GLP STUDY REPORT

TEST FACILITY

STC (Dongguan) Company Limited
68 Fumin Nan Road,
Dalang, Dongguan, Guangdong,
China. (Zip code 523770)

SPONSOR

WINGRAM INDUSTRIAL COMPANY LIMITED
RM708, TECHNOLOGY PARK, NO.18 ON LAI STREET, SHATIN, N.T., HONG KONG

CONFIDENTIAL

STUDY TITLE

Skin Irritation Test of BioAcetate S70 according to ISO 10993-10:2010.

TEST ARTICLE NAME

BioAcetate S70

TEST ARTICLE IDENTIFICATION

CP-MD-4738
CSD NO.: CL20220109567

TABLE OF CONTENTS Page

Summary

The test article, BioAcetate S70, was evaluated for primary skin irritation in rabbits. This study was conducted based on the requirements of ISO 10993-10, Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization (2010). The test articles were extracted in 0.9% sodium chloride injection and Sesame oil. Two 2.5 cm ×2.5 cm sections of absorbent gauze patches with 0.5 mL test extracts/ control extracts were topically applied to the skin of each of three rabbits and left in place for 4 hours. The sites were graded for erythema and edema at 1, 24, 48 and 72 hours after removal of the single application.

There was no erythema and no edema observed on the skin of the animals treated with the test extracts. The Primary Irritation Index for the test extracts was calculated to be 0.0. The response of the test article was categorized as negligible.

Therefore, the test article, BioAcetate S70, passed the conditions based on the requirements of ISO 10993-10.

Study Director Approval: _____

Colin Mo

Test Facility Management Approval: _____

Yena Zhuang

Statement of GLP Compliance

There were no deviations to the provisions of the FDA Good Laboratory Practice (GLP) Regulations (21 CFR, Part 58) and OECD Series on Principles of Good Laboratory Practice (GLP). noted during the course of the study.

Study Director: _____ 2022.03.10

Colin Mo Date

1. Introduction

1.1 Purpose

The purpose of this study was to evaluate the test article for the potential to cause skin irritation in the rabbit.

1.2 Testing Guidelines

This study was based on the requirements of the International Organization for Standardization 10993-10, Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization (2010).

1.3 Dates

Test Article Received:	2022.01.25
Treatment Started:	2022.02.13
Observations Concluded:	2022.03.10

1.4 GLP Compliance

The study initiated by protocol signature on 2022.02.10 was conducted in accordance with the provisions of the FDA Good Laboratory Practice (GLP) Regulations, 21 CFR 58 and OECD Series on Principles of Good Laboratory Practice (GLP). A Statement of Quality Assurance Activities was issued with this report.

2. Identification of Test and Control Articles

The test article provided by the sponsor was identified and handled as described below:

Table 1 - Test Article

Name	BioAcetate S70
Size	N/A
CAS	N/A
Model	S70
Lot	N/A
Initial State	Not Sterilized
Strength, Purity and Composition	N/A
Color	N/A
Physical Description of the Test Article	Solid
Manufacture Date	N/A
Expiration Date	N/A

Table 2 - Negative Control Article

Name	0.9% Sodium chloride injection(SC) Sesame oil(SO)
Purity, Composition, and Other Characteristics	SC Composition: 500mL water:4.5g NaCl; sodium chloride CAS No.: 7647-14-5/water CAS No.: 7732-18-5 SO: Composition: CAS No.: 8008-74-0

Table 3 - Reagents

Name	Brand	Lot
SC	GUANGXIYUYUAN	H21062604
SO	HENRY LAMOTTE	1000015882

3. Test System

3.1 Test System

Species:	Rabbit (Oryctolagus cuniculus)
Strain:	New Zealand White
Source:	Guangzhou huadu district huadongxinhua animal farm
Sex:	Male and Female(female were nulliparous and nonpregnant)
Age:	Young adult
Acclimation Period:	Minimum 5 days
Number of Animals:	6
Identification Method:	Name Card

3.2 Test System Management

The rabbit (animal) is specified as an appropriate animal model for evaluating potential skin irritants by the current ISO testing standards. The rabbit is widely used for this purpose and relative ranking of irritant scores can be determined.

4. Facility & Personnel

4.1 Facility

DGMD Rabbit room

STC (Dongguan)

68 Fumin Nan Road, Dalang,

Dongguan, Guangdong,

China. (Zip code 523770)

4.2 Personnel

Associates involved in this study was appropriately qualified and trained.

