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FINAL REPORT

Study Name: Disposable Medical Face Masks -Skin Sensitization Test

Study Number: MED202008586-08-EN

Sponsor

Name: Changzhou Huankang Medical Device Co., Ltd.

Address: 22 Changhe Road, Changzhou, Jiangsu, China

Testing Facility

Name: EPIN Suzhou Ltd.

Address: No.558 Fenhu Avenue, LiLi Town, Wujiang District, Suzhou, China

Digitally signed by Guțan Ghenadie
Date: 2021.04.22 12:03:05 EEST
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SUPPLEMENTARY EXPLANATION

1. Please apply for rechecking within 15 days after receiving the report if there is any objection.
2. The report is only valid with the dated signatures by person responsible and cross-page seal.
3. The results in this report relate only to the article tested.
4. The test report shall not be reproduced except in full, without written approval of EPIN Suzhou Ltd.
5. ILAC-G8:09/2019 was employed as the decision rules of statement conformity, where applicable.

TEST ARTICLE CONFIRMATION AND SIGNATURE

Edited by: Eric Zhang Date: 2020-10-28
Eric Zhang (Report Drafter)

Checked by: Look Lu Date: 2020-10-28
Look Lu (Study Director)

Approved by: Julie Wang Date: 2020.10.28
Julie Wang (Authorized Signatory)

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SUMMARY

1. Purpose

To evaluate the potential of test article extracts to cause skin sensitization in the guinea pig.

2. Process Description

Test article was whole sampled by 3 cm^2: 1 mL, extraction condition was 37 °C, 72 h. Extraction solvents were 0.9% sodium chloride (SC) and sesame oil (CO).

A pair of 0.1 mL intradermal injections was made into each animal in the clipped intrascapular region. At 7 d after completion of the intradermal induction phase, administered the test article extracts by topical application to the intrascapular region of each animal, used a patch of area approximately 8 cm^2 (absorbent gauze), so as to cover the intradermal injection sites. Secured with an occlusive dressing. Removed the dressings and patches after (48±2) h. Treated the negative control animals similarly, used the negative liquid alone. If the test article extracts did not produce irritation, pretreated the area with 10% sodium dodecyl sulfate massaged into the skin (24±2) h before the patch was applied.

At 14 d after completion of the topical induction phase, challenged all animals with the test extract. Administered all animals by topical application to sites that were not treated during the induction stage, used absorbent gauze (2.5 cm×2.5 cm) soaked. Secure with an occlusive dressing. Removed the dressings and patches after (24±2) h.

Observed the appearance of the challenge skin sites of the test and control animals (24±2) h and (48±2) h after removal of the dressings. Described and scored the skin reactions for erythema and oedema according to the Magnusson and Kligman grading.

3. Results

The positive rate of all test groups was 0%.

The positive rate of all negative control groups was 0%.

No abnormal clinical symptoms were observed in all animals except skin reactions.

4. Conclusion

Under the conditions of this study, the test article extract showed no signification evidence of causing skin sensitization in the guinea pig.

1. STUDY SUMMARIES

1.1. Study Name (Study No.)

Disposable Medical Face Masks - Skin Sensitization Test (MED202008586-08-EN).

1.2. Study Purpose

To evaluate the potential of test article extracts to cause skin sensitization in the guinea pig.

1.3. Referred Standard

- ISO 10993-10: 2010

  Biological evaluation of medical devices—Part 10: Tests for irritation and skin sensitization

- ISO 10993-12: 2012

  Biological evaluation of medical devices—Part 12: Sample preparation and reference materials

- ISO 10993-2: 2006

  Biological evaluation of medical devices—Part 2: Animal welfare requirements

1.4. Testing Facility

Name:	EPIN Suzhou Ltd.
Address:	No.558 Fenhu Avenue, Lili Town, Wujiang District, Suzhou, China

1.5. Sponsor

Name:	Changzhou Huankang Medical Device Co., Ltd.
Address:	22 Changhe Road, Changzhou, Jiangsu, China
ATTN:	Yecheng Zhai
Contact Information:	+86 150 2166 5265/519 8890 9800/hk@huankang.com

1.6. Study Protocol Alteration Treatment

Before the study start, the study protocol was approved by Study Director and sponsor. Any study alteration should be approved by Study Director.

1.7. Deviation(s) and Incident(s) Treatment

If any deviation or incident occurred during the test, the related information would be recorded timely and a deviation report should be submitted with the final report to interpretate the specific effect(s) on the final result

caused by the deviation or incident.

