Transducer Protector

Irritation Test:

Animal Intracutaneous Reactivity Test

FINAL REPORT

Client: Finetech Research and Innovation Corporation
Testing Institution: SGS Taiwan Ltd.
Report No. : UB/2013/70737A-06
Report Date: 2013/09/24

Note:

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3. The results shown in this test report refer only to the article(s) tested.
4. The report is the Chinese version of translations UB/2013/70737A-07

STUDY SCHDULE

Irritation Study: Animal Intracutaneous Reactivity Test

Transducer Protector

Report No.: UB/2013/70737A-06

Test article registration date：2013/07/16

Experimental starting date：2013/09/16

Experimental completion date：2013/09/19

Animal in-grouping: 2013/09/13

Test article administration: 2013/09/16

Observation of dermal reaction: 2013/09/17~2013/09/19

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.)

INFORMATION FOR TEST ARTICLE

SGS

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.

版次：3.1 試驗-對照物質資料表 Information for test article-control article
發行日期：2013.06.14

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STATEMENT OF GLP COMPLIANCE

All study activities performed by SGS Taiwan 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 makes 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 — 2013.10.31

Howard Kao / SGS Taiwan Ltd. — Date Completed

Deputy of
Facility Manager:

Amy Liu — 2013.10.31

Amy Liu / SGS Taiwan Ltd. — Date Completed

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 final report of testing.

QA Manager:

Amy Liu / SGS Taiwan Ltd.

2013.10.31

Date Completed

ARCHIVING

All the study-related protocol and the final report will be kept in archives room of SGS (TAIWAN) LTD for 5 years. Agent authorized by the sponsor can apply for the review according to SGS procedure.

Archiving Room Address:

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

ABSTRACT

The study was to investigate the response of intracutaneous irritation of "Transducer Protector" extract on New Zealand White Rabbits. The experiment was performed by following ISO 10993-10. After shaving fur of animals, inject the test article extract into five sites on one side of the back of each rabbit, and the control solution (0.9% saline and cottonseed oil) on the other. Dermal reactions were observed at the time sites of 24th, 48th and 72nd hrs.

The results showed that there were no significant clinical signs and gross findings in either the control or treatment group, and there were no mortalities. Furthermore, the final test sample score value was less than 1. Therefore, a single topical application of 0.2 ml of "Transducer Protector" extract did not cause intracutaneous irritation on New Zealand White Rabbits.

PURPOSE

This study was to follow ISO 10993-10 guideline for irritation study. The study was to evaluate the possibility of local irritant reaction after a single topical application of test article "Transducer Protector" extract on the intracutaneous of New Zealand White Rabbits. Simultaneously, this study also was to evaluate the reversibility when the injury is not serious.

EXPERIMENTAL DESIGN

A. Animals

1. Species/Strain	New Zealand White Rabbit
2. Resource	ANIMAL HEALTH RESEARCH INSTITUTE
3. Body weights (sex)	>2 kg (female)(3~12 month)
4. Quarantine/acclimation	Once animals were introduced in-house, they were subjected to quarantine and acclimated before treatment. Rabbits were selected by veterinarians based on health status.

B. Feeding and care

1. Environment

Temperature (Humidity)	23±3 ℃(30~70%)

2. Cage and animal no.

Quarantine/acclimation	1 rabbit/cage
Study period	1 rabbit/cage

3. Feed

Name	Altromin 2023
Brand	Altromin, Germany
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 are labeled by ear-marking.

2. Group identification

Cages are 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., Keeper and Deputy.

D. Grouping

Group	Control	Treatment
Number of animals	3	3
Treated article	1. 0.9% saline 2. cottonseed oil	Test article extract (solvent- 0.9% saline and cottonseed oil)

Remark: The control solution and the test article were applied on the different regions of the same rabbit.

A. Administration of test article and control solution

1. Preparation

Polar preparation:

According to ISO 10993-12 guidelines, the ratio of the test article to the extract was 0.2 g sample /ml extract. 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.

Non-polar preparation:

According to ISO 10993-12 guidelines, the ratio of the test article to the extractant was 0.2 g sample /ml extractant. In the study, the test article was immersed in cottonseed oil (SIGMA C7767) for 72 hrs at 50°C with constant agitation (100 rpm). The pH adjustment, filtration and centrifugation are not conducted.

Furthermore, the appearance of the extracts was not different than the control group for polar and non-polar extraction of the test article.

2. Method, route and frequency of administration

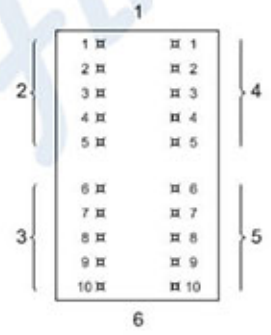
A single dose of the test article and control solution was injected intracutaneously into each rabbit.

3. Volume of administration

0.2 ml of test article extract and 0.2 ml of control solution was administered.