Test Facility Management: Yena Zhuang

Study Director: Colin Mo

Quality Assurance Unit: Jason Huang

Veterinary: Cassie Lin

Technicians: White Bai

5. Animal Management

5.1 Husbandry, Housing and Environment

Conditions conformed to STC Standard Operating Procedures. Animals were housed in groups in stainless steel or plastic suspended cages identified by a card indicating the animal numbers, test code, sex, animal code and date dosed.

The animal housing room is conventional system lab. The lab animal using license: SYXK(Guangdong province)2019-0159. The animal housing room temperature and relative humidity were monitored daily. The temperature for the room was set to 18-26 ℃ and the relative humidity was set to 40-70%. There were no significant temperature or relative humidity excursions that adversely affected the health of the animals.

The light cycle was controlled (12 hours light, 12 hours dark).

5.2 Food, Water and Contaminants

Food: Laboratory animal formula feed (rabbit), Jiangsu Xietong Pharmaceutical Bio-engineering Co., Ltd., was provided daily.

Water: The water quality met the "Sanitary standard for drinking water" (GB5749-2006)

Food and water were sterile. No contaminants present in the feed and water impacted the results of this study.

5.3 Personnel

Associates involved in this study were appropriately qualified and trained.

5.4 Veterinary Care

Standard veterinary medical care was provided in this study.

5.5 IACUC

This procedure has been approved by the STC Institutional Animal Care and Use Committee (IACUC), and is reviewed at least annually by the same committee.

5.6 Selection

Only healthy, animals free from irritation or other dermatological lesions that could interfere with the test were selected.

6. Method (DGMD-DOP-EXP-010-2A and DGMD-DOP-EXP-028-2A)

6.1 Test and Control Article Preparation

The preparations of the test article and the negative control were subjected to the extraction conditions as described below. The extracts were continuously agitated during extraction.

Table 4 - Extraction

Vehicle	Treatment Group	Extraction Ratio	Article Amount	Volume of Vehicle	Extraction Condition
SC	Test	0.2g/mL	4.487g	22.4 mL	50±2°C for72±2 h
	Control	N/A	N/A	20.0 mL	
SO	Test	0.2g/mL	4.520g	22.6 mL	
	Control	N/A	N/A	20.0 mL	

The following table contains a description of the test and control article extracts before and after extraction.

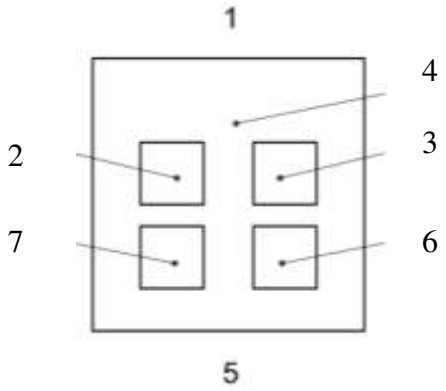
Table 5 - Condition of Extracts

Vehicle	Time Observed	Extract	Condition of Extracts		
			Color	Clarity	Particulates
SC	Before Extraction	Test	Colorless	Clear	None
		Control	Colorless	Clear	None
	After Extraction	Test	Colorless	Clear	None
		Control	Colorless	Clear	None
	Prior to Use	Test	Colorless	Clear	None
		Control	Colorless	Clear	None
SO	Before Extraction	Test	Colorless	Oily	None
		Control	Colorless	Oily	None
	After Extraction	Test	Colorless	Oily	None
		Control	Colorless	Oily	None
	Prior to Use	Test	Colorless	Oily	None
		Control	Colorless	Oily	None

The extracts were maintained at ambient temperature <24 hours before use for all phases. The extracts were not centrifuged, filtered, or otherwise altered prior to dosing.

6.2 Test Procedure

The animals were weighed and the fur on the back of each animal was clipped with an electric clipper 18 hours prior to treatment. On the day of treatment, four sites, two on each side of the back and positioned cranially and caudally, were designated on each animal. The sites were free of blemishes that could interfere with the interpretation of results. The appropriate extracts were applied to the 2.5 cm × 2.5 cm absorbent gauze patches. 0.5 mL extract was used to saturate the gauze. A control patch of gauze moistened with the extract vehicle was applied as well. And then all the application sites were covered with a bandage (semi-occlusive or occlusive) for a minimum of 4 h. Animals were returned to their cages after treatment. After the 4-hour exposure, the binders, tape, and patches were removed. The sites were gently wiped with a gauze sponge dampened with deionized water in an attempt to remove any remaining residue.



Key

1	cranial end	5	caudal end
2	test site	6	test site
3	control site	7	control site
4	clipped dorsal region		

6.2.1 Laboratory Observations

1. Animals were observed daily for general health.
2. Body weights were recorded for each animal at pretreatment.
3. Dermal observations for erythema and edema were recorded at 1, 24, 48 and 72 hours after patch removal in accordance with the criteria in Appendix 1.

