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苏州大学
卫生与环境技术研究所
最终报告

报告编号：SDWH-M201702771-4

参照 ISO 10993-10:2010 方法进行

无纺布单面胶

的皮肤刺激试验

0.9%氯化钠注射液浸提

委托单位

上海锐泉医疗器械有限公司

制造商

上海锐泉医疗器械有限公司

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目 录

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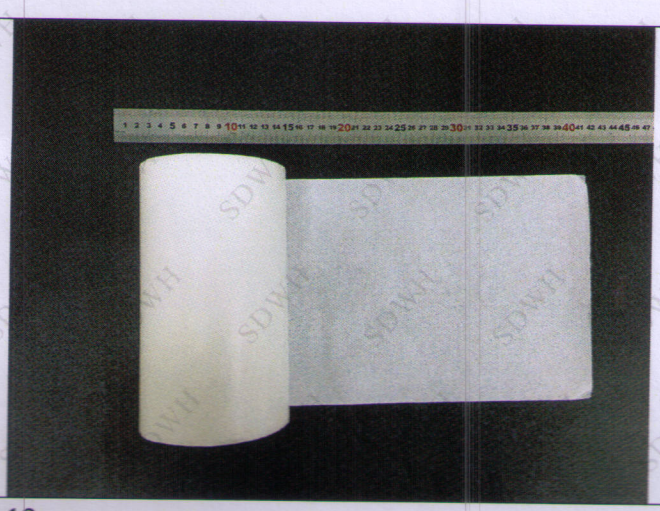
试验样品	
接样日期：	2017-10-12
试验计划书编号：	SDWH- PROTOCOL- M201702771-4
试验计划书生效日期：	2017-10-24
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编制：_____ 2017-11-07 日期

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1.0 摘　要

试验样品无纺布单面胶浸提液与试验系统直接接触，观察其潜在的皮肤刺激反应。

将试验样品浸提液 0.5ml 滴到 2.5cm×2.5cm 大小的吸收性纱布片上，贴敷在动物背部，经(1±0.1) h, (24±2) h, (48±2) h 和 (72±2) h 后，观察皮肤红斑和水肿等反应情况。

试验组皮肤刺激反应未超过对照组；对兔皮肤原发性刺激指数为 0。

在本次试验条件下，试验样品浸提液在兔皮肤反应类型为无刺激作用。

2.0 目　的

用兔来检测表面接触引起的皮肤刺激反应，并类推到人类，但试验结果并不代表样品真正的皮肤刺激反应危险性。

3.0 参考标准

医疗器械的生物学评价第 10 部分:刺激与皮肤致敏试验 ISO10993-10:2010

医疗器械的生物学评价第 12 部分:样品制备和参照样品 ISO10993-12:2012

医疗器械的生物学评价第 2 部分:动物保护要求 ISO10993-2:2006

4.0 执行规范

ISO/IEC 17025:2005《检测和校准实验室能力的通用要求》CNAS-CL01 检测和校准实验室能力认可准则（中国合格评定国家认可委员会 实验室认可证书 No. CNAS L2954）

实验室资质认定评审准则（江苏省质量技术监督局资质认定计量认证证书 CMA 151000100270）

5.0 对照和试验样品确定

5.1 试验样品

名称：无纺布单面胶

来样原始状态：未灭菌

CAS 编号：未提供

型号：未提供

规格：未提供

批号：H20170612001

样品材料：无纺布

包装材质：未提供

性状：固体

颜色：未提供

密度：未提供

稳定性：未提供

溶解度：未提供

保存条件：室温

试验样品信息是由样品委托单位提供。

5.2 阴性对照

名称：0.9%氯化钠注射液（SC）

制造商：河北天成药业股份有限公司

规格：500ml

批号：A17021908

性状：液体

颜色：无色
保存条件：室温

5.3 阳性对照

名称：20%十二烷基硫酸钠
制造商：国药集团化学试剂有限公司
规格：500g
批号：20150113
浓度：20%
溶剂：0.9%氯化钠注射液
配制日期：2017-07-04
性状：液体
颜色：无色透明
保存条件：室温

6.0 试验系统鉴别

种属：新西兰白色纯种大白兔
数量：3 只
性别：雌性
重量：试验开始体重不低于 2.0kg
健康状况：健康未使用、初成年，未产且无孕
饲养：按组饲养在笼子内，做好标识编号、试验代号、试验开始日期。
动物鉴别：苦味酸染色
笼子：不锈钢笼子
适应期：在实验环境下 7 天

