GLP Final Report

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STUDY TITLE
Skin Sensitization Study
Guinea Pig Maximization Test

TEST ARTICLE
Vinyl Examination gloves
Model: clear, powder, L

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Summary

The test article, Vinyl Examination gloves, clear, powder, L, was evaluated for the potential to cause delayed dermal contact sensitization in a guinea pig maximization test. The test article was extracted in polar extract (0.9% sodium chloride (SC)) and non-polar extract (Sesame Oil (SO)). Each extract was intradermally injected and occlusively patched to ten test guinea pigs (per extract). Each extraction vehicle was similarly injected and occlusively patched to five control guinea pigs (per vehicle). Following a recovery period, the test and control animals received a challenge patch of the appropriate test article extract and the vehicle control. All sites were scored for dermal reactions at 24 and 48 hours after patch removal.

Under the condition of this study, the test article extracts showed no evidence of causing delayed dermal contact sensitization in the guinea pig. The test article was not considered a sensitizer in the guinea pig maximization test.

Approved by: _____ 2021.04.27

Lee Fu, Authorized Signatory
Study Director

Date

GLP STATEMENT

This nonclinical laboratory study was conducted in accordance with the United States Food and Drug Administration Good Laboratory Practice Regulations, 21 CFR Part 58.

There was no deviation to the protocol or provisions of GLP Regulation noted during the course of the study.

Approved by: _____ _____

Lee Fu, Authorized Signatory
Study Director

2021.04.27
Date

1. Generals

1.1 Purpose

The purpose of this study was to evaluate the potential of the test article to cause delayed dermal contact sensitization in the guinea pig maximization test.

1.2 Guidelines

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

1.3 Dates

Test Article Received:	01/27/2021
Initiated:	03/05/2021
Completed:	04/03/2021

2. Materials

Test Article	Vinyl Examination gloves
Model	clear, powder, L
Manufacturer	Same as sponsor
Manufacturer Address	Same as sponsor
Identification Number	20210120
Status	Non-sterile
Physical Description	Solid
Composition	Vinyl
Stability	Stability was determined by and on file with the sponsor.
Expiration Date (or Shelf Life)	Stable during the study.
Strength	Not applicable, no active ingredient
Purity	Not applicable, no active ingredient
Storage Condition	Room Temperature
Note	Information regarding the test article was provided by sponsor in the Sample Submission Form.

Extraction Vehicle (Control)	0.9% sodium chloride
Polar	
Manufacturer	China Otsuka Pharmaceutical Co.,Ltd.
Lot Number	20E3502 (Intradermal Induction/ Topical Induction/ Challenge)
Physical Description	Clear, Colourless, Liquid
Composition	NaCl
Strength	250ml/bottle
Purity	Conforms to China Pharmacopoeia
Stability	Marketed product, stability is characterized by its labelling
Storage Condition	Room Temperature

Extraction Vehicle (Control)	Sesame Oil

Non-Polar

Manufacturer	Société Industrielle des Oléagineux
Lot Number	19C0302 (Intradermal Induction/ Topical Induction/ Challenge)
Physical Description	Clear, Yellow to Green, Liquid
Composition	Sesame Oil
Strength	56.5 Kg/barrel
Purity	Pure
Stability	Marketed product, stability is characterized by its labelling
Storage Condition	Room Temperature

Reagent	FREUND'S COMPLETE ADJUVANT
Manufacturer	Sigma-Aldrich, Inc.
Lot Number	SLCD6299

Reagent	Sodium Dodecyl Sulfate (SDS)
Manufacturer	Beijing Chreagen Biotechnology Co., Ltd
Lot Number	A102031

Reagent	Medical Vaseline
Manufacturer	ShanDong LIRCON Medical Technology Incorporated Company
Lot Number	200301

Sample Preparation Prior to the extraction, test article was removed from the package, and covered in the extraction vehicle.

Extraction Procedure The test article and the control blank (extraction vehicle without the test article) were subjected to the extraction conditions as described below. The extracts were continuously agitated during extraction.

Group	**Polar (SC)**		**Non-Polar (SO)**	
Intradermal Induction	**Test**	**Control**	**Test**	**Control**
Extraction Ratio	6 cm^2:1ml	N.A	6 cm^2:1ml	N.A
Sample Amount	400 cm^2	N.A.	400 cm^2	N.A.
Extraction Vehicle Volume	66.7 ml	20.0 ml	66.7 ml	20.0 ml
Extraction Condition	50℃ 72 hours			
Condition of Extracts	Clear	Clear	Clear	Clear
	No Particulate	No Particulate	No Particulate	No Particulate

Note: All extracts were not centrifuged, filtered or otherwise altered prior to dosing. It was dosed immediately after extraction.

