Transducer Protector

Skin Sensitization Study (Maximization Test)

FINAL REPORT

Client: Finetech Research and Innovation Corporation
Testing Institution: SGS Taiwan Ltd
Report No. : UB/2013/70737A-04
Report Date: 2013.11.06

Note:

1. The content of this report is invalid if it is not presented as the entire report.
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3. The results shown in this test report refer only to the test article(s) tested.
4. The report is the Chinese version of translations UB/2013/70737A-05

STUDY SCHEDULE

Skin Sensitization Study (Maximization Test):

Transducer Protector

Report No.:	UB/2013/70737A-04
Test article registration date:	2013/08/05
Animal grouping:	2013/10/04
Experimental starting date:	2013/10/07
Induction phase I:	2013/10/07
Induction phase II:	2013/10/14
Challenge phase:	2013/10/29
Clinical sign observation (24h):	2013/10/31
Clinical sign observation (48h):	2013/11/01

Testing Institution

Name: SGS TAIWAN LTD.

Address: No. 38, Wu Chyuan 7th Rd., New Taipei Industrial Park, Wu Ku Dist., New Taipei City 24890, Taiwan (R. O. C.)

Subcontract Lab

Name: LEON Biotechnology Company Limited Biocompatibility Testing Laboratory

Address: 4F.-2, No. 288-8, Xinya Rd., Qianzhen Dist., Kaohsiung City 806, Taiwan (R.O.C.)

Client / Sponsor

Name: Finetech Research and Innovation Corporation

Address: No.29, Anle St., Xiushui Township, Changhua County 504, Taiwan (R.O.C.)

TEST ARTICLE INFORMATION

INFORMATION FOR ☒ TEST ARTICLE/ ☐ CONTROL ARTICLE

Sponsor Company Name	Finetech research and innovation corporation
Sponsor Address	No.29, Anle St., Xiushui Township, Changhua County 504, Taiwan (R.O.C.)
Contract study item	☒ Base on the contract ☐ Others _____
Name of Test article/ Control article	Transducer Protector
Batch/Lot number	☐ Base on the specific number on the package : _____ ☐ Base on the date on the package : _____ ☐ Base on the arrived date ☑ Others : N/A
Specification & Amount	10pcs/pack * 7packs (e.g.10ml / bottle * 6 bottles)
Retention amount (Note 2)	The amount of the same lot is sufficient for ☐ One test ☐ Two test (for retention)
External features	External features: ☐ liquid ☐ powder ☐ tablet ☐ capsule ☒ Other column Color : translucent white
Major components & Purity	Major components: Polypropylene meterial housing with membrane Purity: _____
Solvent and solubility	N/A
Storage condition	☒ Room temperature ☐ 4℃ ☐ Dry ☐ Light sensitive ☐ Others _____
Expiration date(Note 3)	☐ Date: ____/____/____(YYYY/MM/DD) or ☒ Period : 2 year 0 month 0 day
Attachment(Note 4)	☐ Certificate of Analysis ☐ Material Safety Data Sheet ☐ Stability Test Result ☐ Other : _____ ☒ No attachment (Note4)
Sterilization	Has been sterilized ☐ YES ☒ NO (If Yes, please select the following item) Methods ☐ EOsterilization ☐ Gamma sterilization ☐ Steam sterilization ☐ Other_____
Categorization of devices (The column is only for device used)	1. ☒ Contact with intact skin or mucosa (cumulative contact duration) ☒ Short-term (no greater than 4 hr) ☐ Long-term (exceeding 4 hr) Maximum duration is_____hrs 2. ☐ Implanted device
Specific requirement (Note 5)	N/A

Sponsor Signature/ Date : Golden Li 2013. July 12th.

Note 1. Above all information is disclosure by the sponsor.
Note 2. If the sponsor doesn't provide the retention of test article/control article, the retention of a reserved test article/control article from each batch of test article /control article is the responsibility of the Sponsor.
Note 3. If the effective period is less than 5 years, the test article/control article will be retained till the expiry date. If the effective period is longer than 5 years, the test article/control article will be retained for 5 years only.
Note 4. Determination and documentation of identity, strength, purity, stability, composition, method of synthesis, fabrication, derivation or other characteristics of the test article/control article are the responsibility of the Sponsor.
Note 5. The test article/control article which has been destroyed or cutting will be discarded after the end of experiment. For retention or return of the kind of test article/control article, please indicate in the "special requirement". The human intake suggests or dose requested by the sponsor also can fill in the "special requirement". Note treatment method after test if the test article need to be retreated
Note 6. The code number of test article is the same as the report number.
Note 7. Note 'N/A' if not applicable. Do not leave blank.