7.0 饲养和护理

动物来源：苏州高新区镇湖实验动物科技有限公司 [许可证号：SCXK（苏）2013-0002]
垫料：NA
饲料：实验兔全价颗粒饲料，苏州高新区镇湖实验动物科技有限公司
水：自来水（符合 GB 5749-2006 卫生标准）
室温：18-26℃
相对湿度：30%-70%
光照：每天需要 12 小时光照，全光谱日光灯
人员：检测人员有相应检测资质。
选择：选择健康未使用过的动物。
食物、水中无干扰试验数据污染物存在。

8.0 试验系统确认

依据现行试验标准，新西兰大白兔被指定作为评价原发性皮肤刺激作用合适的动物模型。该试验采用 20%的十二烷基硫酸钠作为皮肤刺激反应的阳性对照已经在苏州大学卫生与环境技术研究所试验得到证实。

9.0 给药途径确认

将试验样品浸提液 0.5ml 滴到 2.5cm×2.5cm 大小的吸收性纱布片，然后将纱布片直接与兔背部

皮肤接触，被认为是最佳接触方式。

10.0 试验设计

10.1 样品制备

样品制备见下表。

无菌操作取样		惰性容器内无菌震荡浸提			最终浸提液	
取样方式	实际取样	浸提比例	SC	条件	pH	是否澄清
随机取样	表面积 120cm^2	6cm^2 : 1ml	20.0ml	37℃，72h	6.0	澄清

浸提前后浸提液状态未发生改变。浸提完成后 4℃保存，24h 内用于测试。浸提液 pH 值未经调整，未经过滤，离心，稀释等处理过程。不加供试品，同条件制备阴性对照液。

10.2 仪器设备

卧式大容量恒温振荡器（SDWH897），校正有效期（2018-07-11）
高压灭菌器（SDWH2097），校正有效期（2017-11-23）
电子秤（SDWH442），校正有效期（2018-09-03）
钢直尺（SDWH463），校正有效期（2018-09-10）

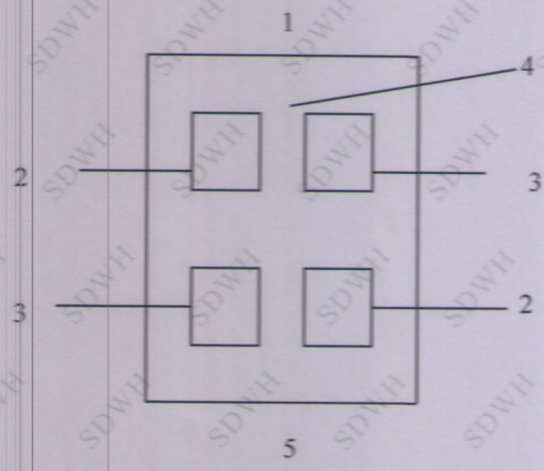
10.3 试剂

0.9%氯化钠注射液（河北天成药业股份有限公司，批号：A17021908）

10.4 试验步骤

试验前 4-24 小时将动物背部脊柱两侧被毛除去（约 10cm×15cm），作为试验和观察部位。

将试验样品浸提液和溶剂对照液各 0.5ml 分别滴到 2.5cm×2.5cm 大小的吸收性纱布片上备用。按图 1 所示，分别将浸透样品浸提液和溶剂对照液的纱布片直接接触兔脊柱两侧的皮肤，然后用绷带固定贴敷至少 4 小时。接触期结束后取下敷贴片。



1—头部；2—试验部位；3—对照部位；4—去毛的背部区域；5—尾部

图 1 皮肤应用部位

10.5 结果观察

取下敷贴片后(1±0.1) h, (24±2) h, (48±2) h 和 (72±2) h 观察敷贴部位及周围皮肤组织反应，包括红斑、水肿和坏死等记录之。根据红斑、水肿发生情况可记分为 0、1、2、3、4 标准记分等级。

详见表 1。

表 1　皮肤刺激反应记分标准

红　斑	记分	水　肿	记分
无红斑现象	0	无水肿现象	0
轻度红斑(勉强可见)	1	轻度水肿(勉强可见皮肤增厚)	1
明显红斑(淡红色)	2	明显水肿(隆起而轮廓清楚)	2
中度红斑(鲜红色)	3	中度水肿(隆起近 1mm)	3
重度红斑(紫红色伴有轻微焦痂形成)	4	重度水肿(隆起大于 1mm)	4
刺激反应最高积分			8