Table 6 - Classification System for Skin Reaction

Erythema and Eschar Formation	Numerical Grading	Edema Formation	Numerical Grading
No erythema	0	No edema	0
Very slight erythema (barely perceptible)	1	Very slight edema (barely perceptible)	1
Well-defined erythema	2	Well-defined edema (edges of area well-defined by definite raising)	2
Moderate erythema	3	Moderate edema (raised approximately 1 mm)	3
Severe erythema (beet redness) to eschar formation preventing grading of erythema	4	Severe edema (raised more than 1 mm and extending beyond exposure area)	4
Total possible score for irritation			8

Table 7- Irritation Response Categories in the Rabbit

Irritation Response Categories in the Rabbit	
Response Category	Mean Score
Negligible	0-0.4
Slight	0.5-1.9
Moderate	2.0-4.9
Severe	5-8

All times and temperatures reported herein are approximate and are within ranges established by the external standards described in the References section of this report and/or STC standard operating procedures.

7. Evaluation

The Primary Irritation Index of the test was calculated following test completion for each animal. The erythema and edema scores obtained at the 24, 48 and 72-hour intervals were added together and divided by the total number of observations. This calculation was conducted separately for the test and control article for each animal. The score for the control was subtracted from the score for the test article to obtain the Primary Irritation Score. The Primary Irritation Score for each animal was added together and divided by the number of animals to obtain the Primary Irritation Index. The Primary Irritation Index was characterized based on the definitions.

8. Results

All the animals were clinically normal throughout the study. Individual results of dermal scoring are presented in Appendix 1. No irritation was observed on the skin of the animals. The Primary Irritation Index of the test article was calculated to be 0.0. The irritation calculations are shown below:

Table 8 - Irritation Calculations of SC group

Animal Number	Test Score Average	Control Score Average	Individual Primary Irritation Score	Combined Primary Irritation Score (CPIS)	Primary Irritation Index (CPIS/3)	Response Category
2021112506	0	0	0	0	0	Negligible
2021102819	0	0	0			
2021102817	0	0	0			

Table 9 - Irritation Calculations of SO group

Animal Number	Test Score Average	Control Score Average	Individual Primary Irritation Score	Combined Primary Irritation Score (CPIS)	Primary Irritation Index (CPIS/3)	Response Category
2021122139	0	0	0	0	0	Negligible
2021122141	0	0	0			
2021122149	0	0	0			

9. Conclusion

There was no erythema and no edema observed on the skin of the animals treated with the test article. The Primary Irritation Indexes for the test article extracts were both calculated to be 0.0. The response of the test article extracts was categorized as negligible.

Results and conclusions apply only to the test article tested. Any extrapolation of these data to other articles is the sponsor's responsibility.

10. Quality Assurance

Inspections were conducted at intervals adequate to assure the integrity of the study in conformance with 21 CFR 58.35(b)(3) and OECD Series on Principles of Good Laboratory Practice (GLP) No 4: Quality Assurance and GLP. The final report was reviewed for

conformance to Section 58.185, Subpart J, of the GLP Regulations and OECD Series on Principles of Good Laboratory Practice (GLP). A Statement of Quality Assurance Activities was issued with the report.

11. Records

All raw data pertaining to this study and a copy of the final report are retained in designated STC archive files in accordance with STC SOPs. All of the files was storage in DGSTC MD Archiving room.

This includes:

- ✓ Agreement of Medical Devices Testing including the Study director assignment (DGMD/888/01 Rev04)
- ✓ Study plan and study plan training record (DGMD-FORM-OAP-001-2A and DGMD-FORM-OAP-002-2A)
- ✓ Final report
- ✓ All raw data and observations(DGMD-FORM-EXP-36-2A and DGMD-FORM-EXP-09-2A)
- ✓ Samples of test and reference items and test sample login form (DGMD-FORM-ART-01-2B)
- ✓ The Records of test system management: Animal quarantine (DGMD-FORM-ANI-002-2A and DGMD-FORM-ANI-003-2A)
- ✓ The Records of test system usage: Animal quality certificate and Animal ethical review records (DGMD-FORM-ANI-001-2A)
- ✓ Records of critical reagent: Saline and Oil (DGMD-FORM-MAT-001-2A
- ✓ Records of all inspections performed by Quality Assurance Program (DGMD-FORM-QAU-002-2A and DGMD-FORM-COE-004-2A）
- ✓ All relevant correspondence/communication (especially for multi- site studies)
- ✓ Records of qualifications training, experience and job descriptions of personnel in the study (this will be archived in Personnel technical file)
- ✓ Records and reports of the maintenance and calibration of apparatus (this will be archived in the equipment file)

- ✓ Validation documentation for computerized systems (this will be archived in the equipment file)
- ✓ Master schedules in use at the time of the study (this will be archived in the facility management file)
- ✓ Historical file of all Standard Operating Procedures (this will be archived in the facility management file)
- ✓ Environmental monitoring records (this will be archived in the animal lab management file)

12. ISO Compliance

All procedures were compliance to ISO 17025.