1.8. Major Laboratory Personnel (s)

Study Director:	Look Lu
Main Operation Personnel:	Ann Feng, Cheery Zhou

1.9. Schedule of the Study

Test Article Received Date:	2020-08-26
Protocol Effective Date:	2020-09-01
Technical Initiation Date:	2020-09-11
Technical Completion Date:	2020-10-05
Final Report Completion Date:	2020-10-28

2. TEST MATERIAL

2.1. Test Article

2.1.1. General information[1)]

Name:	Disposable Medical Face Masks
Initial State:	Sterile, EO
Size:	175*95mm
Model:	HK-Z01
Lot/ Batch#:	20200820
Physical State:	Solid
Color:	N/S[2)]
Density:	N/S
Stability:	N/S
Solubility:	N/S
Storage Condition:	Room temperature
Test Article Material:	N/S
Packaging Material:	N/S
Manufacturer Name:	Changzhou Huankang Medical Device Co., Ltd.

Manufacturer Address: 22 Changhe Road, Changzhou, Jiangsu, China

1) The information about the test article was supplied by the sponsor wherever applicable.
2) N/S means not supplied by the sponsor.

2.1.2. Retention of test article(s)

Reserve Volume:	10 pcs
Storage Location:	Sample Reserve Room

2.1.3. Handling of residual test article(s)

Tested Article(s):	Destroy and Waste
Untested Article(s):	Destroy and Waste

2.2. Negative Control

2.2.1. Polar control information

Name:	0.9% Sodium Chloride (SC)
Size:	500 mL
Lot/ Batch#:	B20031901A
Physical State:	Liquid
Color:	Colorless
Storage Condition:	Room Temperature
Manufacturer:	Kelun Pharmaceutical

2.2.2. Non-polar control information

Name:	Corn oil (CO)
Size:	500 mL
Lot/ Batch#:	C10822722
Physical State:	Pale yellow oily liquid
Storage Condition:	Room temperature
Manufacturer:	Macklin

2.3. Positive Control

Name:	2, 4-Dinitrochlorobenzene (DNCB)

Size:	100 g
Content:	98%
Lot/ Batch#:	160310
Physical State:	Pale yellow solid
Storage Condition:	Room temperature
Manufacturer:	PERFEMIKER
Induction Concentration:	0.5%
Challenge Concentration:	0.1%

2.4. Animal

2.4.1. Animal information

Species:	Hartley Guinea Pig
Microbial Levels:	Conventional
Number/Sex:	30/Male
Weight:	>300 g
Manufacturer:	Zhenhu Experimental Animal Technology Co., Ltd. of Suzhou
Production License#:	SCXK(Su)2015-0007
Quality Certificate#:	No.202012686

2.4.2. Animal feeding conditions

Breeding Density:	5 animals per cage
Cages:	Plastic cage
Animal Identification:	Stain with neutral magenta and identified by a cage card
Acclimation Period:	At least 5 days under the same conditions as for the actual test
Fodder:	Name: Guinea pig maintain feed
	Manufacturer: Beijing Keaoxieli
	Daily 40 g quantitative uptake per animal
Padding:	Name: Corn cob
	Manufacturer: Suzhou Anweierkang
	Periodic replacement

Vegetable/ Fruit:	Manufacturer: Supermarket
	Every afternoon rationing

2.4.3. Animal room environmental conditions

Temperature:	18℃-29℃
Relative Humidity:	40%-70%RH
Ventilation Rate:	≥8/h
Lights:	12 hours light/dark cycle, full spectrum fluorescent lights

2.5. Main Instruments and Reagents

2.5.1. Main instruments

Name	No.	Calibration Due Date
Electronic Balance	EPB-036	2021-02-24
Shaking Bath	EPB-184	2020-12-19
Clean Bench	EPB-143	2021-02-24
Electronic Balance	EPB-070	2021-02-25

2.5.2. Main reagents

Name	Lot/ Batch#	Manufacturer
FCA	SLCC 6223	SIGMA
Sodium Dodecyl Sulfate	20170712	Sinopharm Chemical Reagent Co., Ltd

2.6. Justification of the Test System

The albino guinea pig has been used historically for sensitization studies. The guinea pig is believed to be the most sensitive animal model for this type of study. 2, 4-Dinitrochlorobenzene (DNCB) is recommended as the positive substance by guiding principle. 2, 4-Dinitrochlorobenzene (DNCB) has been substantiated at EPIN Suzhou LTD. once every 3 months with this method.