Group	**Polar (SC)**		**Non-Polar (SO)**	
Topical Induction	**Test**	**Control**	**Test**	**Control**
Extraction Ratio	6 cm^2:1ml	N.A	6 cm^2:1ml	N.A

Sample Amount	400 cm^2	N.A.	400 cm^2	N.A.
Extraction Vehicle Volume	66.6 ml	20.0 ml	66.6 ml	20.0 ml
Extraction Condition		50℃ 72 hours		
Condition of Extracts	Clear	Clear	Clear	Clear
	No Particulate	No Particulate	No Particulate	No Particulate

Note: All extracts were not centrifuged, filtered or otherwise altered prior to dosing. It was dosed immediately after extraction.

Group	**Polar (SC)**		**Non-Polar (SO)**	
Challenge	**Test**	**Control**	**Test**	**Control**
Extraction Ratio	6 cm^2:1ml	N.A	6 cm^2:1ml	N.A
Sample Amount	400 cm^2	N.A.	400 cm^2	N.A.
Extraction Vehicle Volume	66.7 ml	20.0 ml	66.7 ml	20.0 ml
Extraction Condition		50℃ 72 hours		
Condition of Extracts	Clear	Clear	Clear	Clear
	No Particulate	No Particulate	No Particulate	No Particulate

Note: All extracts were not centrifuged, filtered or otherwise altered prior to dosing. It was dosed immediately after extraction.

3. Test Systems and Justification

Species:	Guinea pig (Caviaporcellus)
Breed:	Hartley
Source:	Tianjin Yuda Laboratory Animal Breeding Co., Ltd.
Sex:	Male and Female, Females were nulliparous and non-pregnant.
Body Weight Range:	300-500 grams at injection
Age:	Young adults
Acclimation Period:	Minimum 5 days
Number of Animals:	30, which were divided as follows: 10 SC Test Group, 5 SC Control Group and 10 SO Test Group, 5 SO Control Group
Identification Method:	Ear tag
Justification:	The Hartley albino guinea pig (animal) has been used historically for sensitization studies (Magnusson and Kligman, 1970). The guinea pig is believed to be the most sensitive animal model for this type of study. The susceptibility of the Hartley strain to a known sensitizing agent, 1-chloro-2,4-dinitrobenzene (DNCB) has been substantiated at MID-LINK with this method. Detail information is provided in Attachment 3: Periodic Positive Control Study Record.

4. Animal Management

Husbandry, Housing and Environment	Conditions conform to MID-LINK Standard Operating Procedures. Animals with same sex and in same group were housed in group in a box cage with an identification card indicating the animal number, test code.
Food, Water and Contaminants	A commercially available mouse feed was provided daily. Potable water was provided ad libitum through species appropriate water containers. No contaminant present in the feed

	and water was expected to impact the results of this study.
Personnel	Associates involved in this study were appropriately qualified and trained.
Veterinary Care	Standard veterinary medical care is provided during the study, if applicable.
Selection	Only healthy, previously unused animals were selected.

5. Methods

On the first day of treatment, 15 animals (10 tests, 5 controls) per extract were weighed. The fur from the dorsoscapular area of the animals was removed with an electric clipper.

Intradermal Induction

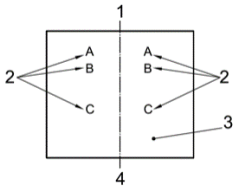
Three pair of intradermal injections of 0.1ml was administered to the animals within an approximate 2 cm × 4 cm area over the dorsoscapular region (as shown in Fig 1 Location of Injection Sites) as follows:

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

Site B: The undiluted test extract for test group and corresponding blank vehicle for control group;

Site C: The test sample at the concentration used at site B, emulsified in a 50:50 volume ratio stable emulsion of Freund's complete adjuvant and the solvent (50 %); inject the control animals with an emulsion of the blank liquid with adjuvant.;

Fig 1 Location of Injection Sites



Remark:

1- cranial end,
2- 0.1 ml intradermal injections,
3- clipped intrascapular region and
4- caudal end

Topical Induction

At 6 days after completion of the Intradermal Induction injection, the injection sites were clipped free of fur again and treated with a 10% (w/w) sodium dodecyl sulfate (SDS). The SDS suspension was applied in an amount sufficient to coat the skin unless the animal exhibit excessive redness and/or swelling at site B. After 24 hours any remaining SDS residue was gently wiped from the area with gauze. Following removal of the SDS, an approximate 2 cm × 4 cm filter paper patch, saturated with the undiluted test extract (test animals) or corresponding blank vehicle (control animals) was applied to intrascapular region and secured with a nonreactive tape. The trunk of each animal was then wrapped snugly with an elastic band for (48 ±2) hours.

