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CNAS L13034

Skin Sensitization Test

Closed-patch test (Buehler test)

Final Report

Verification

Report Number: CSTBB21031029

Article Name: Ostomy bag

Method Standard: ISO 10993-10: 2010

Sponsor

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CONTENTS

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Abstract

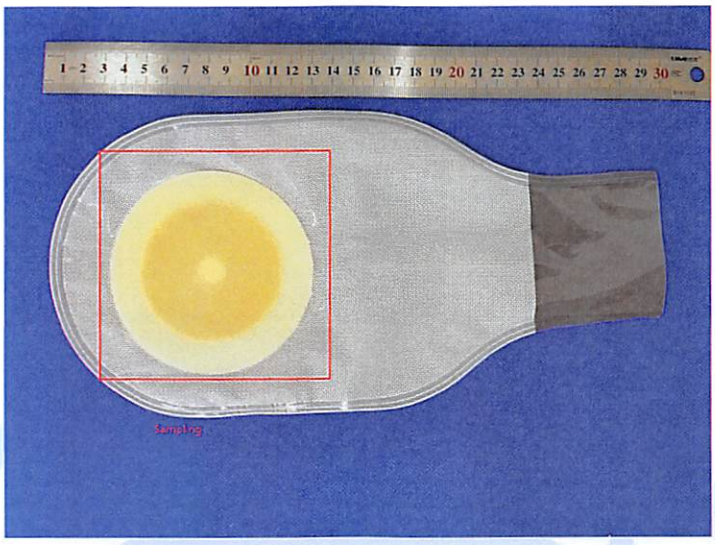
In this study, we took guinea pigs to observe the skin sensitization of the test article according to ISO 10993-10: 2010.

Administer the test sample by topical application to the clipped left upper back region of each animal using appropriate patches. Remove the restrainer of any occlusive dressings and patches after (6±0.5) h. Perform this procedure on three days a week for three weeks. Treat the control animals similarly, using the blank liquid alone.Administer the test sample by topical application to the clipped left upper back region of each animal using appropriate patches. Remove the restrainer of any occlusive dressings and patches after (6±0.5) h. Perform this procedure on three days a week for three weeks. Treat the control animals similarly, using the blank liquid alone.The erythema and edema of the challenge site were observed to test the sensitization response of the test article. According to the Magnusson and Kligman scales, the response to erythema and edema at each application site of the skin was described and scored 24 hours and 48 hours after the challenge phase.

The results showed that the guinea pigs in the negative control group 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 (DNCB). 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 has no potential skin sensitization on guinea pigs in the extraction method.

Study Verification and Signature



Protocol Number	SST2103020108BB
Protocol Effective Date	2021-03-22
Technical Initiation Date	2021-03-26
Technical Completion Date	2021-04-30
Final Report Completion Date	2021-05-07

Personnel Betty 2021-05-07
Date Completed

Approved Maoxuan Ye 2021-05-07
Study Director Date Completed

Supervisory
Test Facility Manager Date Completed

CCIC Huatongwei International Inspection (Suzhou) Co., Ltd.

1.0 Purpose

The test was designed to evaluate the potential of a test article to cause skin sensitization. The test is used as a procedure for screening of contact allergens in guinea pigs and extrapolating the results to humans, but it does not establish the actual risk of sensitization.

2.0 Reference

Biological evaluation of medical devices-Part 2: Animal welfare requirements (ISO 10993-2:2006)

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 materialsy (ISO 10993-12:2021)

3.0 Test and control articles

Groups	Test article	Negative Control Article	Positive Control
Name	Ostomy bag	0.9% Sodium Chloride Injection(SC)	2, 4-Dinitrochlorobenzene (DNCB)
Manufacturer	Zhejiang Ailebao Medical Technology CO.,LTD	Guangxi Yuyuan Pharmaceutical Co., Ltd	TOKYO CHEMICAL INDUSTRY CO., LTD
Size	14.8*29.9cm	500 ml	25 g
Model	1OP60	/	/
Lot Batch#	Not provided	H20120305	H2UKD-DM
Test Article Material	hydrocolloid、bag	/	/
Physical State	Solid	Liquid	Solid
Color	Pale yellow	Colorless	Light yellow
Package material	PE bag	/	/
Sterilized or Not	Yes	/	/
Concentration	/	0.9 %	Induction Concentration: 0.1 % Challenge Concentration: 0.05 % Dissolved in ethanol
Total Surface/Weight	442.52 cm^2 /15.12 g	/	/
Storage Condition	Room Temp.	Room Temp.	Room Temp.
The information about the test article was supplied by the sponsor wherever applicable.			

4.0 Identification of test system

4.1 Test animal

Species: Hartley Guinea Pig (Cavia Porcellus)

Number: 15 (10 Test +5 Control)

Sex: either sex

Initial body weight: 300.0~500.0 g

Health status: Healthy, not previously used in other experimental procedures. Female animals were nul liparous and not pregnant.