兔刺激反应类型	
反应种类	积分
无刺激作用	0-0.4
轻度刺激	0.5-1.9
中度刺激	2.0-4.9
严重刺激	5-8

注：其它副反应出现在皮肤刺激区域的应予记录和报告。

10.6 结果评价

仅使用(24±2) h, (48±2) h 和 (72±2) h 的观察数据进行计算。

将每只动物在每一规定时间的红斑和水肿刺激记分相加后再除以观察总数 6（2 个试验点×3 个观察时间），即为每只动物原发性刺激记分。

三只试验动物原发性刺激记分的平均数即为原发性刺激指数。

计算出对照原发性刺激记分，将试验样品原发性刺激记分减去该记分，即得出原发性刺激记分。该值即为试验样品的原发性刺激指数。

10.7 结　果

实验过程中动物未出现异常症状或死亡。据观察，试验组一侧皮肤反应未超过空白对照组一侧皮肤反应，原发性刺激指数为 0。见表 2。

10.8 结　论

在本次试验条件下，试验样品浸提液在兔皮肤反应类型为无刺激作用。

11.0 记录存储

所有与本次试验有关的原始数据和记录都被保存在指定的 SDWH 档案文件中。

12.0 保密协议

签订检测委托合同即认为双方接受保密协议。

13.0 试验偏离声明

本次试验严格按照方案执行，未发生影响实验数据有效性的偏离。

表 2　皮肤反应结果观察

编号	试验组别		间隔时间(小时)：记分=左侧/右侧			
			1±0.1	24±2	48±2	72±2
1	试验样品组	红斑	0/0	0/0	0/0	0/0
		水肿	0/0	0/0	0/0	0/0
	阴性对照组	红斑	0/0	0/0	0/0	0/0
		水肿	0/0	0/0	0/0	0/0
2	试验样品组	红斑	0/0	0/0	0/0	0/0
		水肿	0/0	0/0	0/0	0/0
	阴性对照组	红斑	0/0	0/0	0/0	0/0
		水肿	0/0	0/0	0/0	0/0
3	试验样品组	红斑	0/0	0/0	0/0	0/0
		水肿	0/0	0/0	0/0	0/0
	阴性对照组	红斑	0/0	0/0	0/0	0/0
		水肿	0/0	0/0	0/0	0/0
原发性刺激指数			0			

表 3　皮肤刺激反应阳性对照

编号	试验组别		间隔时间(小时)：记分=左侧/右侧			
			1±0.1	24±2	48±2	72±2
1	阳性对照组	红斑	1/1	3/3	3/3	4/4
		水肿	1/1	2/2	2/2	1/1
	阴性对照组	红斑	0/0	0/0	0/0	0/0
		水肿	0/0	0/0	0/0	0/0
2	阳性对照组	红斑	1/1	3/3	4/3	4/4
		水肿	2/1	3/2	3/1	2/1
	阴性对照组	红斑	0/0	0/0	0/0	0/0
		水肿	0/0	0/0	0/0	0/0
3	阳性对照组	红斑	1/1	3/3	4/3	4/3
		水肿	2/1	3/2	3/2	2/1
	阴性对照组	红斑	0/0	0/0	0/0	0/0
		水肿	0/0	0/0	0/0	0/0
原发性刺激指数			5.3			

注：阳性对照每六个月进行一次，数据引用 SDWH-M201701444-1（完成日期：2017-07-07）。

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Sanitation & Environment Technology Institute, Soochow University, Final Report

Report Number: SDWH- M201702771-4

Skin Irritation Test of
Non-woven tape
Using ISO 10993-10:2010 Test Method
0.9% Sodium Chloride Injection Extract

