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SUD COSMETICS
Pharma & Beauty Group
Alexandra BACO
ZA Les Plaines Sud
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FRANCE

Study report #21E1462
Related to quote #21D1462

BIOMETROLOGICAL EVALUATION OF THE MOISTURIZING EFFECT OF A COSMETIC PRODUCT

SERUM NOURRISSANT Ref. 3069.03 Batch #201106.002

CLINICAL INVESTIGATION CENTER	
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Document 1/1 including 26 pages

TABLE OF CONTENTS

KEY ELEMENTS OF THE STUDY #21E1462

BIOMETROLOGICAL EVALUATION OF THE MOISTURIZING EFFECT OF A COSMETIC PRODUCT

Claim

- Moisturizing effect until t4h.

Objective

To evaluate, for the studied product its moisturizing effect two and four hours after a standardized application.

Methodology

- Open, intra-individual study; each subject is her own control;
- Treated zone / Non-treated zone.

Kinetics

	Evaluation zone	t0	t2h and t4h
Information of the subject about study conditions and collection of her informed consent.	Legs	•	
Verification of inclusion and non-inclusion criteria.		•	
Acclimatization during about 30 minutes.		•	
Definition of two studied zones on the legs (one treated and one non-treated).		•	
Measurements using Corneometer®.		•	•
Application of the studied product at the laboratory.		•	

Dates

Product reception	Study date
September 1st, 2021	September 15, 2021

Product

Reference	Form	Application zone
SERUM NOURRISSANT Ref. 3069.03 Batch #201106.002	Transparent yellow solution (oil)	Defined treated zone on the legs

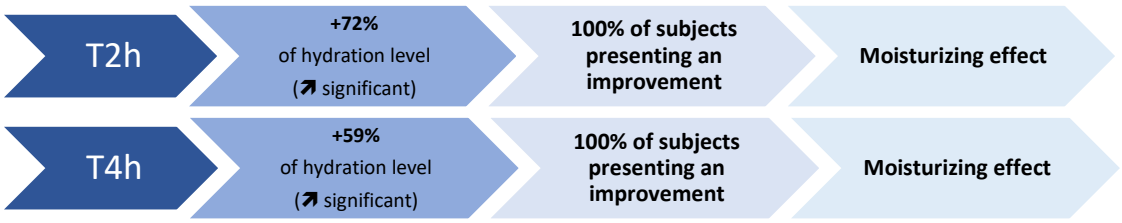
Study Population

Specific inclusion criteria

- **Sex:** female;
- **Age:** between 18 and 65 years old;
- **Phototype:** I to IV;
- Subjects with dry to very dry skin on the legs (cutaneous hydration rate 35-50 A.U. for dry skin and <35 A.U. for very dry skin, verified using Corneometer®);
- Subjects without hair on the external side of the legs.

Number of subjects analyzed	Average age
11	44±4 years (between 22 and 64 years old)

<table>
<tr><td>Conclusion</td><td colspan="3">Under these study conditions, after a standardized application and compared to a non-treated zone, the product “SERUM NOURRISSANT Ref. 3069.03 Batch #201106.002” presented a <u>significant moisturizing effect until t4h:</u>

Nevertheless, it should be noted that the galenic form of the product (greasy substance) takes part in the water concentration of the superficial layers of the epidermis by its occlusive effect.</td></tr>
<tr><td rowspan="2">Project Manager Assistant</td><td>Name</td><td>Date</td><td>Signature</td></tr>
<tr><td>Olga CZECHOWSKA</td><td>September 29, 2021</td><td>  </td></tr>
</table>

ELEMENTS CLES DE L'ETUDE N°21E1462

EVALUATION BIOMETROLOGIQUE DE L'EFFET HYDRATANT D'UN PRODUIT COSMETIQUE

Allégation

- Effet hydratant jusqu'à t4h.

Objectif

Evaluer l'effet hydratant du produit étudié deux et quatre heures après une application standardisée.

Méthodologie

- Etude en ouvert et en intra-individuel, chaque volontaire étant son propre témoin ;
- Zone traitée / Zone non-traitée.

