



瑞德生物科技有限公司
MASTER LABORATORY CO.,LTD.

Pyrogen Study in Rabbits

Master Laboratory Co., Ltd. Animal Laboratory

Address: 3F, No. 221, Sec. 1, Zhongxing Rd., Zhudong Township,

Hsinchu County 31053, Taiwan (R.O.C.) TEL: (886-2)25176117



**Centrifuge Tubes 15, 50mL
Pyrogen Study in Rabbits
STUDY REPORT**

Sponsor: Finetech Research & Innovation Corp.

Testing Institution: Master Laboratory Co., Ltd.

September 2021



FINAL REPORT

Report No.: 21S250T09-01-R01

Report No.: 21S250T09-01-R01

Experimental starting date: 08.24.2021

Test article registration date: 08.26.2021

Animal in-housing: 08.24.2021

Extraction of test article: 08.29.2021

Experimental administration date: 09.01.2021

Body temperature measurement after administration: 09.01.2021

Animal sacrifice date: 09.01.2021

Experimental completion date: 09.01.2021

Study Announcement

1. The study report is valid for the test article used only, and shall not be partly recopied or extracted for another object.
2. The study report is invalid without the endorsement of Master Laboratory Co., Ltd.



SIGNATURE OF STUDY PERSONNEL

Study Director

Bo Han Huang
Bo Han Huang

09.10.2021
Date

Facility Management

Alan Hsieh
Alan Hsieh

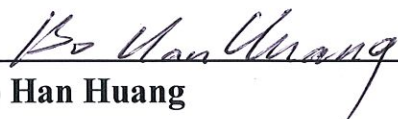
09.10.2021
Date

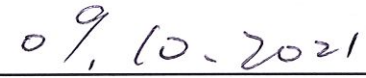


GLP COMPLIANCE STATEMENT

The study met with the technical requirements of the protocol, and the applicable guidance and regulations, which included the Good Laboratory Practice for Non-Clinical Laboratory Studies (FDA, 21 CFR, Part 58, 2019), OECD Principles of Good Laboratory Practice (No. 1, 1997) and Good Laboratory Practice for Non-Clinical Laboratory Studies (Food and Drug Administration, R.O.C., 2019), except the parts of test article identification and related analyses (21 CFR §58.105, §58.113, FDA; 6.2.2-6.2.5, OECD GLP No.1, 6.2.2-6.2.5, TFDA GLP). To the best of our knowledge, there were no deviations from the approved study plan and no adverse problem that would affect the integrity of this study or the interpretation of the study result.

Study Director


Bo Han Huang


Date



QUALITY ASSURANCE STATEMENT

The Quality Assurance personnel had inspected the conduct of different phases of the study according to a predetermined study schedule. To the best of our knowledge, there were no deviations from the study plan and standard operating procedures that would affect the integrity of this study. This report has been audited by the QA personnel in accordance with the appropriate standard operating procedures of Master Laboratory Co., Ltd. described the methods and procedures used in the study, and the reported results accurately reflect the raw data generated during this study.

Listed below are the phases in this study that were audited by the QA personnel and the dates the audits were performed and findings reported to facility management (FM).

Inspection record:

Date of inspection	Phase	Date Reported to SD	Date Reported to FM
08.23.2021	Study protocol, Personnel quality and test article. (Study base)	08.23.2021	08.23.2021
09.03.2021	Study system, study report, raw data, and final report. (Study base)	09.03.2021	09.03.2021

Quality Assurance unit in charge

Ying Chun Chen
Ying Chun Chen

09.10.2021
Date



Contract Research Organization and Sponsor Information

1. CRO:

- a. Title: Master Laboratory Co., Ltd.-Animal laboratory
- b. Address: 3F, No. 221, Sec. 1, Zhongxing Rd., Zhudong Township, Hsinchu County 31053, Taiwan, R.O.C.

2. Study Director:

- a. Name: Bo Han Huang
- b. Address: 3F, No. 221, Sec. 1, Zhongxing Rd., Zhudong Township, Hsinchu County 31053, Taiwan, R.O.C.