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SGS

STATEMENT OF GLP COMPLIANCE

All study activities performed by SGS Taiwan and LEON Biotechnology Company Limited Biocompatibility Testing Laboratory are carried out in compliance with the GLP (Good Laboratory Practices) for Nonclinical Laboratory Studies (Department of Health, Taiwan, 2006), current OECD Principles of Good Laboratory Practice (Organization for Economic Cooperation and Development, Paris, ENV/MC/CHEM (98) 17) and U.S. Food and Drug Administration Good Laboratory Practice Regulations, 21 CFR Part 58. (1987).The study is conducted in accordance with the protocol and standard operating procedures and monitored in conformity with the protocol. All laboratory data are accurately recorded and verified. SGS Taiwan and LEON Biotechnology Company Limited Biocompatibility Testing Laboratory make no GLP compliance claim for characterization and verification of the test article identity and properties; this is the responsibility of the sponsor.

Study Director:

Howard Kao 2013.11.08

Howard Kao / SGS Taiwan Ltd. Date Completed

Deputy of
Facility Manager: Amy Liu 2013.11.08

Amy Liu / SGS Taiwan Ltd. Date Completed

SGS

QUALITY ASSURANCE STATEMENT

This study was audited by Quality Assurance personnel of SGS Life Science Service. The QA inspection report includes review of study plan, result of a study-based audit and results of audit of raw data and study report. The audit report was issued upon the completion of each testing.

QA:

Amy Liu / SGS Taiwan Ltd.

2013.11.08
Date Completed

ARCHIVING

All the study-related records, protocol and the final report will be kept in archives room of SGS (TAIWAN) LTD and study-related raw data will be kept in archives cabinet of LEON Biotechnology Company Limited Biocompatibility Testing Laboratory for 5 years. Furthermore, retention of the test articles will be in Sample Storage Room of SGS (TAIWAN) LTD for 5 years. All of the records and test articles are handled according to GLP guideline. Agent authorized by the sponsor can apply for the review according to SGS procedure.

Archives Room Address

SGS TAIWAN LTD.: No. 38, Wu Chyuan 7th Rd., New Taipei Industrial Park, Wu Ku Dist., New Taipei City 24890, Taiwan (R. O. C.)

LEON Biotechnology Company Limited Biocompatibility Testing Laboratory:

4F.-2, No. 288-8, Xinya Rd., Qianzhen Dist., Kaohsiung City 806, Taiwan (R.O.C.)

Archiving List	
Final Report	Final Report Copy
Raw Data*	Skin Sensitization Study (Maximization Test) Data Sheet
Records	Application Form Information for test article-control article and other supplementary record
Protocol	Protocol

*kept in archives cabinet of LEON Biotechnology Company Limited Biocompatibility Testing Laboratory

ABSTRACT

The study was to investigate the response of skin sensitization of "Transducer Protector" extracts on guinea pigs. The experiment was performed by following ISO 10993-10. After polar extraction of the test article, the extracts were applied twice in induction phase and once in challenge phase. Approximately 24 hrs and 48 hrs after challenge phase, neither the control nor the test group showed significant skin response on the treated areas, according to the criteria of "Magnusson and Kligman scale". The results indicated that the "Transducer Protector" extracts did not produce skin sensitization in guinea pigs.

PURPOSE

When direct contact with human tissues is anticipated, medical device should be carefully tested for biocompatibility according to the nature and duration of the contact to avoid potential physiological damage caused by hypersensitive substances produced or contaminated during manufacture. In this study, guinea pig skin sensitization study (Maximization test) was performed to evaluate the possibility of skin sensitization after topical applications of the test article "Transducer Protector" extracts on the skin of guinea pigs. The experiment is performed by following ISO 10993-10. After polar extraction of the test article, the extracts are applied twice in induction phase and once in challenge phase.