Cinétiques

	Evaluation zone	t0	t2h et t4h
Information du volontaire sur les conditions de l'étude et recueil de son consentement éclairé.	Jambes	•	
Vérification des critères d'inclusion et de non-inclusion.		•	
Acclimatation pendant environ 30 minutes.		•	
Détermination de deux zones d'étude sur les jambes (une traitée et une non-traitée).		•	
Mesures à l'aide du Cornéomètre®.		•	•
Application du produit étudié au laboratoire.		•	

Dates

Réception du produit	Date d'étude
01/09/2021	15/09/2021

Produit

Référence	Forme	Zone d'application
SERUM NOURRISSANT Ref. 3069.03 Batch #201106.002	Solution jaune transparente (huile)	Zone traitée définie sur les jambes

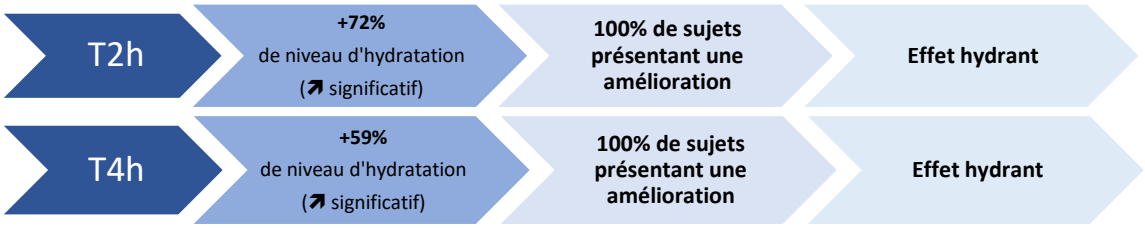
Population d'étude

Critères d'inclusion spécifiques

- **Sexe :** féminin ;
- **Age :** entre 18 et 65 ans ;
- **Phototype :** I à IV ;
- Volontaires présentant une peau sèche à très sèche au niveau des jambes (taux d'hydratation cutanée entre 35-50 U.A. pour la peau sèche et <35 U.A. pour la peau très sèche, vérifié à l'aide du Cornéomètre®) ;
- Absence de pilosité sur la face externe des jambes.

Nombre de volontaires analysés	Age moyen
11	44 ± 4 ans (entre 22 et 64 ans)

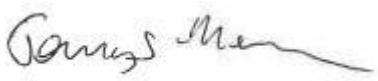
<table>
<tr><td>Conclusion</td><td colspan="3">Dans les conditions de cette étude, après une application standardisée et en comparaison à une zone non traitée, le produit "SERUM NOURRISSANT Ref. 3069.03 Batch #201106.002" <u>a présenté un effet hydratant significatif jusqu'à t4h :</u>

Néanmoins, il est à noter que la forme galénique du produit testé (corps gras) participe à la concentration en eau des couches superficielles de l'épiderme par son effet occlusif.</td></tr>
<tr><td rowspan="2">Chef de projet adjoint</td><td>Nom</td><td>Date</td><td>Signature</td></tr>
<tr><td>Olga CZECHOWSKA</td><td>29/09/2021</td><td>Czechowska</td></tr>
</table>

1 QUALITY CONTROL STATEMENT

The person responsible for the final quality control certifies that the study above was conducted as closely as possible to Good Clinical Practice (GCP-ICH), in compliance with the study protocol and EUROFINS Dermscan/Pharmascan standard operating procedures and that the study report reflects raw data.

	QUALITY CONTROL ASSESSOR
Last name	**TOMYS-MARCZYKOWSKA**
First name	**Małgorzata**
Date	**September 29, 2021**
Signature	

2 STUDY PROCESS

EUROFINS Dermscan/Pharmascan is certified ISO: 9001-2015.

EUROFINS Dermscan/Pharmascan benefits from a governmental Research Tax Credit from the French Ministry of Research.

The study is carried out on a cosmetic product whose safety has been assured by the Sponsor.

The European Directive 2001/20/EC and regulations issued by the Minister of Health (Order of the Minister of Health of May 2, 2012 regarding Good Clinical Practice, Dz.U. 2012, item 491) is not applicable. Therefore, this study is considered as non-interventional and does not require the Ethics Committee Approval and the Competent Authority Authorization.

+ See ethical requirements and regulatory standards in **Appendix 8.**

This study was conducted under the following conditions:

2.1 POPULATION

2.1.1 Selection

INCLUSION CRITERIA
Specific
• **Sex:** female; • **Age:** between 18 and 65 years old; • **Phototype:** I to IV; • Subjects with dry to very dry skin on the legs (cutaneous hydration rate 35-50 A.U. for dry skin and <35 A.U. for very dry skin, verified using Corneometer®); • Subjects without hair on the outer side of the legs.
General
• Healthy subject; • Subject having given her free informed, written consent.