3. TEST DESIGN

3.1. Extract Preparation

3.1.1. Extraction process

Test phase	Sampling Manner	Actual Sampling*	Ratio	Solvent	Amount	Conditions
Intradermal induction	Whole	332.5 cm^2	3 cm^2: 1 mL	SC	110.8 mL	37°C, 72 h
		332.5 cm^2	3 cm^2: 1 mL	CO	110.8 mL	37°C, 72 h
Topical induction		332.5 cm^2	3 cm^2: 1 mL	SC	110.8 mL	37°C, 72 h
		332.5 cm^2	3 cm^2: 1 mL	CO	110.8 mL	37°C, 72 h
Challenge		332.5 cm^2	3 cm^2: 1 mL	SC	110.8 mL	37°C, 72 h
		332.5 cm^2	3 cm^2: 1 mL	CO	110.8 mL	37°C, 72 h

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

*: The surface area is 332.5 cm^2 per test article. (provided by sponsor)

3.1.2. Final extract treatment

Final extract	Presence of particles or Not	Color and Clear or Not	Additional processing prior to the testing or Not
SC	Not	Colorless and Clear	Not
CO	Not	Pale yellow and Clear	Not

Note: Used the final extracts immediately.

3.2. Grouping

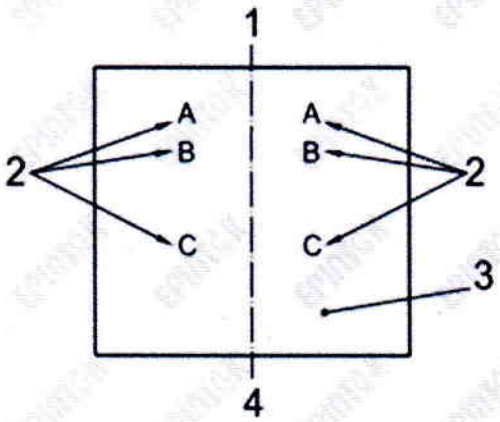
Took 30 guinea pigs and divided them into four groups.

Group No.	Group Name	Amount	Sex	Numbered list
1	Negative control (SC)	5	♂	1101-1105
2	Test group (SC)	10	♂	2106-2115
3	Negative control (CO)	5	♂	3116-3120
4	Test group (CO)	10	♂	4121- 4130

3.3. Experimental Process

3.3.1. Intradermal induction phase I

A pair of 0.1 mL intradermal injections was made for each of the following, into each animal, at the injection sites (A, B and C) as shown in **Figure 1** in the clipped intrascapular region.



1. Cranial end 2. 0.1 mL intradermal injections 3. Clipped intrascapular region 4. Caudal end

Site A: 50:50 (volume ratio) stable emulsion of Freund's complete adjuvant mixed with the chosen solvent.

Site B: The test article extract, the negative control animals were injected with the solvent alone.

Site C: The test article extract, emulsified in a 50:50 volume ratio stable emulsion of Freund's complete adjuvant and the solvent (50%), the negative control animals were injected with an emulsion of the negative liquid with adjuvant.

Figure 1 Location of intradermal injection sites

3.3.2. Topical induction phase II

At 7 d after completion of the intradermal induction phase, administered the test article extract by topical application to the intrascapular region of each animal, used a patch of area approximately 8 cm^2 (absorbent gauze), so as to cover the intradermal injection sites. Secured with an occlusive dressing. Removed the dressings and patches after (48±2) h. Treated the negative control animals similarly, used the negative liquid alone. If the test article extract did not produce irritation, pretreated the area with 10% sodium dodecyl sulfate massaged into the skin (24±2) h before the patch was applied.

3.3.3. Challenge phase

At 14d after completion of the topical induction phase, challenged all animals with the test article extract. Administered all animals by topical application to sites that were not treated during the induction stage, used absorbent gauze (2.5 cm×2.5 cm) soaked. Secured with an occlusive dressing. Removed the dressings and patches after (24±2) h.

3.3.4. Observation of animal

Observed the appearance of the challenge skin sites of the test and control animals (24±2) h and (48±2) h after removal of the dressings. Full-spectrum lighting was used to visualize the skin reactions. Described and graded the skin reactions for erythema and oedema according to the Magnusson and Kligman grading given in **Table 1** for each challenge site and at each time interval.

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

3.3.5. Other observed endpoints

Clinical symptoms except dermal reactions were observed every day.

Weighting all the test animals at the beginning and end of the test.

4. EVALUATION CRITERION

1) 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.
2) 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.
3) If the response is equivocal, rechallenge is recommended to confirm the results from the first challenge.
4) Occasionally, the test group has a greater number of animals showing a response than the controls, although the intensity of the reaction is not greater than that exhibited by the controls. In these instances, a rechallenge might be necessary to define the response clearly. A rechallenge shall be carried out 1 week to 2 weeks after the first challenge. The method used shall be as described for the first challenge, using a naive side on the animal.
5) The outcome of the test is presented as the frequency of positive challenge results in test and control animals.

