Determination of Cutaneous Tolerance and Sensitization on Healthy Participants by Human Repeat Insult Patch Test (HRIPT)

Final Report
Study N°22W-0718-03

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This final report was prepared by a clinical testing laboratory with a quality management system registered to ISO 9001.

This report is composed of 10 pages including appendices (2 pages).

September 2nd, 2022

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SUMMARY

Human Repeat Insult Patch Test
STUDY 22W-0718-03

Sponsor Code: NZ

Test: Determination of the cutaneous tolerance (irritation potential) and sensitization to a soap tested on fifty (50) healthy participants by HRIPT.

Product tested: Inodore | Unscented
Customer Lot#: 1091521
Evalulab Lot#: 220627.NZ.01

Date: August 22nd, 2022

Results: Under the conditions of the test procedure referenced herein, the test product referenced above has produced no significant signs of cutaneous irritation or intolerance and no signs of sensitization.

Hence, the test product may be considered as non-irritant and hypo-allergenic.

Signatures:

Doctor Michel Journet, M.D.
Dermatologist F.R.C.P (C)

Noor Mantash, B. Sc.
Investigator, Evalulab Inc.

Marilou Nadeau, B. Sc.
Quality Assurance Director, Evalulab Inc.

STUDY OBJECTIVE

To carry out a "Human Repeat Insult Patch Test" (HRIPT).
This test determines the cutaneous irritation (contact dermatitis) and sensitization (contact allergy) potential of a topical product applied to the skin of 50 healthy participants. It consists of repetitively applying 10 patches during an induction period of 3 weeks, followed by a rest period and a challenge period.

PROTOCOL

1. Ethics Committee

This standard procedure and associated documents were reviewed and approved prior to the commencement of the study, by an Ethics Committee (an independent organization whose responsibility is to ensure the protection of the rights, safety and well-being of the subjects participating in the study).

2. Duration

The study took place between July 11th, 2022, and August 19th, 2022.

3. Investigation Site

Evalulab Inc. located at 5475 rue Paré, Suite 206, Mont-Royal, Quebec, H4P 1P7, Canada.

4. Personnel

This study was conducted by Evalulab Inc., represented by Noor Mantash, B. Sc. – Clinical Research Associate & Adriana Aguirre Garzon, B. Sc. – Laboratory Technician, under the control of Doctor Michel Journet, M.D. – Dermatologist.

5. Test Product

Upon reception, the test product was registered in the "Receptions Book" and assigned a code, followed by its storage at ambient humidity and temperature in its original container (as received) in an area allocated for this purpose.

Two samples of 130g were received.

Description of the product tested:		Description of control used:
Product name:	Inodore | Unscented	Pure Vaseline USP
Category:	Soap	
Client lot #:	1091521	
Evalulab lot #:	220627.NZ.01	
Application:	The product was diluted at 10% and generously applied on the entire surface of the patch. The total area of application is about 2.25 cm^2.	

6. Material

The patches used in this study were TruMed® semi-occlusive, cotton "BBA149-129 Absorbent" with "3M 1530 Tape" adhesive backing.

7. Quality Assurance

Good Clinical Practice (GCP) is defined by the totality of the pronouncements put in place for ensuring the quality and authenticity of the trials and the obtained data on one hand and the respect for the ethics on the other.

The data obtained for each participant is recorded in individual Case Report Forms. The data entry is made in black ink. In case of errors or omissions, the initial entry is crossed out and initialed by the investigator.

All recorded data is validated by the investigator, who assumes responsibility for the quality of the work presented and verifies that all gathered data is in agreement with the protocol.

The records obtained during the study will be kept by Evalulab Inc. for a period of 2 years.

8. Adverse Events or Severe Adverse Events

An "Adverse Event" is defined as any noxious and unintended response observed in a participant testing a product that does not necessarily have to have a causal relationship with the test product or the treatment in question.
The risks for adverse events associated with this test may vary amongst the participants. Participants may be subject to a rash (intense redness), cracking, exfoliation effect, dryness, or even pain if the test product is strongly irritant or if the participant is particularly sensitive to the product. Participants may also develop an allergic reaction to the test products or to their components.
The term "Severe Adverse Event" refers to all medical manifestations, related or not to the test products, that may lead to death, persistent or significant disability that requires hospitalization or prolongation of a hospitalization period, or provoke invalidity, significant or permanent incapacity, or translate to congenital anomaly or malformation.
Participants were asked to immediately communicate any reactions to Evalulab.

No "Severe Adverse Event" occurred during the entire length of the study.

