FINAL REPORT

ASSESSMENT OF DERMAL COMPATIBILITY (irritant potential)

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

Study N°	**CF024/14-01**
Study Protocol code	**REL/0185/2014/CLI/SAB**
Sponsor	**Chase Life Extension Foundation Ltd** **64 Stapleford Cres, Browns Bay** **0630 Auckland - New Zealand**
Analyzed substance	**TA Serum 818** **Batch: F7NCT/200114**

Study Director:
Dr. Samuele Burastero, _____

Medical Doctor, Board Certified Specialist in Allergology and Clinical immunology, Researcher at the Scientific Institute San Raffaele Hospital

Date: **15/05/2014**
Address: Istituto Scientifico Ospedale san Raffaele
Via Olgettina, 58
20132 – Milano (MI)
Italy

Dermatological supervision:

Prof. Paolo D. Pigatto, _____

Associate Professor of Dermatology, University of Milan, Board Certified Specialist in Dermatology

Date: **15/05/2014**
Address: University of Milan
Via Galeazzi, 4
20161 – Milano (MI)
Italy

Quality Assurance:
Dr.ssa Valentina Zanoletti, _____
Chemistry and Pharmaceutical Technonlogy
Date: **15/05/2014**
Address: Abich S.r.l. - Clinical and Cosmetological Trials Center
Via Bruno Buozzi, 4
20090 - Vimodrone (MI) - Italy

Assay Center Director:
Dr. Stefano Todeschi, _____
Biologist and Specialist in Clinical Pathology
Date: **15/05/2014**
Adress: Abich S.r.l. - Clinical and Cosmetological Trials Center
Via Bruno Buozzi, 4
20090 - Vimodrone (MI) - Italy

Other professionals involved in the study:

Dr.ssa Mariana Tritapepe - Biologist_____

Dr.ssa Giulia Caccia - Biologist_____

AUTHENTICITY OF RESULTS

I hereby declare that the study concerned by this report was carried out under my responsibility, according to the experimental protocol and the quality plan of the Abich Cosmetic Lab. and according to the rules of Good Clinical Practices (GCP).
All observations and data recorded during this test are reported in this study report.
I certify the re-reading of this report and do agree with its content.

The Medical Director

Dott. Samuele Burastero _____

Date **15/05/2014**

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SUMMARY

This study was performed with test substance **TA Serum 818 Batch: F7NCT/200114** *in order to evaluate its compatibility with human skin (irritant potential) under normal conditions of use and reasonable foreseeable misuse conditions, according to COLIPA guidelines ("Guidelines for the Assessment of Skin Tolerance of Potentially Irritant Cosmetic Ingredients" Edition of 1997).*
To this purpose, the test substance was used in a single application by a closed patch epicutaneous assay, on the healthy skin of the back, in 20 volunteers.

The test substance was left in contact with the skin for 48 hours.
Fifteen minutes and 24 hours after patch removal the skin reactions were evaluated according to defined parameters (erythema, desquamation, oedema and vesicles) and scored with gravity values ranging from 0 to 3. This allowed to extrapolate the Average Irritation Index.
Any other undesirable local reactions and subjective effects were also observed and registered.
The test was conducted under the direction of a Medical Doctor, Board Certified Specialist in Allergology with proven experience in Clinical Studies and with the supervision of a Medical Doctor Board Certified in Dermatology.

The calculation of Mean Irritation Index (MII), under the adopted experimental conditions, allowed to classify the test substance

TA Serum 818 Batch: F7NCT/200114

as **NOT IRRITANT**

The study was performed in the facilities of the Abich Assay Center, Via Buozzi, 4, 20090-Vimodrone, MI, Italy.The study started the 03/02/2014 *and ended the* 07/02/2014.

INTRODUCTION

On behalf of **Chase Life Extension Foundation Ltd,** *on the test substance* **TA Serum 818 Batch: F7NCT/200114,** *a study was conducted in order to collect the data on topic tolerability after a single prolonged application of the test substance.*
This kind of test is suitable to highlight any possible irritation risks under normal conditions of use as well as in reasonable foreseeable misuse conditions.
This test may not exclude the allergenic potential of the tested product.

DISCLAIMER

According to COLIPA guidelines, the test was performed with the assumption that the Sponsor under its responsibility provided to the personnel of the Abich Assay Center, truthful information on any ingredient of the test product endowed with potential toxicological relevance.
On the basis of such information, a general assessment of the toxicological information concerning the product was preliminarily carried out and ethical implications as to its use during the present study have been considered.