Sponsor
shanghai Rui Quan medical instrument Co.,Ltd

Manufacturer
shanghai Rui Quan medical instrument Co.,Ltd

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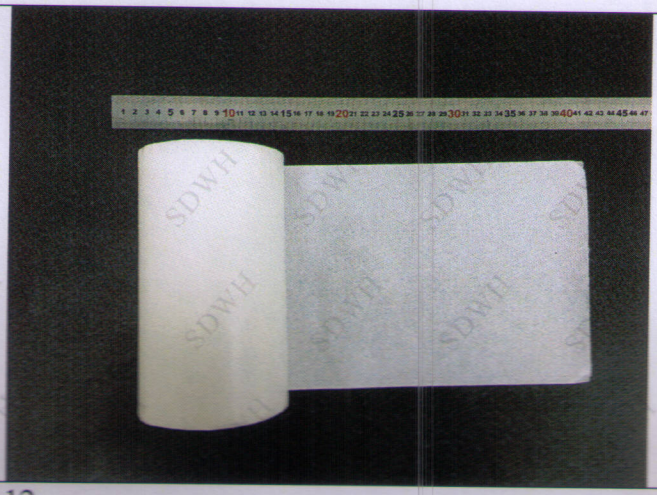
Test Article	
Test Article Receipt:	2017-10-12
Protocol No:	SDWH- PROTOCOL- M201702771-4
Protocol Effective Date:	2017-10-24
Technical Initiation Date:	2017-10-27
Technical Completion Date:	2017-11-03
Final Report Completion Date:	2017-11-07

Edited by : _____ 2017-11-07
Date

Checked by : _____ 2017-11-07
Study Director Date

Approved by : _____ 2017-11-08
Authorized Signatory Date

Sanitation & Environment Technology Institute, Soochow University

1.0 Summary

The extract of test article Non-woven tape was evaluated for skin irritation. The test and control extracts 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 extract 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

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 the laboratories (Quality and Technical Bureau of Jiangsu Province Metrology Accreditation Certificate CMA 151000100270)

5.0 Identification of test and control articles

5.1 Test article

Name: Non-woven tape
Test article initial state: Not sterilized
CAS Code: Not supplied by sponsor (N/S)
Model: N/S
Size: N/S
Lot/ Batch: H20170612001
Test Article Material: Non-woven
Packaging Material: N/S
Physical State: Solid
Color: N/S
Density: N/S
Stability: N/S
Solubility: N/S
Storage Condition: Room Temperature
The information about the test article was supplied by the sponsor wherever applicable.

5.2 Negative Control

Name: 0.9% sodium chloride injection (SC)
Manufacturer: Hebei Tiancheng Pharmaceutical Company Limited.
Size: 500ml

Lot/ Batch#: A17021908
Physical State: Liquid
Color: Colourless
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: 2017-07-04
Physical State: Liquid
Color: Colourless
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) 2013-0002>
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

The patches (about 2.5cm×2.5cm) which moistened by test article extract, and directly applying to

the rabbit skin is considered to be the best mean of contact.

10.0 Experiment design

10.1 Sample and Control Preparation

See the table below for test article extract preparation.

Aseptic Sampling		Aseptic Agitation Extraction In Inert Container			Final Extract	
Sampling Manner	Actually sampling	Ratio	SC	Condition	pH	Clear or Not
Random sampling	Surface area 120cm^2	6cm^2 : 1ml	20.0ml	37℃，72h	6.0	Clear

There was no change in the extraction solvent (pre- and post-extraction).

The extract was stored at 4℃ and tested within 24h after extraction without the process of pH value adjustment, filtering, centrifugation, dilution, etc.

The vehicle (without the test article) was similarly prepared to serve as the control.

10.2 Equipment

Horizontal Large Capacity Constant Temperature Vibrator (SDWH897), Calibration Expire (2018-07-11)

Autoclave (SDWH2097), Calibration Expire (2017-11-23)

Electronic Scale (SDWH442), Calibration Expire (2018-09-03)

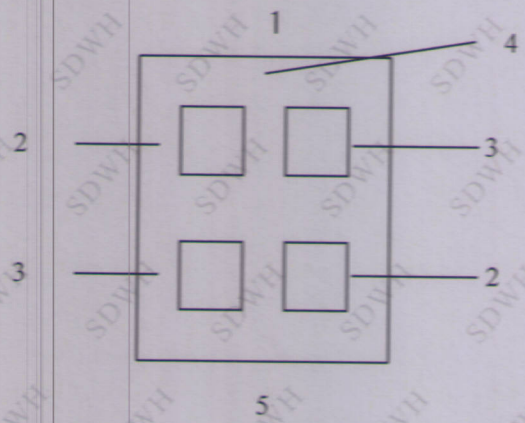
Steel Straight Scale (SDWH463), Calibration Expire (2018-09-10)

10.3 Reagents

0.9% sodium chloride injection (Hebei Tiancheng Pharmaceutical Company Limited. Lot No: A17021908)

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 0.5ml extract (s) of test article or control to 2.5cm×2.5cm 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.

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
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

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 extract 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	3/3	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	3/3	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			5.3			

Note: Positive control performed once every six months, see SDWH-M201701444-1(Completed Date: 2017-07-07).