F. Procedure

1. Prior to study, furs of animal's backside were one-way clipped with an electric animal shaver, so that a sufficient distance on both sides of the spine for injection of the extract was allowed. Animals with scratches or skin diseases on the clipped skin surfaces were rejected from the study.
2. Test article administration: On the treatment day, inject 0.2 ml of the test article extract (solvent-0.9% saline) at five sites. Similarly, inject 0.2ml of test article extract (solvent-cottonseed oil) at five sites on posterior side of each rabbit (As shown in figures below).
3. Control solution administration: On the treatment day, inject 0.2 ml of 0.9% saline at the other five sites.Similarly, Inject 0.2 ml of cottonseed oil at five sites on posterior side of each rabbit (As shown in figures below).



Key
1 cranial end
2 0.2 ml injections of polar extract
3 0.2 ml injections of non-polar extract
4 0.2 ml injections of polar solvent control
5 0.2 ml injections of non-polar solvent control
6 caudal end

(ISO 10993-10)

G. Animal observations and items for examination

1. Irritant reaction evaluation

Based on "Grading system for intracutaneous reaction" (Appendix 1), the dermal reactions at the treated areas were observed and recorded, including erythema, edema, irritation, corrosion, recovery and other toxicity, at the time sites of 24th,48th and 72nd hrs after the injection of the test article extract and control solution.

2. Determination of dermal reaction

After the 72hrs grading, all erythema grades plus edema grades were totaled separately for

each test article and 0.9% saline and cottonseed oil. To calculate the score of a test sample or blank on each animal, divide each of the totals by 15 (3 scoring time sites × 5 test or blank sample injection sites). To determine the overall mean score for each test sample and each corresponding blank, add the scores for the three animals and divide by three. The final test sample score can be obtained by subtracting the score of the blank from the test sample score. The requirements of the test were met if the final test sample score was 1.0 or less. If at any observation period the average reaction to the test sample was questionably greater than the average reaction to the blank, repeat the test using three additional rabbits. The requirements of the test were met if the final test sample score was 1.0 or less.

3. Animal management

   Autopsy would be performed immediately for those animals found dead.

RESULTS

The results showed that there were no significant clinical signs and gross findings in either the control or treatment group, and there were no mortalities (Figure 1~3; Table 1-1~1-2). The final test sample score values of all groups were less than 1(polar=0; non-polar=0).

CONCLUSION

The study results showed that a single application of "Transducer Protector" extract induced neither significant clinical signs nor dermal gross changes on New Zealand White Rabbits at each time point. Furthermore, the final test sample score value was less than 1.0. Therefore, a single topical application with 0.2 ml of "Transducer Protector" extract did not cause irritation on New Zealand White Rabbits.

REFERENCES

1. 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.