3. Study personnel:

- a. Name: Kuo Shu Huang
- b. Address: 3F, No. 221, Sec. 1, Zhongxing Rd., Zhudong Township, Hsinchu County 31053, Taiwan, R.O.C.

4. Quality Assurance personnel:

- a. Name: Ying Chun Chen
- b. Address: 3F, No. 221, Sec. 1, Zhongxing Rd., Zhudong Township, Hsinchu County 31053, Taiwan, R.O.C.

5. Sponsor:

- a. Title: Finetech Research & Innovation Corp.
- b. Address: No. 29, Anle St., Andong Vil., Xiushui Township, Changhua County 504, Taiwan



CONTENTS

Summary..... 8

Introduction..... 9

Materials and Methods..... 9

Results..... 14

Conclusion..... 14

References..... 15

Table..... 16

Appendixes..... 17



SUMMARY

The present study was performed in compliance with USP 43/NF38:2020 <151> to evaluate the pyrogen limits of test article “Centrifuge Tubes 15, 50mL” extracts in the New Zealand White Rabbits by single dose (10 ml/kg) injection in ear vein. The body temperatures of rabbits were measured five times after the single dose intravenous injection. The body temperatures of the administered rabbits were increased within acceptable ranges, pyrogen study responses were negative, the difference between the control temperature and the highest temperature among the five-time measurements was not over 0.5°C. According to the results, the test article extracts met the requirements for the absence of pyrogens.



INTRODUCTION

The testing was performed in compliance with USP 43/NF38:2020 <151> to evaluate pyrogen limits of the test article extracts in the New Zealand White Rabbits. The body temperatures of rabbits were measured five times after a single dose (10 ml/kg) intravenous injection in ear vein.

MATERIALS AND METHODS

1. Animals

1.1. Species/Strain: New Zealand White Rabbit

1.2. Resource: Hui Jun

1.3. Body weights (Gender): > 1.5kg (Male)

1.4. Quarantine/acclimation: (MSAT-SOP-AM-001)

Animals were subjected to be quarantined and acclimated before treatment.

Veterinarian ensured the animal health status before the treatment.

1.5. Reasons chosen for animal study:

New Zealand white rabbit was proven to be suitable for pyrogen studies, and widely used in single dose pyrogen studies.

1.6. Groups

Group	Dosage of administration (ml/kg)	Gender	Number
Preliminary test	10	Male	3



2. Feeding and care (MSAT-SOP-AM-002)

2.1. Housing: Rabbit room

2.2. Environment:

a. Temperature: $19 \pm 3^{\circ}\text{C}$

b. Humidity: $50 \pm 20\%$

c. Light Cycle: 12 hours light and 12 hours dark

2.3. Cage and animal number.

a. Quarantine/acclimation: 1 rabbit/cage

b. Study period: 1 rabbit/cage

2.4. Feed

a. Name: Prolab Rabbit Diet

b. Brand: Lab Diet, U.S.A.

c. Way to supply: *ad libitum*

d. Source: PMI Nutrition International, U.S.A.

2.5. Drinking water

a. Sort: RO Water

b. Way to supply: *ad libitum*

3. Individual and group identification (SOP: MSAT-SOP-AM-025)

3.1. Individual identification: Tested animals were identified by ear-marking.

3.2. Group identification: Cages were properly labeled for identification including the Study Title/No., Administration, Observation Period, Room No., Cage No., Quantity/cage, Species, Strain, Gender, In House Date, In House Age, Animal ID No., Keeper and Deputy.



4. Test article and extraction vehicle

4.1. Test article: Centrifuge Tubes 15, 50mL, Lot. 210326

4.2. Extraction vehicle (Saline): CHI SHENG CHEMICAL CORPORATION, Lot. P5152; Solutio Natrii Chloridi Isotonica 0.9% 500 ml

5. Temperature measuring machine:

5.1. Vendor: LUTRON ELECTRONIC ENTERPRISE CO., LTD.

5.2. Brand: PRECISION 0.01 DEGREE THERMOMETER

6. Administration of test article

6.1. Preparation (MSAT-SOP-GE-014): According to ISO 10993-12:2021 guideline.

Measured the surface area of test article, and immersed it in saline for 72 ± 2 hr at $50 \pm 2^\circ\text{C}$ with constant agitation (100 rpm) with an extraction ratio of $3 \text{ cm}^2/\text{ml}$. After extraction, the extract was used immediately; the appearance of test article extract was clear and colorless without particulates present.

