ASSESSMENT OF DERMAL COMPATIBILITY (irritant potential)

Occlusive patch test in a single application (duration 48 h) on 20 volunteers

Study N°	CADD013/19-04
Study Protocol code	REL/CA0147/2019/CLI
Sponsor	DCP DERMOSCIENCE INC. 1275 Gay-Lussac, Bureau 102 Boucherville, Québec, J4B 7K1, Canada
Analyzed substance	**Discreet Face** **Batch: (L) 8346**
Date of final report	**February 27th, 2019**

1) TEST MATERIAL :

The test substance consists of a cream for cosmetic use.

Name:	**Discreet Face**
Batch:	(L) 8346
Abich sample code:	CA0013/19-04
INCI Composition:	See annex
PaO/ expiration date:	n/a
Storage conditions:	Room temperature

The characterization of the test substance is under responsibility of the Sponsor.

2) AIM OF THE TEST

The objective of the study was the assessment of the local skin tolerance of the test product.

3) HANDLING

Upon arrival at Abich Inc the test sample was assigned a unique laboratory code number and entered in Abich Software identifying the lot number, description, sponsor, date received and tests requested.

4) INDEPENDENT ETHICS COMMITTEE (IEC)

An independent body constituted of medical professionals and non-medical members, whose responsibility it is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial and to provide public assurance of that protection by among other things, reviewing and approving/providing favorable opinion on the trial protocol, the suitability of the investigator(s), facilities and the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

5) REGULATORY ASPECT

This study has been carried out in compliance with the most recent recommendations of the Helsinki Declaration (Helsinki Declaration 64th WMA General Assembly, Fortaleza, Brazil, October 2013) and has followed the "Guidelines for the Assessment of Skin Tolerance of Potentially irritant Cosmetic ingredients", COLIPA, 1997.

In particular, to respect the ethical requirements imposed by the human studies, the following criteria were applied:
- Volunteers were recruited according to the recruitment criteria of inclusion and exclusion specified below (see Section 7.1 and 7.2);

- All volunteers were informed about the purpose and type of study, the possible risks, and freely gave their informed consent;
- Before the volunteers were exposed to the product, information on the toxicological profile of the product were obtained by the sponsor (see section on Limitation of Liability, above);
- All necessary precautions have been taken to avoid excessive skin reactions or adverse effects on the health of volunteers during the study;
- Security measures have been prepared in case of adverse reactions.

6) GENERAL PRINCIPLE

The principle of the study is based on the single application of 0.07-0.1 ml of test product on the intact skin of the back of adult volunteers. The product is kept in contact with the skin for 48 hours under occluded patch.

Products are tested pure or diluted depending on product type and intended use. In most cases are tested pure. The rinsing products are diluted at 1%, at 5% or at 10%, depending on the kind of product. The hydrophilic products are diluted in demineralized water while lipophilic products are diluted in mineral oil.

Powders are placed in the small area of the device for occlusive application and a drop of demineralized water or mineral oil is added to facilitate the homogeneous dispersion on the application surface and to ensure a good contact with the skin.

Solid materials are reduced into small pieces of dimensions suitable to be applicable onto the test discs of the occlusive device.

The observation of the effects caused by the application of the test substance is performed 15 minutes and 24 hours after the patch removal.

The assessment is made by comparison with a "negative control", prepared as follows:
-If the product is tested pure: empty patch;
-If the product is tested diluted: patch with about 0.07-0.1 ml of demineralized water or mineral oil (depending on the used solvent).

7) PANEL FEATURES

7.1 Inclusion Criteria of subject in a Study

- Individuals who are enlisted in the Abich Inc laboratory database.
- Individuals who are not under a doctor's care.
- Individuals who are healthy and do not suffer from chronic or dermatologic disorder that would affect the study in anyway.
- Individuals who have agreed to the study after reading, understanding and signing the informative form, informed consent from C.I.