13. References

Code of Federal Regulations (CFR), Title 21, Part 58, Good Laboratory Practice for Nonclinical Laboratory Studies

OECD Series on Principles of Good Laboratory Practice (GLP)

International Organization for Standardization (ISO) 10993-1, Biological evaluation of medical devices -Part 1: Evaluation and testing within a risk management process (2018).

International Organization for Standardization (ISO) 10993-2, Biological evaluation of medical devices -Part 2: Animal welfare requirements (2006).

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

International Organization for Standardization (ISO) 10993-12, Biological evaluation of medical devices -Part 12: Sample preparation and reference materials (2021).

International Organization for Standardization/International Electrotechnical Commission (ISO/IEC) 17025, General requirements for the competence of testing and calibration laboratories (2017).

Appendix 1 – Dermal Observations

Table 10 - Dermal Observations of SC group

Animal number	Weight (g)	Group	Observation	Interval (hours)			
				1	24	48	72
2021112506	3556.2	Test	Erythema	0	0	0	0
			Edema	0	0	0	0
		Control	Erythema	0	0	0	0
			Edema	0	0	0	0
2021102819	4017.4	Test	Erythema	0	0	0	0
			Edema	0	0	0	0
		Control	Erythema	0	0	0	0
			Edema	0	0	0	0
2021102817	4226.8	Test	Erythema	0	0	0	0
			Edema	0	0	0	0
		Control	Erythema	0	0	0	0
			Edema	0	0	0	0

Table 11- Dermal Observations of SO group

Animal number	Weight (g)	Group	Observation	Interval (hours)			
				1	24	48	72
2021122139	3274.3	Test	Erythema	0	0	0	0
			Edema	0	0	0	0
		Control	Erythema	0	0	0	0
			Edema	0	0	0	0
2021122141	3302.7	Test	Erythema	0	0	0	0
			Edema	0	0	0	0
		Control	Erythema	0	0	0	0
			Edema	0	0	0	0
2021122149	3617.5	Test	Erythema	0	0	0	0
			Edema	0	0	0	0
		Control	Erythema	0	0	0	0
			Edema	0	0	0	0

Appendix 2 - Periodic Positive Control Study for Primary Skin Irritation Test

What was tested:
sodium dodecyl sulfate (SDS) （Brand: Macklin, Lot:C12089309）

Dates:
Treatment Started: 2022.02.14
Observations Concluded: 2022.02.17

Purpose:
A periodic positive control study of within three months was conducted for the Primary Skin Irritation Test to meet the following objectives: 1) confirm the methodology in ISO 10993-10:2010, Biological Evaluation of Medical Devices - Part 10: Tests for Irritation and Skin Sensitization, 2) substantiate the potential of SDS to cause irritant effects, 3) verify proper training of the technicians performing these studies, and 4) substantiate the susceptibility of the rabbit strain to primary skin irritation test.

Methods:
The test utilized young adult, 3 male rabbits supplied by Guangzhou huadu district Huadong xinhua animal farm. The weight at study initiation ranged from 2kg to 4kg. Two 25 mm x 25 mm sections of absorbent gauze patches with 0.5ml 20% (w/w) concentration of SDS was topically applied to the skin of each of three rabbits and left in place for 4 hours. The sites were graded for erythema and edema at 1, 24, 48 and 72 hours after removal of the single application.

Results:
All of the three sites demonstrated a positive skin irritation to the known skin irritant, SDS. None of the control sites of animals demonstrated an irritation response. The Irritation Calculations are shown below:

Animal Number	Test Score Average	Control Score Average	Individual Primary Irritation Score	Combined Primary Irritation Score (CPIS)	Primary Irritation Index (CPIS/3)	Response Category
2021120916	8	0	8	24	8	Severe
2021120908	8	0	8			
2021072903	8	0	8			

Conclusion:

The known skin irritant SDS produced evidence of causing primary skin irritation in the New Zealand White strain of rabbit. Therefore, the following objectives were met: 1) the methodology in ISO 10993-10:2010, Biological Evaluation of Medical Devices, Part 10: Tests for Irritation and Skin Sensitization was confirmed, 2) the potential for SDS to cause skin irritation was substantiated, 3) proper training of the technicians performing this study design was verified and 4) the susceptibility of the New Zealand White rabbit strain to skin irritation was substantiated.

