confidentiality Agreement

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

13.0 Deviation statement

There were no deviations from the approved study protocol which were judged to have any impact on the validity of the data.

Table 2 Dermal Observations

Rabbit No	Group		Interval (hours): score=left site/right site			
			1±0.1	24±2	48±2	72±2
1	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	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	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		Interval (hours): score=left site/right site			
			1±0.1	24±2	48±2	72±2
1	Positive control	Erythema	1/1	2/2	3/3	4/4
		Oedema	1/1	2/2	2/2	1/1
	Negative Control	Erythema	0/0	0/0	0/0	0/0
		Oedema	0/0	0/0	0/0	0/0
2	Positive control	Erythema	1/1	2/3	4/3	4/4
		Oedema	2/1	3/2	3/1	2/1
	Negative Control	Erythema	0/0	0/0	0/0	0/0
		Oedema	0/0	0/0	0/0	0/0
3	Positive control	Erythema	1/1	3/3	4/3	4/3
		Oedema	2/1	3/2	3/2	2/1
	Negative Control	Erythema	0/0	0/0	0/0	0/0
		Oedema	0/0	0/0	0/0	0/0
Primary irritation index			5.1			

Note: Positive control performed once every six months, see SDWH-M201800001-1(Completed Date: 2018-01-06).