7.2 Exclusion Criteria of subject in a Study

Prior to the beginning of the study, the following criteria were applied:

- Individuals under the legal age, 18 years old;
- Individuals under a doctor's care;
- Individuals who are not healthy and suffer from acute, chronic or dermatologic disorder that would affect the study in anyway;
- Female subjects who are pregnant or nursing;
- Individuals taking chronic or occasional medication which may affect the skin response to the product;
- Individuals with skin diseases which may interfere with the objective of the present study;
- Individuals who were diagnosed with chronic skin allergies;
- Individuals taking part in other studies simultaneously using the same test site or subject that did not have an appropriate rest period between studies.

After the beginning of the study, the following withdrawal criteria were applied:

- Individuals did not follow the conditions as described in the Study Information Sheet;
- Individuals who suffered any illness, an accident or developed any condition which could affect the outcome of the study;
- Individuals who did not longer wish to participate in the study.

For the duration of the study the volunteers were asked not to shower before the removal of the patch and to avoid exposure to UV rays on the test site.

The volunteers were also asked to report to the staff of the Abich Inc laboratory the use of any drug, particularly-anti-inflammatory drugs, steroids and antihistamines.

7.3 Recruitment

The study was performed on 20 healthy volunteers, male and female who have been identified from the volunteers' database of the Abich Inc laboratory. The selection was made by advertising on university bulletin board and website.

7.4 Informed Consent and Medical History Form

Before the beginning of the study, each volunteer has read and signed an informative form (informed consent form, C.I.). Each volunteer has had the opportunity to ask any kind of questions regarding the study. The aim of the test, the procedure and the possible risks related were explained. Only after signature of the informed consent the participation in the study was permitted. The originals of these informed consent forms were archived at the Abich Inc laboratory. All individuals signed also a consent allowing to treat personal data according to the Canadian law.

8) EQUIPMENT

The test product was applied by means by an occlusive application test (model: model Finn Chambers on Scanpor®), in sufficient amount to fill one test disk (approximately 0.07-0.1 ml)15 minutes before occluded application to the skin of the back of each volunteer.

9) EXPERIMENTAL PLAN

9.1 Structure of the study

The study was performed in single blind mode.

9.2 Environmental conditions

The study was performed in standard environmental conditions for each observing / reading time specified, maintaining temperature and humidity constant.

9.3 Area to be tested

The product has been applied on the upper back skin.

9.4 Patch test application method

Patch test application was performed with an occlusive method.

9.5 Preparation of the sample

Products are tested pure or diluted depending on product type and intended use. The use of the tested product **Discreet Face Batch: (L) 8346** is pure. The amount of substance applied to each disc of reaction was approximately 0.07-0.1 ml.

10) ASSAY METHODOLOGY

10.1 Application method

The portion of skin designed for the assay performance was cleaned up with demineralized water and dried with cellulose cotton wool tissue; the samples were applied on the back of the volunteers.

The fine positioning of the patch depended on the presence of naevi or congenital dyschromia, which were avoided.

In parallel to the application of products to be studied, a "negative" control patch was applied (empty or containing mineral oil or demineralized water).

10.2 Patch application period

The samples remained on the volunteer's skin for 48 hours. The application area was kept dry for the whole experimental time.

10.3 Finn chambers removal

After the scheduled application period expired, the patch was removed and the area was wiped from residues. Fifteen minutes and 24 hours after patch removal, the application area was carefully examined a technician from Abich Inc laboratory in order to evaluate skin reactions.

In particular, the following parameters were considered: erythema, desquamation, oedema and vesicles.

Each parameter was scored with values ranging from 0 to 3 to express differences in severity of the observed reactions.

11) OBSERVATION

11.1 Adverse events/Severe adverse events

In this final report, an "adverse event" is defined as any unintended or harmful response that is observed in a volunteer who is testing a product, which may not necessarily be due to the product or treatment in question. Volunteers participating in this test may be subject to a variety of adverse events such as cracking, rash, dryness or pain if the test product is strongly irritant or if the volunteer is particularly sensitive to the product. Moreover, potential development of an allergic sensitization may occur due to the test product or its ingredients.

A "severe adverse event" is referred to any unmedical occurrence such as death or persistent disability that will require the affected subject to be hospitalized or cause significant or permanent incapacity, which may or may not be related to the test product.

No adverse events of any kind were reported during the course of this study.

12) READ-OUTS

Skin reactions were evaluated 15 minutes and 24 hours after patch removal.
Skin irritation was scored according to the scale illustrated in Table 1.