EXPERIMENTAL PROCEDURE

1. *TEST SUBSTANCE*

The test substance consists of an opaque light yellow gel.

Name:	TA Serum 818
Batch:	F7NCT/200114
Abich sample code:	0824/14-03
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. *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 type of product. 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 satisfactory 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 solvent).*
Clinical analysis is performed according to a scale proportional to the severity of irritation for each of the considered irritation phenomena (i.e.,erythema, desquamation, edema, vesicles).
The Mean Irritation Index is the average of the cumulative irritation values of the entire panel of volunteers.

4. *REGULATORY ASPECT*

This study has been carried out in compliance with the most recent recommendations of the 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, in order to comply with the ethical requirements imposed by the human studies, the following criteria were applied:
- volunteers were recruited according to the inclusion and exclusion criteria specified below (see Section 5.2);
- all volunteers were informed about the purpose and type of study and 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 were prepared in case of adverse reactions.

5. *PANEL FEATURES*

5.1. Volunteers recruitment

The study was performed on 20 healthy volunteers, males or females, of age between 18 and 65 years, who have been identified from the volunteers database of the Abich Assay Centre.
Before the beginning of the study each volunteer has read and signed an informative form (informed consent form, C.I.). Each volunteers has had the opportunity to ask any kind of questions regarding the study to which was given an exhaustive answer. The volunteer was explained the aim of the test, the procedure and the possible risks related.
Only after signature of the informed consent the participation in the study was permitted. Only volunteers in good general health conditions were included in the study.

The originals of these informed consent forms were archived at the Abich Cosmetic Lab. All patients signed a consent allowing to treat personal data according to the Italian law (Testo unico sulla privacy. D.Lgs 196/2003).

5.2. Exclusion criteria

The following criteria of exclusion were applied:
- *Minors;*
- *Women pregnancy or nursing condition;*
- *Subjects with blemishes, marks, including tattoos, scars, sunburns on the test site(s) which could interfere with scoring;*
- *Medication (local and/or systemic) which may affect skin response;*
- *Signs of irritated skin on test site(s);*
- *Any active skin disease which may interfere with the aim(s) of the present study;*
- *Participation in other simultaneous studies which that might interfere with the test evaluation or participation in a previous study without an appropriate rest period between studies.*

After study start, the following withdrawal criteria were applied:
- *Volunteers who did not follow the conditions as described in the Study Information Sheet;*
- *Volunteers who suffered any illness or accident or developed any condition which could affect the outcome of the study;*
- *Volunteers who did not longer wish to participate in the study.*

For all the duration of the study the volunteers were asked to refrain from exposure to UV rays and to water the areas of application of the patch.
The volunteers were also asked to report to the staff of the Abich Assay Centre the use of any drug, with particular reference to anti-inflammatory drugs, steroids and antihistamines.

6. *MATERIALS*

The test product was applied by means of adhesive strips for patch tests (model Curatest® F, adhesive strips for patch test, Lohmann and Rauscher International GMBH and Co., Rengsdorf, Germany) in sufficient amount to fill one test disk (approximately 0.07-0.1 *ml) before occluded application to the skin of the back of each volunteer.*

7. *EXPERIMENTAL PLAN*

7.1. Structure of the study

The study was performed in single blind mode.

7.2. Environmental conditions

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

7.3. Area to be tested

The product was applied on the skin of the back.

7.4. Patch test application method

Patch test application was performed with an occlusive method.

7.5. Preparation of the sample

The test substance was applied pure.
The amount of substance applied to each disc of reaction was approximately 0.07-0.1 *ml.*

8. *ASSAY METHODOLOGY*

8.1. 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 dischromia, 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).

8.2. Patch application period

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

8.3. 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 by a Medical Doctor specialized in Allergology 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 increasing severity of the observed reactions.

9. LETTURE / 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

10. *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 European Standard UNI EN ISO 10993-10 "Biological evaluation of medical devices - Part 10: Tests for irritation and delayed-type hypersensitivity" Edition of July 2009 (Chapter 6) 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 the this test, do not influence the final interpretation.*

11. ARCHIVING

The study protocol, the raw data and the final report will be kept in the archives of Abich Assay Center , in Via Buozzi, 4, 20090-Vimodrone (MI), both in electronic format and in reduced paper format for a period of 10 years from the issue of the final report.
The control sample of the test substance and eventual specific reference material will be kept for 1 month, unless a specific request is provided by the customer.
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.