Challenge

At 14 days after completion of the topical induction phase, challenge all test and control animals with the test sample. Administer the test sample and a blank by topical application to sites that were not treated during the induction stage, such as the upper flank of each animal. The fur was clipped from the sides and flanks with an electric clipper, using approximate 2 cm × 4 cm filter paper patches or chambers soaked in the test sample at the concentration selected in Intradermal Induction Phase for site C. Dilutions of this concentration might also be applied to other untreated sites in a similar manner. Secure with an occlusive dressing. Remove the dressings and patches after (24±2) h.

Laboratory Observations

Observe 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. Use of natural or full-spectrum lighting is highly recommended in order to visualize the skin reactions. Describe and grade 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: Grading 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

6. Evaluation

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. 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.

7. Results

No evidence of sensitization was observed. The individual body weights at pretreatment are presented in Attachment 1: Individual Body Weight Data and Dermal Reaction.

8. Conclusion

Under the conditions of this study, the test article extracts showed no evidence of causing delayed dermal contact sensitization in the guinea pig. The test article was not considered a sensitizer in the guinea pig maximization test.

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

9. Deviation

There was no deviation during the study.

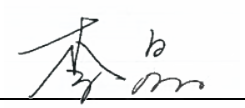
10. Records

All raw data pertaining to this study and a copy of final report are retained in designated Mid-Link’s archive files in accordance with Mid-Link SOP.

STATEMENT OF QUALITY ASSURANCE ACTIVITIES

Phase Inspected	Date Inspected
Application	03/15/2021
Study Data Review	04/06/2021
Final Report Review	04/12/2021

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). Results are included in the Periodic Status Report to Management and Study Director.

QA Representative 

Authorized Signature

2021.04.27

Date

Attachment 1: Individual Body Weight Data and Dermal Reaction

Treatment Group	Animal Number	Pretreatment Body Weight (g)	Dermal Reaction	
			24 Hours	48 Hours
Test (SC)	C5031	368.7	0	0
	C5032	382.5	0	0
	C5033	366.3	0	0
	C5034	386.9	0	0
	C5035	359.4	0	0
	C5036	387.7	0	0
	C5037	365.9	0	0
	C5038	358.2	0	0
	C5039	397.3	0	0
	C5040	368.5	0	0
Control (SC)	C5021	359.4	0	0
	C5022	366.7	0	0
	C5023	386.5	0	0
	C5024	392.3	0	0
	C5025	387.7	0	0
Test (SO)	C5151	369.9	0	0
	C5152	387.6	0	0
	C5153	376.3	0	0
	C5154	369.5	0	0
	C5155	359.3	0	0
	C5156	365.7	0	0
	C5157	386.9	0	0
	C5158	359.4	0	0
	C5159	386.7	0	0
	C5160	369.5	0	0
Control (SO)	C5171	359.3	0	0
	C5172	387.7	0	0
	C5173	369.4	0	0
	C5174	395.2	0	0
	C5175	389.7	0	0

Attachment 2: Illustration of Test Article

Attachment 3: Periodic Positive Control Study Record

Positive Control Article: 2,4-dinitrobenzene (DNCB) (Dissolved in ethanol with 0.1% (w/v) in the concentration of solution);
Negative Control Article: Ethanol.

Dates
Treatment Started: 02/08/2021
Observations Concluded: 03/06/2021

Purpose A periodic positive control study was conducted for the Guinea Pig Maximization Test to meet the following objectives: 1) confirm the methodology in ISO 10993-10, Biological Evaluation of Medical Devices - Part 10: Tests for Irritation and Skin Sensitization and 2) substantiate the susceptibility of the Hartley guinea pig strain provided by to dermal contact sensitization.

Methods The experiment used adult guinea pigs, in which females were asked not to give birth and not to become pregnant. The weight of the animals were ranged from 300 to 500 grams. There were five (5) animals in test group and five (5) in negative control group. The positive control study and scoring was carried out in accordance with same manner of the guinea pig maximization test.

Results

Table A1 Results

Group	Anima Number	Dermal Reaction		Result
		24 Hours	48 Hours	
Test Group	C3861	2	2	+
	C3862	3	2	+
	C3863	1	1	+
	C3864	2	2	+
	C3865	2	3	+
Control Group	C3956	0	0	-
	C3957	0	0	-
	C3958	0	0	-
	C3959	0	0	-
	C3960	0	0	-

Conclusion Under the conditions of this study, the positive control substance showed evidence of causing delayed dermal contact sensitization in the guinea pig.