EXPERIMENTAL DESIGN

A. Animals

1. Species/Strain	Guinea Pig (Hartley strain)
2. Resource	National Laboratory Animal Center
3. Body weights (sex)	300~500 g (male)
4. Quarantine/acclimation	Animals were subjected to quarantine and acclimated before test. Guinea pigs were selected by veterinarians based on health status.

B. Feeding and care

1. Environment	
Temperature	20~26 ℃(30~70%)
2. Cage and animal no.	
Quarantine/acclimation	5 guinea pigs /cage
Study period	5 guinea pigs /cage
3. Feed	
Name	Maintenance diet-Guinea pigs
Brand	Altromin 3023
Way to supply	*ad libitum*
4. Drinking water	
Sort	RO Water
Way to supply	*ad libitum*

C. Individual and group identification

1. Individual identification	Animals were identified by ear-marking.
2. Group identification	Cages were properly labeled for identification including the Study Title/No., Administration/ Observation Period, Room No., Cage No., Quantity/cage, Species, Strain, Sex, In House Date, In House Age, Animal ID No.

D. Administration of test article extracts and control solutions

1. Preparation

Polar: According to ISO 10993-12 guidelines, the ratio of the test article to the extractant is 0.2 g sample/ml. In the study, the test article was immersed in 0.9% saline (TAI YU PHARMACEUTICAL CO., LTD) for 72 hrs at 50°C with constant agitation (100 rpm). The pH

adjustment, filtration and centrifugation are not conducted. The appearance of the extracts was not different from the control solution.

2. Control solution: 0.9% saline

3. Method, route and frequency of administration

Induction phase: Two topical applications: intracutaneous injection and spread to the dermal area (upper backside).

Challenge phase: One topical application: spread to the dermal area (flank).

E. Groups

Animals were divided into control group (5 animals) and test group (10 animals).

Control group: 0.9% saline

Test group : Test article extracts (solvent-0.9% saline).

F. Procedure

1. Prior to the study, furs of animal's backside was clipped from neck to scapular area with an electric animal shaver. Animals with scratches or skin diseases on the clipped skin surfaces were rejected from the study. The clipped area was approximately 8cm^2.
2. Induction phase Ⅰ : On the test day, three kinds of solutions or emulsions were prepared from the control solutions or test article extracts as follows:

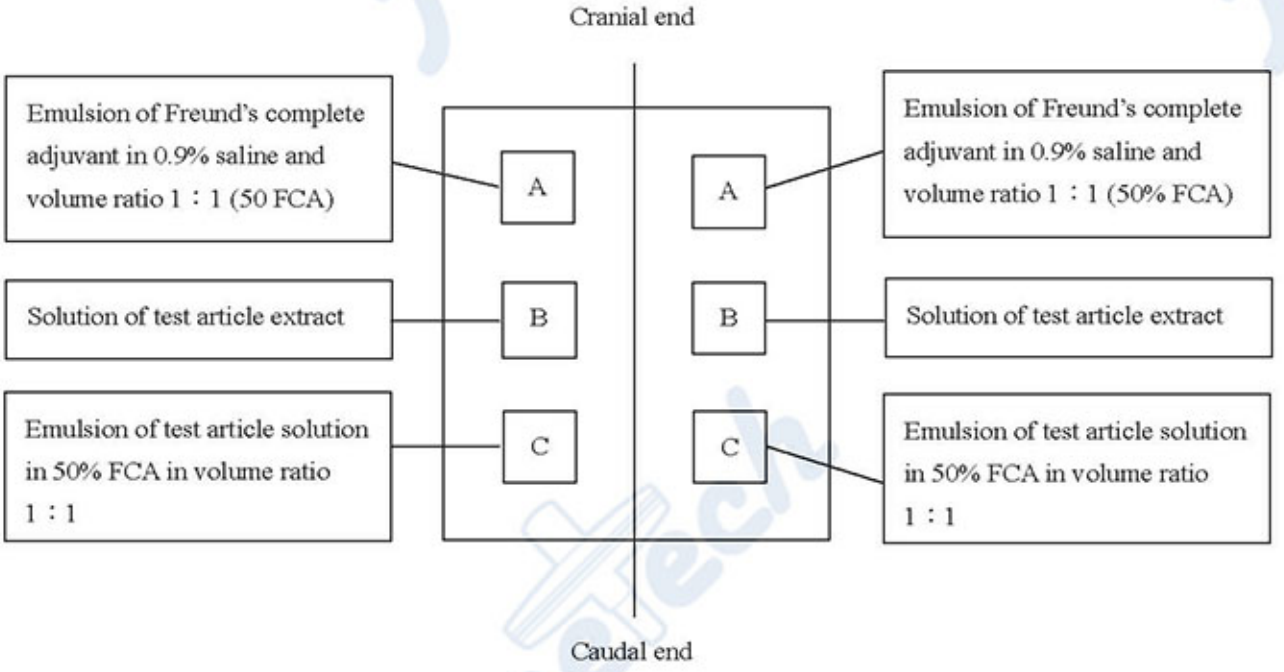
   Polar:

   (A) Emulsion of Freund's complete adjuvant (Sigma F5881) in 0.9% saline and volume ratio 1:1 (50% FCA).

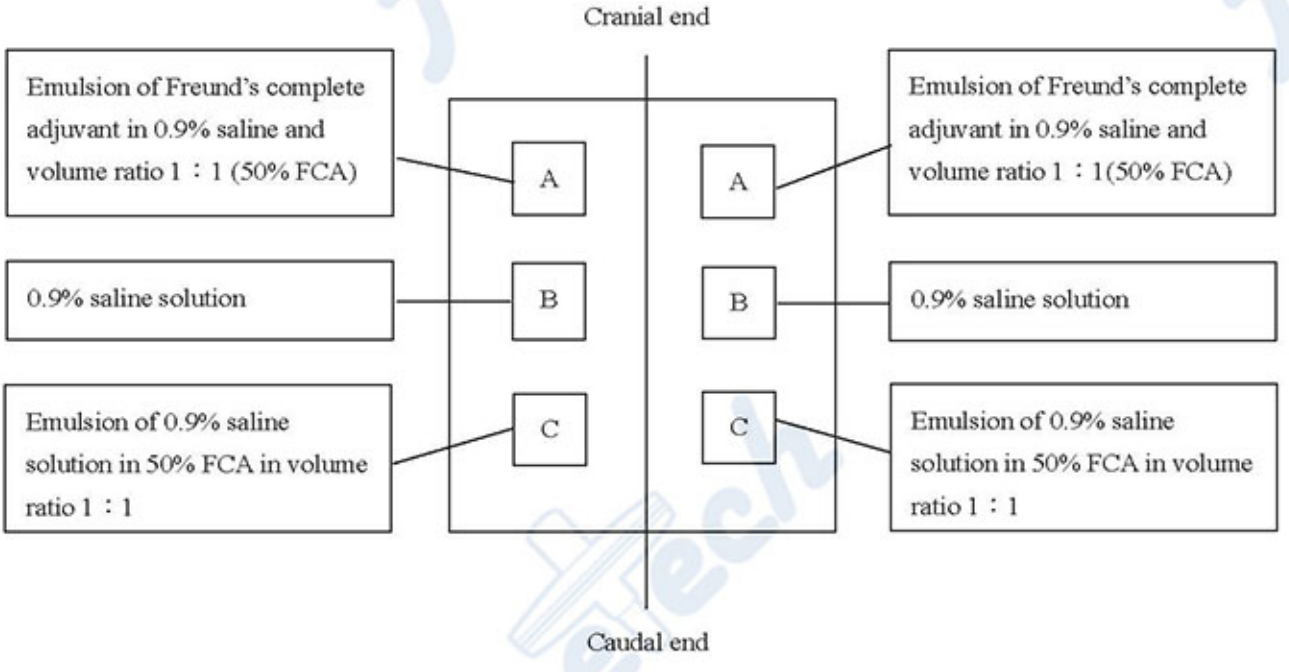
   (B) Solution of either test article extracts or 0.9% saline.

   (C) Emulsion of either test article extracts or 0.9% saline in 50% FCA in volume ratio 1:1.