6.2. The test article extract was injected intravenously into the ear vein of each rabbit with a single dosage of 10 ml/kg.

6.3. The injection volume of test article extract was based on body weights which recorded on the first day of study prior to administration.

7. Procedure (MSAT-SOP-ME-008)

7.1. Three days before the start of the experiment, body temperatures of the 3 rabbits were measured for 4 times. The criteria which rabbits selected for pyrogen study is that body temperature of each rabbit did not exceed 39.8°C and the difference of body temperature is not more than 1°C between the highest and the lowest body temperatures among the four temperature measurements.



- 7.2. Inserted the temperature measuring machine probe into the rectum of the test rabbit to a depth of not less than 7.5 cm and measured with a constant time of 1 minute.
- 7.3. During the study, animals were fasting and only RO water was provided. Not more than 30 minutes prior to the injection of the test article extract, determined the control temperature of each animal using anus thermometer (accuracy $\pm 0.01^{\circ}\text{C}$). Every appliance used in the study was also pyrogen-free.
- 7.4. Three rabbits whose control temperatures did not vary by more than 1°C from each other were collected for use. Any rabbit with a control temperature exceeding 39.8°C was excluded. Test article extract (warm up to $37 \pm 2^{\circ}\text{C}$) was injected into ear vein of the rabbit. The time of administration was not over than 10 minutes. Body temperatures were measured subsequently to the administration at 30-minute intervals between 1 and 3 hours. The differences of the highest body temperature among the five-time measurements and the control temperature were evaluated.

8. Criteria

- 8.1. If the difference between the control temperature and the highest temperature among the five-time measurements was not over 0.5°C , the test article would meet the requirements for the absence of pyrogen.
- 8.2. If any rabbit shows an individual temperature rise of 0.5°C or more, additional 5 rabbits will have to be tested.
- 8.3. If no more than three of eight rabbits show individual temperature rise of 0.5°C or more and if the maximum temperature rise of the eight individuals does not exceed 3.3°C , the materials under examination meets the requirements for the absence of pyrogens.



FINAL REPORT

Report No.: 21S250T09-01-R01

9. Archive of the record and data

- 9.1. All records were retained in the archives of Master Laboratory Co., Ltd. for a period of six years from the issue of the final report. Test article (retained sample) was retained until its expiration date. Archive address: 3F., No. 221, Sec. 1, Zhongxing Rd., Zhudong Township, Hsinchu County 31053, Taiwan (R.O.C.)



RESULTS

1. Body weight (Appendix 1)

Body weights of three animals were above 1.5 kg and were qualified for the study.

2. Control temperature (Table 2 and Appendix 2)

Control temperatures in three animals were 39.34°C, 39.08°C and 39.31°C, respectively.

3. Body temperatures measurement after test article administration (Appendix 3).

4. The elevation of body temperatures of the three rabbits were below 0.5°C (Table 3).

(Animal No. 1001: -0.09°C, Animal No. 1002: 0.08°C and Animal No. 1003: 0.09°C)

CONCLUSION

The study was performed in compliance with USP 43/NF38:2020 <151> to evaluate the pyrogen limits of test article extracts in the New Zealand White Rabbits by single dose (10 ml/kg) injection in ear vein. The body temperatures of rabbits were measured five times after the single dose intravenous injection. The response of pyrogen study was negative; therefore, the test article “Centrifuge Tubes 15, 50mL” extracts under examination met the requirements for the absence of pyrogens.