9. Data Analysis

The tolerance to the product was evaluated by a dermatologist considering the scores, observed reactions, their level of intensity and the reproducibility from one participant to another. The dermatologist specified, if necessary, the irritation or allergic potential of the registered reactions.

10. Amendment to Protocol

There were no amendments to the protocol. However, there was a deviation due to one participant (participant *#01-0718-024*) having forgotten to remove the patch 24 hours after application between the third and fourth observations. This patch was kept on for 48 hours. Nonetheless, this had no impact on the results of the study since the participant did not show any reactions to the products.

11. HRIPT

- **Type of Study**

Monocentric and open-label, meaning the evaluator, participants, and sponsors alike, were aware of the nature of the test material.

- **Participants**

Recruitment of participants

A total of 55 participants were recruited based on the inclusion and exclusion criteria. The profile of each participant is presented in Table I in the Appendices.

Participant Demographics

Sex	Number	Age	Average Age
Male	15	25 to 72	53.33
Female	40	26 to 80	54.08
Total	**55**	**25 to 80**	**53.85**

Informed Consent Form

All participants were required to read, sign and date the electronic Informed Consent Form, sent to them by email before their first laboratory visit, explaining the conditions of the test, the risks involved and briefly describing the product to be tested. The participants who could not properly access and sign the electronic form were given hard copies of the Informed Consent Form which they had to read, sign and date on their first visit. Each participant was informed verbally and in writing of the nature of the test and of the potential risks involved.

Confidentiality

Participation of the subjects in this study is confidential. The information gathered in the course of the study was recorded in individual Case Report Forms, that are numerically coded and do not contain the names of the participants.

Only the employees of Evalulab, auditors of the sponsor, and regulatory bodies (FDA, Health Canada and the Ethics Committee) may have access to the confidential information.

Inclusion Criteria

1. Participants of the feminine or masculine sex, aged 18 years or older,
2. With phototype I to V and with a skin type that does not interfere with the assessment of cutaneous reactions,
3. Healthy and without any dermal anomalies on the areas to be tested that may interfere with the results of the study,
4. With no excessive body hair, especially on the test area,
5. Who will cooperate and be present for a follow-up at every visit, informed and sensitized about the duration and the importance of controls allowing complete compliance with the study protocol,
6. Who have read, signed and dated the Informed Consent Forms upon full knowledge of the risks involved with the study,
7. Women who use a method of contraception (oral contraceptive, condoms, spermicidal creams, an intra-uterine device (IUD), abstinence…), or are in a menopausal status.

Exclusion Criteria

1. Participants with a history of skin irritation or allergies to the type of products to be tested or in general, to glues (sticking plaster), with allergies to certain foods, to certain chemical products, to jewelry, …,
2. With an uncontrolled serious illness, health problem or chronic or progressive disease (asthma, diabetes, cancer, immunological deficiency, ablated organ…),
3. With a history of eczema, dermatitis, psoriasis or significant dermal anomalies on the test area,
4. On medication or having taken medication in the last 7 days prior to the study that could affect skin characteristics or could bias the study (antibiotics, anti-inflammatory drugs, steroids, antihistamines…),
5. Who frequent tanning salons or foresee exposure to the sun during the study,
6. Who abuse alcohol, drugs and/or tobacco,
7. Women, who are pregnant, breast feeding or expecting to become pregnant during the study.

- **Design of the Study**

Induction phase (or repeated skin contact test):

Prior to applying the patches, the test area (upper back, between the two shoulder blades) was carefully examined and wiped with alcohol if necessary (oily skin only). A patch containing the test products and the control were applied to the test area and left in contact with the skin for 48 hours. Care was taken when positioning the patches to minimize the possibility of displacement or rubbing.

The test products were applied on the selected zones every second day, 3 times per week, over 3 consecutive weeks.

This is referred to as the Induction Phase.

Any deviation from the protocol or missed appointment or "non-application" was recorded in the attendance schedule for each participant. "Non-application" should not exceed 144 hours (6 days) and the induction phase should incorporate at least 9 applications over a 4-week period.

The first patch was removed at the laboratory 48 hours after application. The observation area was rinsed with water, dried, and examined for any skin changes, such as redness, irritation, inflammation, etc.

Following the examination, a new patch with "fresh" test product was applied.

With the exception of the first application, subsequent patches were removed by the participants themselves 24 hours after each application. Care was taken to re-apply the patches on the same test area every time. In the event of a significant skin irritation, for example if a reaction ranking between 2 and 4 is observed, a new application site is selected. If the reaction reoccurs and is identical in magnitude in the new test area, the Induction Phase for the test product in question is stopped.