Table 1
Evaluation scale for skin reations

ERYTHEMA	Score
None	0
Light erythema, hardly noticeable	1
Moderate and uniform redness	2
Severe and uniform redness (w/w.o. wounds and/or eschar)	3

OEDEMA	Score
None	0
Slight oedema (edges of area well defined by definite raising)	1
Moderate oedema (raised approximately 1 mm)	2
Severe oedema (raised more than 1 mm and extending beyond the area of exposure)	3

DRYNESS/DESQUAMATION	Score
No dryness/ no desquamation	0
Dryness with light desquamation (smooth skin)	1
Moderate desquamation	2
Severe desquamation	3

VESICLES	Score
None	0
Very small vesicles (barely visible)	1
Clearly visible, small vesicles (well-defined contours)	2
Large, well-defined vesicles	3

13) DATA ANALYSIS AND PRODUCT CLASSIFICATION

Scores assigned for erythema, desquamation, oedema and vesicle were registered for each volunteer. They were cumulatively considered and averaged. This allowed extrapolate the Mean Irritation Index (MII).

The product was classified on the basis of The Mean Irritation Index according to range of values reported in Table 2.

Table2

MII	CLASSES
≤ 0.4	*Not irritant*
0.5 ≤ MII ≤ 1.9	*Lightly irritant*
2.0 ≤ MII ≤ 4.9	*Moderately irritant*
5.0 ≤ MII ≤ 8.0	*Strongly irritant*

Note: results were interpreted according to ISO 10993-10 AMD 1:2004

(Biological evaluation of medical devices - Part 10: Tests for irritation and delayed-type hypersensitivity), which is applies a 0.4 cut-off for positive outcomes. On this basis, the effect of modest reactivity, which is often observed due to the exaggerated exposure conditions of this test, do not influence the final interpretation.

The tolerance to the product was evaluated by a dermatologist – considering the scores, observed reactions, their level of intensity and reproducibility from one volunteer to another.

14) RESULTS

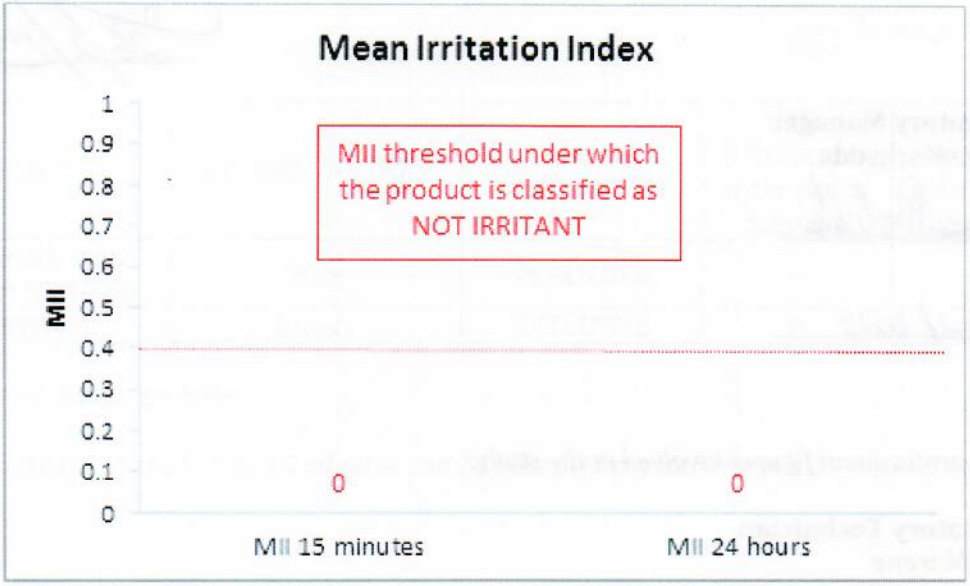
Under the adopted experimental conditions, the tested product **Discreet Face**
Batch: (L) 8346 applied under occlusive conditions on the healthy skin of 20 volunteers, caused a mean irritation index equal to:

- 15 minutes after patch removal;
- 24 hours after patch removal.