12. *RESULTS*

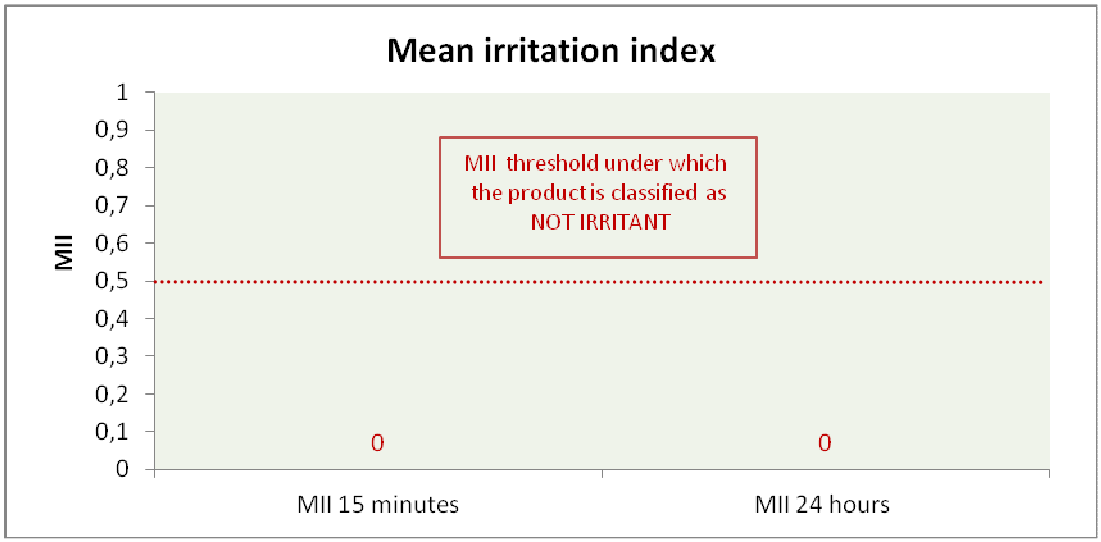
Under the adopted experimental conditions the tested product **TA Serum 818 Batch: F7NCT/200114** *applied under occlusive conditions on the healthy skin of 20 volunteers, caused a mean irritation index equal to:*

- ***0** 15 minutes after patch removal;*
- ***0** 24 hours after patch removal.*

PRODUCT	***CONCENTRATION***	**MII** ***15 minutes after patch removal***	**MII** ***24 hours after patch removal***
TA Serum 818 Batch: F7NCT/200114	*Pure*	0	0
CONTROL	*Empty*	0	0

MII = (*Mean Irritation Index).*

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



13. *DISCUSSION AND CONCLUSIONS*

The calculation of Mean Irritation Index, under the adopted experimental conditions, allowed to classify the test substance

TA Serum 818 Batch: F7NCT/200114

as **NOT IRRITANT**

14. REFERENCES

"Guidelines for the Assessment of Skin Tolerance of Potentially Irritant Cosmetic Ingredients" Edition of 1997

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

ISO 10993-10 AMD 1:2004 (Biological evaluation of medical devices - Part 10: Tests for irritation and delayed-type hypersensitivity)

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Pirila V. : "Chamber test versus patch test for epicutaneous testing". Contact Dermatitis I, 48, (1975).

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Brasch J., Geier H. Henseler T.: "Evaluation of patch test results by use of the reaction index. An analysis of data recorded by the information network of departments of dermatology". Contact Dermatitis, 33:385-380, (1995).

Consensus documents Number 4.
OECD SERIES ON PRINCIPALES OF GLP AND COMPLIANCE MONITORING
"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.

ANNEXES

ANNEX 1

ASSESSMENT OF DERMAL COMPATIBILITY (irritative potential)

Occlusive patch test in a single application (duration 48 h)
Skin reactions 15 minutes and 24 hours after patch removal and MII.