NON-INCLUSION CRITERIA
• Pregnant or nursing woman during the study; • Cutaneous pathology on the study zone (eczema, etc.); • Use of topical or systemic treatment during the previous weeks liable to interfere with the assessment of the efficacy of the study product; • Subject having undergone a surgery under general anesthesia within the previous month; • Excessive exposure to sunlight or UV-rays within the previous month; • Subject enrolled in another clinical trial during the study period (concerns the studied zone); • Subject considered by the investigator to be likely not compliant to the protocol; • Subject who was abroad in a country with a higher incidence rate of COVID-19 than Poland within 14 days before the beginning of the study; • Subject presenting following symptoms: cough, shortness of breath, elevated body temperature – equal and above 37.5°C; • Subject who had contact with any person infected with COVID-19 within 10 days before the beginning of the study; • Subject who is currently during home quarantine recommended by the Sanitary Inspection.

2.1.2 Study requirements and constraints

DURING THE STUDY, THE SUBJECTS	
HAVE TO	**MUST NOT**
• comply with dates and hours of evaluation measurements; • remain in the special conditions of temperature and humidity in the waiting room during the whole study; • have legs exposed and not crossed, trousers leg rolled up during the whole study; • wear mask and disinfect hands during the whole study.	• apply any product to test areas the day of the visit* to the lab; • apply any other similar product to test areas during the whole study; • wash or wipe tested areas during the whole study; • eat, drink and smoke during the whole study.

** a shower with the usual product is allowed the day of the evaluation visit to the lab at least 4 hours before measurements.*

2.1.3 Protocol deviations

A protocol deviation can be defined as any non-adherence to the final protocol, including:

- wrong inclusion (inclusion criteria or non-inclusion criteria not fulfilled);
- start of a prohibited concomitant treatment;
- non-adherence of the subjects to the study schedule (missed or postponed visit);
- missing data for one or several evaluation criteria;
- low compliance of the subject to the study product(s) application;
- premature study end or untraceable subject;
- no respect of the constraints envisaged by the protocol.

Deviations to the protocol should be classified as:

- **minor** if they don't impact the rights, safety or well-being of the subjects. They do not increase the risk for the subject and/or do not have a significant effect on the integrity of the data collected,
- **major (or protocol violations**) if they affect the rights, safety or well-being of participants. They increase the risk for the subject and/or have a significant effect on the integrity of the study data,
- **critical:** any protocol violations as mentioned above necessarily requiring the suspension or the termination of the study.

In case of minor protocol deviation, the technician or the investigator repeats the instructions and reminds the subject to follow protocol requirements / study procedures. In case of persistent or major protocol violations, the subject is declared non-compliant and withdrawn from the study because of non-compliance.

- **No protocol non-adherence was observed during the study.**

2.1.4 Concomitant treatments

- **None of the subjects took new concomitant medications.**

2.1.5 Follow-up

	NUMBER OF SUBJECTS		
	INCLUDED	COMPLETING THE STUDY	ANALYZED
Moisturizing effect	11	11	11

2.1.6 Demographic data

ANALYZED SUBJECTS	SEX	AGE (IN YEARS)			SKIN TYPE ON THE LEGS	PHOTOTYPE	COMMENTS AND DETAILED DATA
		Mean ± SEM	Min.	Max.			
11	Female	44±4	22	64	Very dry: 6 Dry: 5	I : 0 II : 9 III : 2 IV : 0	See **Appendix 7.1**

2.2 INVESTIGATIONAL PRODUCT

2.2.1 Description

Reference	Batch #	Form	Packaging	Confidentiality procedure	Storage temperature
SERUM NOURRISSANT Ref. 3069.03	201106.002	Transparent yellow solution (oil)	1 sample of 90 ml	Encoded	Room temperature

2.2.2 Application

Zone	Frequency	Directions for use
Defined treated zone on the legs.	At the laboratory. Standardized application (2 x 1 µl/cm²).	Light, uniform massage with a fingerstall.

2.2.3 Labelling

Example of labelling of each product by EUROFINS Dermscan/Pharmascan and translation:

DERMSCAN Badanie n°	DERMSCAN Study #
Nr Ochotnika: ND Nr Dermscan: ..... W nagłej potrzebie:	Subject#: NA Dermscan ref.: ..... Emergency telephone number: .....
Warunki przechowywania:	Conservation: .....
Przechowywać z dala od dzieci i ich zasięgu wzrokowego. Stosować pod kontrolą medyczną tylko dla potrzeb badania.	Keep out of reach and sight of children. To be used only under strict medical supervision for clinical trial.