   Make a pair of 0.1 ml intradermal injection of each of the following condition into each animal at the injection sites (A, B and C), as shown in the figure below.
3. Induction phase Ⅱ : One week later, the injection sites were applied with 10% of sodium dodecyl sulfate (SDS) for 24 hours. Then, saturate an appropriate absorbent gauze patch (about 8 cm^2) with the test article extracts or control solutions, and applied the patch to the clipped skin under an occlusive dressing secured by a wrap around the torso of the animal for another 48 hours.
4. Challenge phase: On the challenge day (2 weeks after induction phase II), fur of flank of the animals were clipped. An appropriate site of this hairless area was selected and applied by the patches that soaked with the control solutions or test article extracts. Secure with an occlusive dressing. Remove the dressings and patches after 24 hrs.



Test-1 group, 10 animals (extract solvent-0.9% saline)



Control-1 group, 5 animals (0.9% saline)

G. Animal observations and items for examination

Observe the appearance of the challenge skin sites of the test and control animals 24 hrs and 48 hrs after removal of the dressings. Describe and grade the skin reactions for erythema and oedema according to the Magnusson and Kligman grading given in Appendix 1 for each challenge site and at each time interval. Magnusson and Kligman grades of 1.0 or greater in the test group generally indicate sensitization, provided grades of less than 1.0 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.

RESULTS

Approximately 24 hrs and 48 hrs after challenge phase, neither the control nor the test group showed significant skin response on the treated areas (Figure1). None of the test or control guinea pigs had a mean score increase of 1 or more in the observation period (Table 1).

CONCLUSION

The results indicated that the polar extracts of "Transducer Protector" did not produce skin sensitization in guinea pigs.

RELIABILITY CHECK

The positive control study was finished at 2013.07.25. According to ISO 10993-10 guidelines, positive control shall be performed at least once every six month. α-hexylcinnamicaldehyde (Sigma 291285) were used for positive control substances. The method for the positive control assay was identical to the method described above in this study. For the induction phase, 0.5% and 85% α-hexylcinnamicaldehyde was used. For the challenge phase, 85% α-hexylcinnamicaldehyde was used.

Animals in the positive control group exhibited discrete erythema to confluent erythema at the challenge site. All reactions in the positive control group scored of 1~2, had a 100% incidence and 1.4 severity (24 hour score) are indicated that is positive sensitization reaction.

REFERENCES

1. Good Laboratory Practice for Nonclinical Laboratory Studies (2000) Department of Health, the Executive yuan.

2. Skin sensitization, OECD guideline for the testing of chemicals #406 (1992) OECD.

3. Good Laboratory Practice for Nonclinical Laboratory Studies. Title 21 of the U.S. Code of Federal Regulations, Part 58 (1997) United States Food and Drug Administration.

4. Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization, ISO 10993 (2010).

5. Biological evaluation of medical devices-Part 12：Sample preparation and reference materials ISO 10993 (2012), ISO.

6. Current OECD Principles of Good Laboratory Practice (Organization for Economic Cooperation and Development, Paris, ENV/MC/CHEM (98) 17).

FIGURES

1. Pictures for Observation of Skin Response (Polar)

Control group: 24th h after administration

Control group: 48th h after administration

Test group: 24th h after administration

Test group: 48th h after administration

TABLE

Skin Response Grade of Individual Animal

Group	Sex	Number of animals	24 hrs after challenge phase	48 hrs after challenge phase
Control "0.9% saline"	M	C1	0	0
		C2	0	0
		C3	0	0
		C4	0	0
		C5	0	0
		Mean score	0	0
Test "Transducer Protector Extracts (saline)"	M	130803-GPMT-01	0	0
		130803-GPMT-02	0	0
		130803-GPMT-03	0	0
		130803-GPMT-04	0	0
		130803-GPMT-05	0	0
		130803-GPMT-06	0	0
		130803-GPMT-07	0	0
		130803-GPMT-08	0	0
		130803-GPMT-09	0	0
		130803-GPMT-10	0	0
		Mean score	0	0

F: female; M: male

APPENDIX

Magnusson and Kligman Scale (ISO 10993-10)

Patch test reaction	Grading scale
No visible change	0
Discrete or patchy erythema	1
Moderate and confluent erythema	2
Intense erythema and swelling	3

TEST ARTICLE PHOTO