Animal identification: Ear tag

Cages: Plastic cage

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

4.2 Justification of test system

The albino guinea pig has been used historically for sensitization studies (Magnusson and Kligman, 1 970). The guinea pig is believed to be the most sensitive animal model for this type of study. DNCB is the positive control article recommended in the test instructions. To ensure the sensitivity of the experime ntal system, the positive control article should be verified every three months.

5.0 Animal Management

Animal purchase: Wuxi hengtai experimental animal breeding co. LTD SCXK (SU) 2020-0003

Bedding: Corncob Jiangsu Xietong Pharmaceutical Bio-engineering Co., Ltd.

Feed: Guinea pigs were fed with full-price pellets Jiangsu Xietong Pharmaceutical Bio-engineering 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, or bedding expected to interfere with the test data.

6.0 Equipment and reagents

6.1 Instruments

Electronic scale (SHB017, calibration data: 2021/03/11)

7.0 Experiment design

7.1 Sample preparation

The test article articles were cut into 8 cm^2 and then used in test directly without any treatment. Use a volume of negative control article sufficient to saturate the gauze.

7.2 Test method

7.2.1 Intradermal induction phaseI

Administer the test sample by topical application to the clipped left upper back region of each animal using

appropriate patches. Remove the restrainer of any occlusive dressings and patches after (6±0.5) h. Perform this procedure on three days a week for three weeks. Treat the control animals similarly, using the blank liquid alone.

7.2.2 Challenge phase

At (14±1) d after the last induction application, challenge all test and control animals with the test sample. Administer the test sample by a single topical application to a clipped untested area of each animal using appropriate patches soaked in the test sample. Remove the restrainer and occlusive dressings and patches after (6 ±0.5) h.

8.0 The results observed

The day after challenge exposure, the patch will be removed and the area cleaned gently with gauze if necessary. The site will be wiped gently with a 0.9% saline soaked gauze sponge prior to each scoring period. The challenge sites will be observed for signs of irritation and sensitization reaction, as indicated by erythema and edema. If necessary, the fur will be shaved or clipped in advance for the convenience of dermal score.

Daily challenge observation scores will be recorded approximately 24, and 48 hours after patch removal in accordance with the following classification system for skin reactions:

Table 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

9.0 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.

The outcome of the test is presented as the frequency of positive challenge results in test and control animals.

10.0 Results of the test

All animals were survived and no abnormal signs were observed during the study.Individual results of dermal scoring for the challenge appear in Table 2.

11.0 Conclusion

The test article showed no evidence of causing delayed dermal contact sensitization in the guinea pig. Results and conclusions apply only to the test article tested. Any extrapolation of these data to other articles is the sponsor’s responsibility.

12.0 Record

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

13.0 Confidentiality Agreement

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

14.0 Protocol amendment/deviations

There were no amendments or deviations that occurred during the course of this study.

Table 2 Guinea pig Sensitization Dermal Reactions

Group	No.	Pretest weight(g)	Finished weight(g)	The Challenge patch was removed 24h later		The Challenge patch was removed 48h later		Positive rate
				Erythema	Swelling	Erythema	Swelling	
Test article	1	309.7	366.2	0	0	0	0	0%
	2	317.5	370.8	0	0	0	0	
	3	310.5	371.9	0	0	0	0	
	4	306.1	366.5	0	0	0	0	
	5	318.7	372.6	0	0	0	0	
	6	310.6	370.2	0	0	0	0	
	7	317.3	378.6	0	0	0	0	
	8	310.2	373.9	0	0	0	0	
	9	305.4	367.4	0	0	0	0	
	10	304.9	362.6	0	0	0	0	
Negative Control	11	303.4	366.7	0	0	0	0	0%
	12	312.8	375.0	0	0	0	0	
	13	318.0	378.2	0	0	0	0	
	14	310.1	372.9	0	0	0	0	
	15	318.7	374.8	0	0	0	0	

Table 3 Positive control

Group	No.	Pretest weigh(g)	Finished weigh(g)	The Challenge patch was removed 24 h later		The Challenge patch was removed 48 h later		Positive rate
				Erythema	Swelling	Erythema	Swelling	
Test	1	309.0	370.8	1	0	2	0	100%
	2	304.4	364.9	0	0	1	0	
	3	316.7	379.6	1	1	2	1	
	4	308.3	372.3	1	0	2	1	
	5	305.9	363.2	0	0	1	1	
	6	316.3	377.1	0	0	1	0	
	7	317.5	381.2	1	1	1	2	
	8	306.9	362.0	2	0	2	1	
	9	315.2	367.6	0	0	1	0	
	10	312.0	370.8	1	0	2	1	
Negative Control	11	310.1	374.0	0	0	0	0	—
	12	314.6	372.7	0	0	0	0	
	13	318.3	383.0	0	0	0	0	
	14	305.5	366.3	0	0	0	0	
	15	316.7	371.1	0	0	0	0	

Note：The positive control was CSTBB2103001P2 (Finish date：2021-04-02)