5. ALTERATION AND DEVIATION

Alteration and deviation did not happen in this study.

6. RESULTS

The positive rate of all test groups was 0%.

The positive rate of all negative control groups was 0%.

No abnormal clinical symptoms were observed in all animals except skin reactions.

See **Attached Table 1-2.**

7. CONCLUSION

Under the conditions of this study, the test article extract showed no significant evidence of causing skin sensitization in the guinea pig.

8. ARCHIVING

All correspondence, including original copy of the protocol, original copy of the test report, and all raw data generated during the study (i.e., documentation forms as well as any other notes of raw data, printouts of instruments and computers) are stored in the archives room of the EPIN Suzhou Ltd.

9. ATTACHED TABLE

9.1. Attached Table 1 Sensitization Dermal Reactions

Group	Animal Number	(24±2) h before Phase II Patch Application		Hours Following Challenge Phase		Positive Rate after Challenge Phase
		Left	Right	(24±2) h	(48±2) h	
Negative control (SC)	1101	0	0	0	0	0%
	1102	0	0	0	0	
	1103	0	0	0	0	
	1104	0	0	0	0	
	1105	0	0	0	0	
Test group (SC)	2106	0	0	0	0	0%
	2107	0	0	0	0	
	2108	0	0	0	0	
	2109	0	0	0	0	
	2110	0	0	0	0	
	2111	0	0	0	0	
	2112	0	0	0	0	
	2113	0	0	0	0	
	2114	0	0	0	0	
	2115	0	0	0	0	
Negative control (CO)	3116	0	0	0	0	0%
	3117	0	0	0	0	
	3118	0	0	0	0	
	3119	0	0	0	0	
	3120	0	0	0	0	
Test group (CO)	4121	0	0	0	0	0%
	4122	0	0	0	0	
	4123	0	0	0	0	
	4124	0	0	0	0	
	4125	0	0	0	0	
	4126	0	0	0	0	
	4127	0	0	0	0	
	4128	0	0	0	0	
	4129	0	0	0	0	
	4130	0	0	0	0	

9.2. Attached Table 2 Weight Change and Clinical Observation

Group	Animal Number	Weight (g)		Clinical Observation except Dermal Reactions
		Test Begin	Test End	
Negative control (SC)	1101	346	417	Normal
	1102	319	408	Normal
	1103	328	410	Normal
	1104	336	412	Normal
	1105	309	428	Normal
Test group (SC)	2106	350	446	Normal
	2107	341	427	Normal
	2108	339	403	Normal
	2109	320	416	Normal
	2110	338	407	Normal
	2111	307	387	Normal
	2112	319	402	Normal
	2113	320	435	Normal
	2114	334	404	Normal
	2115	345	411	Normal
Negative control (CO)	3116	347	423	Normal
	3117	308	411	Normal
	3118	349	417	Normal
	3119	320	403	Normal
	3120	338	415	Normal
Test group (CO)	4121	356	411	Normal
	4122	340	428	Normal
	4123	337	443	Normal
	4124	328	428	Normal
	4125	310	406	Normal
	4126	309	417	Normal
	4127	320	402	Normal
	4128	349	415	Normal
	4129	338	403	Normal
	4130	340	414	Normal

9.3. Attached Table 3 Sensitization Dermal Reactions of Positive Group

Group	Animal Number	(24±2) h before phase II patch application		Hours following Challenge phase		Positive rate after challenge phase
		Left	Right	(24±2) h	(48±2) h	
Negative control (DNCB)	5131	0	0	0	0	0%
	5132	0	0	0	0	
	5133	0	0	0	0	
	5134	0	0	0	0	
	5135	0	0	0	0	
Positive control (DNCB)	6136	3	3	3	3	100%
	6137	3	2	2	2	
	6138	3	3	3	3	
	6139	3	3	3	3	
	6140	2	3	3	2	

Note: The data of positive control came from MED202007235-08 (Completed Date: 2020-09-12)

9.4. Attached Table 4 Weight Change and Clinical Observation of Positive Group

Group	Animal Number	Weight (g)		Clinical observation except dermal reactions
		Test began	Test end	
Negative control (DNCB)	5131	350	432	Normal
	5132	337	418	Normal
	5133	323	417	Normal
	5134	324	405	Normal
	5135	316	393	Normal
Positive control (DNCB)	6136	338	416	Normal
	6137	349	424	Normal
	6138	310	388	Normal
	6139	356	432	Normal
	6140	340	417	Normal

Note: The data of positive control came from MED202007235-08 (Completed Date: 2020-09-12)

End of Report