Rest Period (or Incubation Phase):

After the completion of the Induction Phase described above, a Rest Period of 10 to 14 days is scheduled.

Challenge Phase (or Revealing Phase):

All test products are to be included in the Challenge Phase, except when there are strong indications of sensitivity (generally reactions of grade 3 to 4) caused by the test product that are observed during the Induction Phase.

The application site used during the Challenge Phase must be different than the one used in the Induction Phase.

For this phase, the patch was removed at the laboratory, 48 hours after application. The test site was cleaned and examined for any signs of intolerance or irritation.

Important notes:

The participants were to avoid wetting the patches, exposing them to sunlight or other sources of tanning; they were to keep the patches covered with clothing.

The use of topical pharmaceutical products or other skin care products on the test site was not permitted during the study. Ingestion of medication or any treatment that could have altered the results of the study was also prohibited.

- **Observations and Data collection**

The patch zones and their surrounding area were observed for erythema, oedema, vesicles, blisters, ulcerations, dryness and acne (papules). These parameters were evaluated and graded as follows:

Reaction Scale:

0 = No visible reaction,
+ = Barely noticeable erythema,
1 = Mild / slight erythema in the patch zone,
2 = Moderate but well-defined erythema and presence of barely perceptible oedema (more palpable than visible),
3 = Marked erythema, presence of oedema and vesicles,
4 = Severe erythema, presence of vesicles, blisters, and ulcerations.

In addition to the observations made and recorded by Evalulab, the participants were encouraged to observe and report to Evalulab any immediate or delayed reactions such as redness, irritation, itching, or other sensations on the application sites for up to 72 hours after application.

All observations and comments provided by the participants were recorded in their respective Case Report Form. The obtained scores were then entered in a tabular form showing the number of reactions after treatment.

RESULTS

Fifty-five (55) participants, men & women aged 25 to 80 years (Average Age = 53.85), were included in this study.

One participant (*participant #02-0718-004*) dropped out of the study because they were experiencing slight itchiness due to reactions from two products and did not want to continue. Two participants (*participants #01-0718-051* and *#01-0718-054*) were withdrawn from the study due to scheduling conflicts. One participant (*participant #01-0718*-053) was withdrawn due to a stomach flu. Another participant (*participant #01-0718*-055) was removed due to loss of contact.

The final 50 participants completed the study without incident. The data obtained during the study are presented in Table II in the Appendices.

No reaction with the control (Pure Vaseline USP) was observed.

CONCLUSION

Under the conditions of the study described herein, the test product "Inodore | Unscented" has produced no significant signs of cutaneous irritation nor of skin sensitization.

It is therefore considered non-irritant and hypo-allergenic.

Also given the control provided by a dermatologist, the test product may bear the claim "Tested under the control of a dermatologist".

I the undersigned, Noor Mantash, – Clinical Research Associate, declare that the study was conducted in accordance with the principles of *"Good Clinical Practice"*. The recorded results show exactly and completely the raw data of the study.

Signature Date: Mont-Royal – September 2nd, 2022
Noor Mantash, B.Sc.
Investigator, Clinical Research Associate

I the undersigned, Adriana Aguirre Garzon, – Laboratory Technician, declare that the study was conducted in accordance with the principles of *"Good Clinical Practice"*. The recorded results show exactly and completely the raw data of the study.

Signature Date: Mont-Royal – September 2nd, 2022
Adriana Aguirre Garzon, B.Sc.
Laboratory Technician

I the undersigned, Marilou Nadeau, declare having validated the information provided in this report.

Signature Date: Mont-Royal – September 2nd, 2022
Marilou Nadeau, B.Sc.
Quality Assurance Director

APPENDICES

Table I. – Participants' Profile (Study #22W-0718-03)