PRODUCT: **TA Serum 818 Batch: F7NCT/200114**								
	Code	***Age***	***Sex***	**Readings at 15 minutes**				
				ERYTHEMA	*OEDEMA*	*DRYNESS*	*VESICLES*	**TOT**
1	ALCA511	21	F	0	0	0	0	**0**
2	VALA158	31	F	0	0	0	0	**0**
3	ESA8	46	F	0	0	0	0	**0**
4	DOCA447	53	F	0	0	0	0	**0**
5	MACA64	45	F	0	0	0	0	**0**
6	SACA38	36	F	0	0	0	0	**0**
7	LOSE516	23	F	0	0	0	0	**0**
8	MORE267	49	F	0	0	0	0	**0**
9	KADI493	38	F	0	0	0	0	**0**
10	GIMA500	58	F	0	0	0	0	**0**
11	NAMA501	49	F	0	0	0	0	**0**
12	ARSU460	53	F	0	0	0	0	**0**
13	VABA502	20	F	0	0	0	0	**0**
14	MAAP492	45	F	0	0	0	0	**0**
15	DADI412	22	M	0	0	0	0	**0**
16	ROTE181	62	F	0	0	0	0	**0**
17	GITA175	40	M	0	0	0	0	**0**
18	MAVA368	28	M	0	0	0	0	**0**
19	LADA394	23	F	0	0	0	0	**0**
20	ALCA336	26	M	0	0	0	0	**0**
Mean		**38**	**16F,4M**	***TOTAL***				**0**
				MII				**0**

PRODUCT: **TA Serum 818 Batch: F7NCT/200114**								
Vol.	***Code***	***Age***	***Sex***	**Readings at 24 hours**				
				ERYTHEMA	*OEDEMA*	*DRYNESS*	*VESICLES*	**TOT**
1	ALCA511	21	F	0	0	0	0	**0**
2	VALA158	31	F	0	0	0	0	**0**
3	ESA8	46	F	0	0	0	0	**0**
4	DOCA447	53	F	0	0	0	0	**0**
5	MACA64	45	F	0	0	0	0	**0**
6	SACA38	36	F	0	0	0	0	**0**
7	LOSE516	23	F	0	0	0	0	**0**
8	MORE267	49	F	0	0	0	0	**0**
9	KADI493	38	F	0	0	0	0	**0**
10	GIMA500	58	F	0	0	0	0	**0**
11	NAMA501	49	F	0	0	0	0	**0**
12	ARSU460	53	F	0	0	0	0	**0**
13	VABA502	20	F	0	0	0	0	**0**
14	MAAP492	45	F	0	0	0	0	**0**
15	DADI412	22	M	0	0	0	0	**0**
16	ROTE181	62	F	0	0	0	0	**0**
17	GITA175	40	M	0	0	0	0	**0**
18	MAVA368	28	M	0	0	0	0	**0**
19	LADA394	23	F	0	0	0	0	**0**
20	ALCA336	26	M	0	0	0	0	**0**
Mean		**38**	**16F,4M**	***TOTAL***				**0**
				MII				**0**

Vol.	*Code*	*Age*	*Sex*	CONTROL	
				Readings at 15 minutes	**Readings at 24 hours**
1	ALCA511	21	F	0	0
2	VALA158	31	F	0	0
3	ESA8	46	F	0	0
4	DOCA447	53	F	0	0
5	MACA64	45	F	0	0
6	SACA38	36	F	0	0
7	LOSE516	23	F	0	0
8	MORE267	49	F	0	0
9	KADI493	38	F	0	0
10	GIMA500	58	F	0	0
11	NAMA501	49	F	0	0
12	ARSU460	53	F	0	0
13	VABA502	20	F	0	0
14	MAAP492	45	F	0	0
15	DADI412	22	M	0	0
16	ROTE181	62	F	0	0
17	GITA175	40	M	0	0
18	MAVA368	28	M	0	0
19	LADA394	23	F	0	0
20	ALCA336	26	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*

ANNEX2

INCI COMPOSITION

Aqua, Jojoba Esters, Macadamia Integrifolia (Seed) Oil, Ethyl Macadamiate, Isoamyl Laurate, Lecithin, Polyglyceryl-10 Stearate, Helianthus Annuus (Sunflower seed) Oil, phospholipids, Sodium Acrylates Copolymer, Glyceryl Caprylate, Isopropyl myristate, Glycerin, Hydrogenated Polyisobutene, Polyglceryl-6 Caprylate, Caprylhydroxamic acid, Propanediol, phytosphingosine, Sodium Phytate, TAM-818