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

Final Report
Study N°20AV-0928-18

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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).

November 20th, 2020

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SUMMARY

Human Repeat Insult Patch Test
STUDY 20AV-0928-18

Sponsor Code: KL

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

Product tested: Aurafirm N
Customer Lot#: WO0919BAURN
Evalulab Lot#: 200918.KL.01

Date: November 12th, 2020

Results: Under the conditions of the test procedure referenced herein, the test product referenced above has produced no 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)

Nina Abdou, 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 September 28th, 2020 and November 4th, 2020.

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 Rébecca Padey, M.A. – Laboratory Assistant and Nina Abdou, B.Sc. – Investigator and under the control of Doctor Michel Journet, MD 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 (2) units of 100g were received.

Description of the product tested:		Description of control used:
Product name:	Aurafirm N	Pure Vaseline USP
Category:	Raw ingredient	
Client lot #:	WO0919BAURN	
Evalulab lot #:	200918.KL.01	
Application:	The product was used without dilution and was 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.

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 56 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	16	20 to 65	48.75
Female	40	20 to 78	52.73
Total	**56**	**20 to 78**	**51.59**

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 IV (very clear to mat) 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 jewellery, …,
2. With a 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 weeks 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,
+ = Erythema barely noticeable,
1 = Mild / slight erythema in the patch zone,
2 = Moderate but well defined erythema and presence of slight or barely visible oedema,
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-six (56) participants, men & women aged 20 to 78 years (Average Age = 51.59), were included in this study.

Three (3) participants (*participants #01-0928-023, #01-0928-033 and #02-0928-041*) did not complete the study due to schedule inconvenience and one (1) participant (*participant* #01-0928-014) did not comply with the instructions given for the study. For the remaining fifty-two (52) participants, 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 "Aurafirm N" has produced no signs of cutaneous irritation nor of skin sensitization.

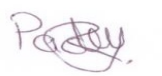
It is therefore considered non-irritant and hypo-allergenic.

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, Nina Abdou, – 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 – November 20th, 2020
Nina Abdou, B.Sc.
Investigator, Laboratory Technician

I the undersigned, Rébecca Padey, declare that the information provided in this report reflects in a complete and exact manner the results obtained during the study.



Signature — Date: Mont-Royal – November 20th, 2020
Rébecca Padey, M.A.
Laboratory Assistant

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

Signature — Date: Mont-Royal – November 20th, 2020
Marilou Nadeau, B. Sc.
Quality Assurance Director

APPENDICES

Table I. – Participants' Profile (Study #20AV-0928-18)

Participant #			Initials	Age	Sex
01	-0928-	001	KO	37	F
01	-0928-	002	SN	52	F
02	-0928-	003	EM	63	M
01	-0928-	004	RO	62	F
01	-0928-	005	JL	31	F
01	-0928-	006	AN	38	F
02	-0928-	007	AD	35	M
01	-0928-	008	AM	73	F
01	-0928-	009	AQ	61	F
01	-0928-	010	CM	50	F
02	-0928-	011	PL	58	M
01	-0928-	012	EB	26	F
02	-0928-	013	BG	64	M
01	-0928-	014	OG	44	F
01	-0928-	015	MC	55	F
01	-0928-	016	EL	49	F
01	-0928-	017	NT	53	F
02	-0928-	018	ED	42	M
01	-0928-	019	JB	61	F
02	-0928-	020	BB	61	M
01	-0928-	021	MA	78	F
01	-0928-	022	SB	63	F
01	-0928-	023	LB	30	F
01	-0928-	024	CT	70	F
01	-0928-	025	RP	54	F
01	-0928-	026	AS	64	F
01	-0928-	027	FM	54	F
02	-0928-	028	AS	64	M
01	-0928-	029	NM	68	F
01	-0928-	030	CP	74	F
01	-0928-	031	CO	70	F
02	-0928-	032	LA	42	M
01	-0928-	033	DC	45	F
01	-0928-	034	SN	62	F
01	-0928-	035	FN	58	F
01	-0928-	036	SL	55	F
01	-0928-	037	PD	66	F
02	-0928-	038	LL	65	M
01	-0928-	039	RC	50	F
02	-0928-	040	JB	41	M
02	-0928-	041	RD	49	M
01	-0928-	042	CA	48	F
01	-0928-	043	DV	64	F
01	-0928-	044	MM	20	F
01	-0928-	045	NR	38	F
02	-0928-	046	LC	43	M
01	-0928-	047	OS	59	F
02	-0928-	048	DY	20	M
01	-0928-	049	RM	57	F
01	-0928-	050	MM	47	F
01	-0928-	051	AA	44	F
02	-0928-	052	LR	44	M
02	-0928-	053	CH	46	M
02	-0928-	054	EP	43	M
01	-0928-	055	LM	45	F
01	-0928-	056	CA	34	F

Table II. – Individual results of HRIPT (Study #20AV-0928-18)

Participant Identification					Induction Period Observations									Challenge Period Observations	
No.			Initials	Sex	#1	#2	#3	#4	#5	#6	#7	#8	#9	48h	72h*
01	-0928-	001	KO	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	002	SN	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	003	EM	M	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	004	RO	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	005	JL	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	006	AN	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	007	AD	M	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	008	AM	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	009	AQ	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	010	CM	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	011	PL	M	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	012	EB	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	013	BG	M	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	014	OG	F	0	0	0	0	0	VS					
01	-0928-	015	MC	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	016	EL	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	017	NT	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	018	ED	M	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	019	JB	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	020	BB	M	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	021	MA	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	022	SB	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	023	LB	F	VS										
01	-0928-	024	CT	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	025	RP	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	026	AS	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	027	FM	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	028	AS	M	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	029	NM	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	030	CP	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	031	CO	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	032	LA	M	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	033	DC	F	VS										
01	-0928-	034	SN	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	035	FN	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	036	SL	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	037	PD	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	038	LL	M	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	039	RC	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	040	JB	M	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	041	RD	M	VS										
01	-0928-	042	CA	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	043	DV	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	044	MM	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	045	NR	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	046	LC	M	0	0	0	0	0	+	0	0	0	0	-
01	-0928-	047	OS	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	048	DY	M	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	049	RM	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	050	MM	F	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	051	AA	F	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	052	LR	M	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	053	CH	M	0	0	0	0	0	0	0	0	0	0	-
02	-0928-	054	EP	M	0	0	0	0	0	0	0	0	0	0	-
01	-0928-	056	CA	F	0	0	0	0	0	0	0	0	0	0	-

* :Optional
VS :Withdrawn from study
0 :No visible reaction
\+ :Erythema barely noticeable,