PRODUCT	*CONCENTRATION*	TYPE OF APPLICATION	MII *15 minutes after patch removal*	MII *24 hours after patch removal*
Discreet Face Batch: (L) 8346	Pure	OCCLUSIVE	0	0
CONTROL	Empty	OCCLUSIVE	0	0

MII = *Mean Irritation Index.*

Graphic 1: *MII of product at 15 minutes and 24 hours after patch removal.*



15) DISCUSSION AND CONCLUSIONS

The calculation of Mean Irritation Index, under the adopted experimental conditions, allowed to classify the test substance **Discreet Face Batch: (L) 8346** as **NOT IRRITANT** to the skin according to reference.

Supervision Dermatologist
Ari Demirjian MD,
FRCPC Professeur adjoint CUSM

Date: 26/2/19

Laboratory Manager
Debora Pischedda

Date: 13/02/2019

Other professional figures involved in the study:

Laboratory Technician
Lucia Marone

Date: 13/02/2019

16) ARCHIVING

The study protocol, the raw data and the final report will be kept at Abich Inc laboratory: 5160, Décarie Boulevard, suite 330, Montréal (Québec) H3X 2H9 - Canada for a minimum period of 5 years from the issue of the final report.

The control sample of the test substance and eventual specific reference material will be kept for 3 months, unless the customer provides a specific request.

The Customer, upon drafting a suitable contract, may request either the extension of the conservation of all or part of the materials for a further period or their restitution.

QA STATEMENT

The volunteers' recruitment is done according to specific internal procedures, according to GCP directive and according to Helsinki Declaration, 2013 requests. The volunteers signed the personal informal consent, they were informed about the complete study plan under development.

The collected data derived from this study is managed according to internal procedures following the GLP directive and is verified by the QA manager who checks the different parts of this study (comparison between raw data and recorded data, laboratory books and files, protocol and report) according to the quality plan of ABICH Inc laboratory (internal audits, periodical calibration status of the instruments if they are involved in the test).

Quality Assurance Chemist

Nina Duru _____

Date 19/02/2019

ANNEXES

ANNEX 1

ASSESSMENT OF DERMAL COMPATIBILITY (irritant potential)
Occlusive patch test in a single application (duration 48 h)
Skin reactions 15 minutes and 24 hours after patch removal and MII.

PRODUCT: **Discreet Face Batch: (L) 8346**

Vol.	Code	Gender	Readings at 15 minutes after the patch removal				
			ERYTHEMA	*OEDEMA*	*DRYNESS*	*VESICLES*	TOT
1	ADAG0500	F	0	0	0	0	**0**
2	ANVA0551	F	0	0	0	0	**0**
3	CABO0576	M	0	0	0	0	**0**
4	CETO0917	M	0	0	0	0	**0**
5	ELCA0554	F	0	0	0	0	**0**
6	IRST0014	F	0	0	0	0	**0**
7	JEBO0577	M	0	0	0	0	**0**
8	JOMA0932	F	0	0	0	0	**0**
9	JUSE0469	M	0	0	0	0	**0**
10	LIDE0399	F	0	0	0	0	**0**
11	LUCE0922	M	0	0	0	0	**0**
12	LYTA0120	F	0	0	0	0	**0**
13	MACH0992	F	0	0	0	0	**0**
14	NACA0467	F	0	0	0	0	**0**
15	NAUR0901	F	0	0	0	0	**0**
16	NERO0600	F	0	0	0	0	**0**
17	OLGH0334	F	0	0	0	0	**0**
18	PARE1048	F	0	0	0	0	**0**
19	PIDO0364	F	0	0	0	0	**0**
20	RASA0400	M	0	0	0	0	**0**
Mean		**14F/6M**	***TOTAL***				**0**
			MII				**0**