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

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

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

5. Acute dermal irritation/corrosion, OECD guideline for the testing of chemicals. #404 (2002) OECD.

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

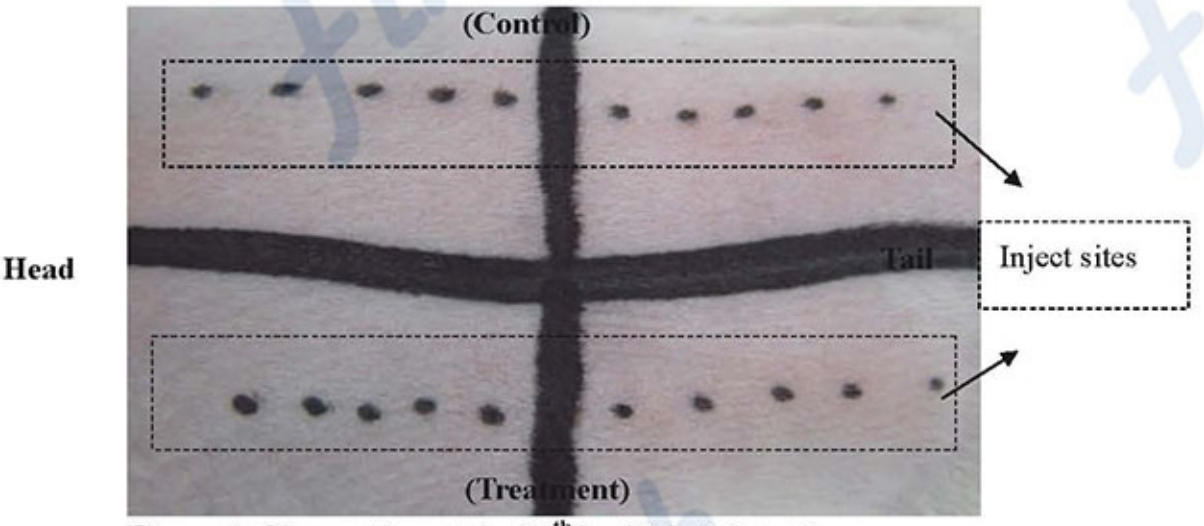


Figure 1. Observation at the 24th h of Administration

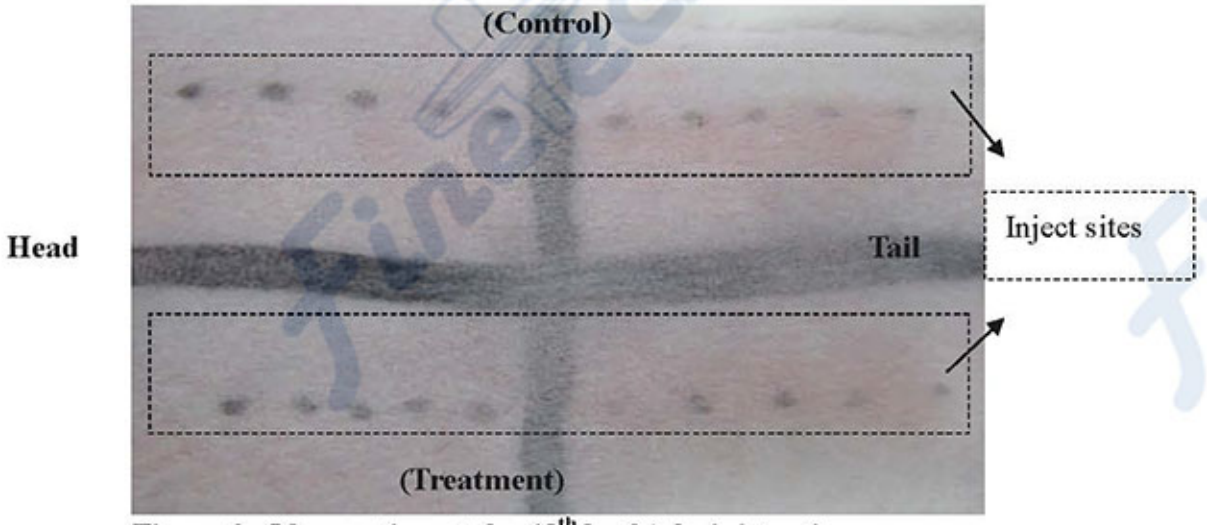


Figure 2. Observation at the 48th h of Administration

Figure 3. Observation at the 72nd h of Administration

Table 1-1. Individual Animal Grade in Clinical Observation (Polar Group)

Applied Regions (Dorsal Skin)	Treated article	Sex	Animal No.	Items for Grading	Clinical Observation (time point/h)		
					24	48	72
Backside (five sites)	Treatment group "Transducer Protector" extract	F	130803-IR-01	Erythema and eschar formation	0	0	0
				Oedema formation	0	0	0
		F	130803-IR-02	Erythema and eschar formation	0	0	0
				Oedema formation	0	0	0
		F	130803-IR-03	Erythema and eschar formation	0	0	0
				Oedema formation	0	0	0
Backside (the other five sites)	Control group "0.9% saline"	F	130803-IR-01	Erythema and eschar formation	0	0	0
				Oedema formation	0	0	0
		F	130803-IR-02	Erythema and eschar formation	0	0	0
				Oedema formation	0	0	0
		F	130803-IR-03	Erythema and eschar formation	0	0	0
				Oedema formation	0	0	0

F: Female

Table 1-2. Individual Animal Grade in Clinical Observation (Non-Polar Group)

Applied Regions (Dorsal Skin)	Treated article	Sex	Animal No.	Items for Grading	Clinical Observation (time point/h)		
					24	48	72
Backside (five sites)	Treatment group "Transducer Protector" extract	F	130803-IR-01	Erythema and eschar formation	1	1	1
				Oedema formation	0	0	0
		F	130803-IR-02	Erythema and eschar formation	1	1	2
				Oedema formation	0	0	0
		F	130803-IR-03	Erythema and eschar formation	1	1	1
				Oedema formation	0	0	0
Backside (the other five sites)	Control group "Cottonseed oil"	F	130803-IR-01	Erythema and eschar formation	1	1	1
				Oedema formation	0	0	0
		F	130803-IR-02	Erythema and eschar formation	1	1	2
				Oedema formation	0	0	0
		F	130803-IR-03	Erythema and eschar formation	1	1	1
				Oedema formation	0	0	0

F: Female

Appendix 1. Grading System for Intracutaneous Reaction (ISO 10993-10)

Dermal Reaction	Grade
Erythema and eschar formation	
No erythema	0
Very slight erythema	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation	4
Oedema formation	
No oedema	0
Very slight oedema	1
Slight oedema (edges of area well defined by definite raising)	2
Moderate oedema (raised approximately 1 mm)	3
Severe oedema (raised more than 1 mm and extending beyond the area of exposure)	4

TEST ARTICLE PHOTO