Participant #			Initials	Age	Sex
01	-0718-	001	MC	56	F
01	-0718-	002	MB	78	F
01	-0718-	003	SB	62	F
02	-0718-	004	DT	65	M
02	-0718-	005	CH	70	M
01	-0718-	006	LB	31	F
01	-0718-	007	ND	59	F
01	-0718-	008	MA	80	F
02	-0718-	009	MC	65	M
01	-0718-	010	FM	55	F
01	-0718-	011	RV	64	F
02	-0718-	012	BG	66	M
01	-0718-	013	GH	74	F
01	-0718-	014	LT	37	F
02	-0718-	015	RS	38	M
01	-0718-	016	CT	39	F
01	-0718-	017	ST	42	F
02	-0718-	018	AE	39	M
01	-0718-	019	CO	72	F
01	-0718-	020	CP	76	F
01	-0718-	021	MM	58	F
01	-0718-	022	SB	65	F
01	-0718-	023	LP	31	F
01	-0718-	024	JM	63	F
01	-0718-	025	MB	35	F
02	-0718-	026	EL	65	M
01	-0718-	027	AZ	61	F
02	-0718-	028	AB	54	M
01	-0718-	029	RO	64	F
01	-0718-	030	JW	72	F
01	-0718-	031	LL	70	F
01	-0718-	032	JC	52	F
01	-0718-	033	SR	66	F
01	-0718-	034	SC	36	F
02	-0718-	035	RG	35	M
02	-0718-	036	WA	68	M
01	-0718-	037	LM	47	F
02	-0718-	038	EP	45	M
02	-0718-	039	AD	37	M
01	-0718-	040	AN	40	F
01	-0718-	041	RM	58	F
01	-0718-	042	LT	42	F
01	-0718-	043	SY	65	F
01	-0718-	044	ML	72	F
01	-0718-	045	SK	60	F
02	-0718-	046	YO	72	M
02	-0718-	047	AG	56	M
01	-0718-	048	AG	29	F
01	-0718-	049	AQ	63	F
02	-0718-	050	SO	25	M
01	-0718-	051	MM	43	F
01	-0718-	052	TM	39	F
01	-0718-	053	NT	54	F
01	-0718-	054	AM	26	F
01	-0718-	055	DP	26	F

Table II. – Individual results of HRIPT (Study #22W-0718-03)

Participant Identification					Induction Period Observations									Challenge Period Observations	
No.			Initials	Sex	#1	#2	#3	#4	#5	#6	#7	#8	#9	48hrs	72h*
01	-0718-	001	MC	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	002	MB	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	003	SB	F	0	0	0	0	0	0	0	0	0	PP	-
02	-0718-	004	DT	M	0	0	0	VS							
02	-0718-	005	CH	M	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	006	LB	F	PP	0	0	0	0	0	0	0	0	0	-
01	-0718-	007	ND	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	008	MA	F	0	0	0	0	0	0	0	0	0	0	-
02	-0718-	009	MC	M	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	010	FM	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	011	RV	F	0	0	0	0	0	0	0	0	0	0	-
02	-0718-	012	BG	M	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	013	GH	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	014	LT	F	0	0	0	0	0	0	0	0	0	0	-
02	-0718-	015	RS	M	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	016	CT	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	017	ST	F	0	0	0	0	0	0	0	0	0	0	-
02	-0718-	018	AE	M	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	019	CO	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	020	CP	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	021	MM	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	022	SB	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	023	FP	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	024	JM	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	025	MB	F	0	0	0	0	0	0	0	0	0	0	-
02	-0718-	026	EL	M	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	027	AZ	F	0	0	0	0	D	0	0	+	0	0	-
02	-0718-	028	AB	M	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	029	RO	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	030	JW	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	031	LL	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	032	JC	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	033	SR	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	034	SC	F	0	0	0	0	0	0	0	0	0	0	-
02	-0718-	035	RG	M	0	0	0	0	0	0	0	0	0	0	-
02	-0718-	036	WA	M	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	037	LM	F	0	0	0	0	0	0	0	0	0	0	-
02	-0718-	038	EP	M	0	0	0	0	0	0	0	0	0	0	-
02	-0718-	039	AD	M	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	040	AN	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	041	RM	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	042	LT	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	043	SY	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	044	ML	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	045	SK	F	0	0	0	0	0	0	0	0	0	0	-
02	-0718-	046	YO	M	0	0	0	0	0	0	0	0	0	0	-
02	-0718-	047	AG	M	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	048	AG	F	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	049	AQ	F	0	0	0	0	0	0	0	0	0	0	-
02	-0718-	050	SO	M	0	0	0	0	0	0	0	0	0	0	-
01	-0718-	051	MM	F	0	VS									
01	-0718-	052	MT	F	0	0		0	0	0	0	0	0	0	-
01	-0718-	053	NT	F	0	0	VS								
01	-0718-	054	AM	F	VS										
01	-0718-	055	DP	F	VS										

* :Optional
\- :Not applicable
VS :Withdrawn from study
0 :No visible reaction
\+ :Barely noticeable erythema
PP :Lost patch
D :Dryness