PRODUCT: **Discreet Face Batch: (L) 8346**

Vol.	*Code*	*Gender*	Readings at 24 hours after the patch removal				
			ERYTHEMA	*OEDEMA*	*DRYNESS*	*VESICLES*	TOT
1	ADAG0500	F	0	0	0	0	**0**
2	ANVA0551	F	0	0	0	0	**0**
3	CABO0576	M	0	0	0	0	**0**
4	CETO0917	M	0	0	0	0	**0**
5	ELCA0554	F	0	0	0	0	**0**
6	IRST0014	F	0	0	0	0	**0**
7	JEBO0577	M	0	0	0	0	**0**
8	JOMA0932	F	0	0	0	0	**0**
9	JUSE0469	M	0	0	0	0	**0**
10	LIDE0399	F	0	0	0	0	**0**
11	LUCE0922	M	0	0	0	0	**0**
12	LYTA0120	F	0	0	0	0	**0**
13	MACH0992	F	0	0	0	0	**0**
14	NACA0467	F	0	0	0	0	**0**
15	NAUR0901	F	0	0	0	0	**0**
16	NERO0600	F	0	0	0	0	**0**
17	OLGH0334	F	0	0	0	0	**0**
18	PARE1048	F	0	0	0	0	**0**
19	PIDO0364	F	0	0	0	0	**0**
20	RASA0400	M	0	0	0	0	**0**
Mean		**14F/6M**	***TOTAL***				**0**
			MII				**0**

Vol.	Code	Gender	CONTROL	
			Readings at 15 minutes	Readings at 24 hours
1	ADAG0500	F	0	0
2	ANVA0551	F	0	0
3	CABO0576	M	0	0
4	CETO0917	M	0	0
5	ELCA0554	F	0	0
6	IRST0014	F	0	0
7	JEBO0577	M	0	0
8	JOMA0932	F	0	0
9	JUSE0469	M	0	0
10	LIDE0399	F	0	0
11	LUCE0922	M	0	0
12	LYTA0120	F	0	0
13	MACH0992	F	0	0
14	NACA0467	F	0	0
15	NAUR0901	F	0	0
16	NERO0600	F	0	0
17	OLGH0334	F	0	0
18	PARE1048	F	0	0
19	PIDO0364	F	0	0
20	RASA0400	M	0	0
Total			**0**	**0**
MII			**0**	**0**

MII	CLASSES
≤ 0.4	*Not irritant*
0.5 ≤ MII ≤ 1.9	*Lightly irritant*
2.0 ≤ MII ≤ 4.9	*Moderately irritant*
5.0 ≤ MII ≤ 8.0	*Strongly irritant*

ANNEX 2

INCI COMPOSITION

Ingredients:

Aqua, Aloe Barbadensis (Aloe Vera) Leaf Juice, Caprylic/Capric Triglyceride, Coco-Caprylate/Caprate, Glyceryl Stearate SE, Propanediol, Butyrospermum Parkii (Shea Butter), Cetyl Alcohol, Glycerin, Stearic Acid, Hamamelis Virgiana (Witch Hazel) Distillate, Phenoxyethanol, Allantoin, Sodium Carboxymethyl Beta-Glucan, Arnica Montana Flower Extract, Calendula Officinalis Flower Extract, Tilia Cordata Flower Extract, Ginkgo Biloba Powder, Helichrysum Italicum (Immortelle) Oil, Jasminum Grandiflorum Flower Extract, 3-O-Ethyl Ascorbic Acid, Tocopheryl Acetate, Panthenol, Tetrasodium Iminodisuccinate, Sodium Hydroxyde.

17) REFERENCES

Declaration WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI
Ethical Principles for Medical Research Involving Human Subjects
Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington 2002 (Note of Clarification on paragraph 29 added)
55th WMA General Assembly, Tokyo 2004 (Note of Clarification on Paragraph 30 added)
59th WMA General Assembly, Seoul, October 2008
64th WMA General Assembly, Fortaleza, Brazil, October 2013

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"Quality assurance and GLP" 26 Oct. 1999.
Consensus documents Number 5.
OECD SERIES ON PRINCIPALES OF GLP AND COMPLIANCE MONITORING
"Compliance of laboratory suppliers with GLP principles" 28 Sept. 2000.
Consensus documents Number 7.
OECD SERIES ON PRINCIPALES OF GLP AND COMPLIANCE MONITORING
"The application of to GLP principles to short term studies" 15 Sept. 1999.
Consensus documents Number 8.
OECD SERIES ON PRINCIPALES OF GLP AND COMPLIANCE MONITORING
"The role and responsibility of the Study Director in the GLP studies" 15 Sept. 1999.