REFERENCES

1. Good Laboratory Practice for Nonclinical Laboratory Studies (2019) Food and Drug Administration, R.O.C.
2. Good Laboratory Practice for Nonclinical Laboratory Studies. Title 21 of the U.S. Code of Federal Regulations, Part 58 (2019) United States Food and Drug Administration.
3. Pharmacopeia US: Pyrogen Test, USP 43/NF38:2020 <151>.
4. Biological evaluation of medical devices-Part 11: Tests for systemic toxicity ISO 10993 (2017).
5. Biological evaluation of medical devices-Part 12: Sample preparation and reference materials ISO 10993 (2021).
6. Biological evaluation of medical devices-Part 12: Sample preparation and reference materials EN ISO 10993 (2021).
7. General requirements for the competence of testing and calibration laboratories. ISO/IEC 17025 (2017).



Table 1. Body temperature of Rabbits before study day

Animal number	Body temperature (°C) before study day			
	1 st	2 nd	3 rd	4 th
1001	39.23	39.35	39.33	39.28
1002	39.10	39.17	39.24	39.22
1003	39.34	39.26	39.38	39.40

Table 2. Control Temperature of rabbits

Animal number	Control temperature (°C)
1001	39.34
1002	39.08
1003	39.31

Table 3. Body Temperature Elevation

Animal number	Body temperature elevation after administration (°C)
1001	-0.09
1002	0.08
1003	0.09

Remark: Temperature elevation: the highest body temperature (Among five-time measurement) subtract control temperature.



FINAL REPORT

Report No.: 21S250T09-01-R01

Appendix 1. Individual Body Weight

Dosage (ml/kg)	Gender	Animal number	Weight (g)	Injection Volume (ml)
10	Male	1001	2483	25
		1002	2177	22
		1003	2123	21

Appendix 2. Control Temperature Records

Animal number	Body temperature before administration (°C)		Control Temperature (°C)
	1 st	2 nd	
1001	39.44	39.34	39.34
1002	39.31	39.08	39.08
1003	39.38	39.31	39.31

Remark: Measured body temperature readings recorded for the rabbit in 30 minutes before the administration. The final body temperature was the control temperature.

Appendix 3. Body Temperature Records (After Administration)

Animal number	Body temperature (°C) after administration					
	1 st	2 nd	3 rd	4 th	5 th	HBT-CT
1001	39.21	39.25	39.14	39.21	39.25	-0.09
1002	39.03	39.06	39.01	39.16	39.13	0.08
1003	39.35	39.30	39.34	39.40	39.31	0.09

Remark: Body temperatures were measured 1, 1.5, 2, 2.5 and 3 hr after administration for five times at half-hour intervals.

HBT: highest body temperature

CT: control temperature



Appendix 4. Test Article Information Sheet

Master Laboratory Co., Ltd.

Information for Test Article/ Control Article

Sponsor Company	Finetech Research & Innovation Corp.
Sponsor Address	No. 29, Anle St., Andong Vil., Xiushui Township, Changhua County 504, Taiwan
Contract Study item	<input checked="" type="checkbox"/> Base on the contract
Name of test article	Centrifuge Tubes 15 · 50mL
Major components	PP
Sample status	<input checked="" type="checkbox"/> Sterilized (<input type="checkbox"/> Gamma <input checked="" type="checkbox"/> EO <input type="checkbox"/> Steam) <input type="checkbox"/> Not Sterilized
Storage condition	<input checked="" type="checkbox"/> Room temperature (10°C~30°C) <input type="checkbox"/> 4°C <input type="checkbox"/> Others: _____
Expiry day	2024/03/25
Specific requirement	-
Lot number	<input type="checkbox"/> Base on the specific number on the package: _____ <input checked="" type="checkbox"/> Others: <u>210326</u>
Extract by	<input type="checkbox"/> Weight (0.2g/ml) Total weight of each test article: _____ <input checked="" type="checkbox"/> Surface (Sample thickness: <input checked="" type="checkbox"/> >1.0mm <input type="checkbox"/> 0.5-1.0mm <input type="checkbox"/> <0.5mm) Total area surface of each test article: _____
Absorption	<input checked="" type="checkbox"/> Non absorption <input type="checkbox"/> Water absorption rate: _____ / Oil absorption rate: _____
Sponsor Signature	<u>葉宜昭 2021.8.26</u>



Appendix 5. Test Article