Appendix 3 – Photograph(s) of Test Articles

Statement of Quality Assurance Activities

Phase Inspected	Date Inspected	Study Director Notification Date	Management Notification Date
Study Plan Review	2022.01.30	2022.01.30	2022.01.30
Onsite Inspection：Extraction in the 1st day	2022.02.13	2022.02.13	2022.02.13
Onsite Inspection：Animal acclimatization	2022.02.13	2022.02.13	2022.02.13
Onsite Inspection：Test substance application 1st day	2022.02.16	2022.02.16	2022.02.16
Onsite Inspection：Observation conclude	2022.02.19	2022.02.19	2022.02.19
Study Data Review	2022.03.10	2022.03.10	2022.03.10
Final Report Review	2022.03.10	2022.03.10	2022.03.10

Based on a review of this study, it has been concluded that this report accurately describes the methods and standard operating procedures, and that the reported results accurately reflect the raw data of the study. This study has been reviewed in accordance with the provisions of the FDA Good Laboratory Practice Regulations (21 CFR, Part 58) and OECD Series on Principles of Good Laboratory Practice (GLP).

Quality Assurance Unit Representative: Jason

Jason Huang — 2022.03.10 Date

******* END OF STUDY REPORT *******

Conditions of Issuance of Test Reports

1. All samples and goods are accepted by The STC (Dongguan) Company Limited (the "Company") solely for testing and reporting in accordance with the following terms and conditions. The Company provides its services on the basis that such terms and conditions constitute express agreement between the Company and any person, firm or company requesting its services (the "Clients").

2. Any report issued by the Company as a result of this application for testing service (the "Report") shall be issued in confidence to the Clients and the Report will be strictly treated as such by the Company. It may not be reproduced either in its entirety or in part and it may not be used for advertising or other unauthorized purposes without the written consent of the Company. The Clients to whom the Report is issued may, however, show or send it, or a certified copy thereof prepared by the Company to his customer, supplier or other persons directly concerned. Subject to clause 3, the Company will not, without the consent of the Clients, enter into any discussion or correspondence with any third party concerning the contents of the Report, unless required by the relevant governmental authorities, laws or court orders.

3. The Company shall be at liberty to disclose the testing-related documents and/or files anytime to any third-party accreditation and/or recognition bodies for audit or other related purposes. No liabilities whatsoever shall attach to the Company's act of disclosure.

4. The Company shall not be called or be liable to be called to give evidence or testimony on the Report in a court of law without its prior written consent, unless required by the relevant governmental authorities, laws or court orders.

5. The results in Report apply only to the sample as received and do not apply to the bulk, unless the sampling has been carried out by the Company and is stated as such in the Report. The Clients provide the sample's relevant information, and the Company will not be liable for or accept responsibility for the truth of the sample information.

6. When a statement of conformity to a specification or standard is provided, the ILAC-G8 Guidance document (and/or IEC Guide 115 in the electrotechnical sector) will be adopted as a decision rule for the determination of conformity unless it is inherent in the requested specification or standard, or otherwise specified in the Report.

7. In the event of the improper use the report as determined by the Company, the Company reserves the right to withdraw it, and to adopt any other additional remedies which may be appropriate.

8. Sample submitted for testing are accepted on the understanding that the Report issued cannot form the basis of, or be the instrument for, any legal action against the Company.

9. The Company will not be liable for or accept responsibility for any loss or damage howsoever arising from the use of information contained in any of its Reports or in any communication whatsoever about its said tests or investigations.

10. Clients wishing to use the Report in court proceedings or arbitration shall inform the Company to that effect prior to submitting the sample for testing.

11. Subject to the variable length of retention time for test data and report stored hereinto as to otherwise specifically required by individual accreditation authorities, the Company will only keep the supporting test data and information of this test report for a period of six years. The data and information will be disposed of after the aforementioned retention period has elapsed. Under no circumstances shall we provide any data and information which has been disposed of after the retention period. Under no circumstances shall we be liable for damages of any kind, including (but not limited to) compensatory damages, lost profits, lost data, or any form of special, incidental, indirect, consequential or punitive damages of any kind, whether based on breach of contract of warranty, tort (including negligence), product liability or otherwise, even if we are informed in advance of the possibility of such damages.

12. Issuance records of the Report are available on the internet at www.stc.group. Further enquiry of validity or verification of the Reports should be addressed to the Company.