Legend: ND: nie dotyczy
NA: not applicable

2.2.4 Storage

Until the beginning of the study, product is kept at room temperature in a dedicated air-conditioned room, which is locked and access controlled.

2.2.5 Attribution to the subjects

➔ *Product*

The same product reference is applied for all the subjects.

➔ *Measurements and application zones*

The measurements and application zones of the study product are randomized.
+ See details in **Appendix 7.2.**

2.2.6 Handing-out

Not applicable. The standardized applications are done by the technician at the investigation center.

2.2.7 Future

As far as possible, one sample of the study product is kept by the investigation center for a period of six months after its receipt.

- **By default, the products (used and not used) are destroyed at the end of the study according to the current internal EUROFINS Dermscan/Pharmascan procedures.**

2.3 STUDY STAGES

At t0:

Subjects:
- come to the laboratory without having applied any product to the legs since the previous evening;
- are informed about the trial objectives, the procedures and the risks of the study;
- sign two copies of the Consent Form;
- acclimatize during about 30 minutes in the air-conditioned waiting room, the legs being bared.

Technician:
- conducts an epidemiological interview;
- verifies the inclusion and exclusion criteria;
- defines two zones on the legs for Corneometer® measurements, according to the randomization list presented in the **Appendix 7.2**:
  - one zone treated by the studied product,
  - one non-treated zone being the control;
- measures the cutaneous hydration rate using Corneometer® on two previously defined zones;
- applies the product to the previously defined treated zone.

At t2h and t4h after the product application:

Technician:
- measures the cutaneous hydration rate using Corneometer® on two zones defined at t0.

Ambient conditions during measurements:
- room temperature: 22±2°C;
- relative humidity: between 35% and 55%.

Remarks:

- before each measurement each zone is wiped three times with a tissue paper (concerns the studied part of the zone at each kinetic);
- the probe of Corneometer® is disinfected after each subject.

2.4 DATA ANALYSIS

The following data are analyzed:

	Parameter(s)	Unit(s)	Variation(s) t_i-t_0 Kinetics	Statistical analysis (tick if yes)	Expected result(s)
Corneometer®	Hydration rate	A.U.	ti-t0 (ti=t2h, t4h)	X	↗: moisturizing effect ➔: non-drying effect

Legend:
A.U.: arbitrary units

Individual data are presented in raw value tables. These tables also show the descriptive statistics: means, medians, minima, maxima, standard errors of the means (SEM) and confidence intervals of 95% (95% CI).

Variation tables present raw variations, percentage variations, descriptive statistics and the results of the statistical analysis (p).

2.4.1 Calculation formulas

The variations (Δ) and in percentage on the mean (Δ%) are calculated according to the following formulas:

Treated zone	Non-treated zone
$\Delta TZ = (TZ_{ti} - TZ_{t0})$	$\Delta NTZ = (NTZ_{ti} - NTZ_{t0})$
$\Delta\% \, TZ = \frac{(TZ_{ti} - TZ_{t0})}{TZ_{t0}} X100$	$\Delta\% \, NTZ = \frac{(NTZ_{ti} - NTZ_{t0})}{NTZ_{t0}} X100$

$$\Delta\Delta = \Delta TZ - \Delta NTZ$$

$$\Delta\Delta\% = \Delta\% \, TZ - \Delta\% \, NTZ$$

with:
- TZ: value obtained on the zone treated by the tested product
- NTZ: value obtained on the non-treated zone
- t0: before product application
- ti: at each measurement time after product application

2.4.2 Statistical method

PAIRED STUDENT T-TEST

Analysis conditions	p-value	H0	Conclusion
Type I error (α) = 5% in bilateral mode	**p ≤ 0.05**	Rejected	Statistically significant difference
Null hypothesis (H0) = no difference between means	**p > 0.05**	Not rejected	No statistically significant difference

2.4.3 Statistical software

The software used is Excel 2016.

2.5 AUDIT AND TRIAL MONITORING VISIT

An audit and/or trial monitoring visit may be carried out at the Sponsor's request or by the appropriate regulatory authority. The aim of the monitoring visit is to verify that the study is conducted according to the determined protocol and current regulations.

- **No monitoring visit occurred for this study.**

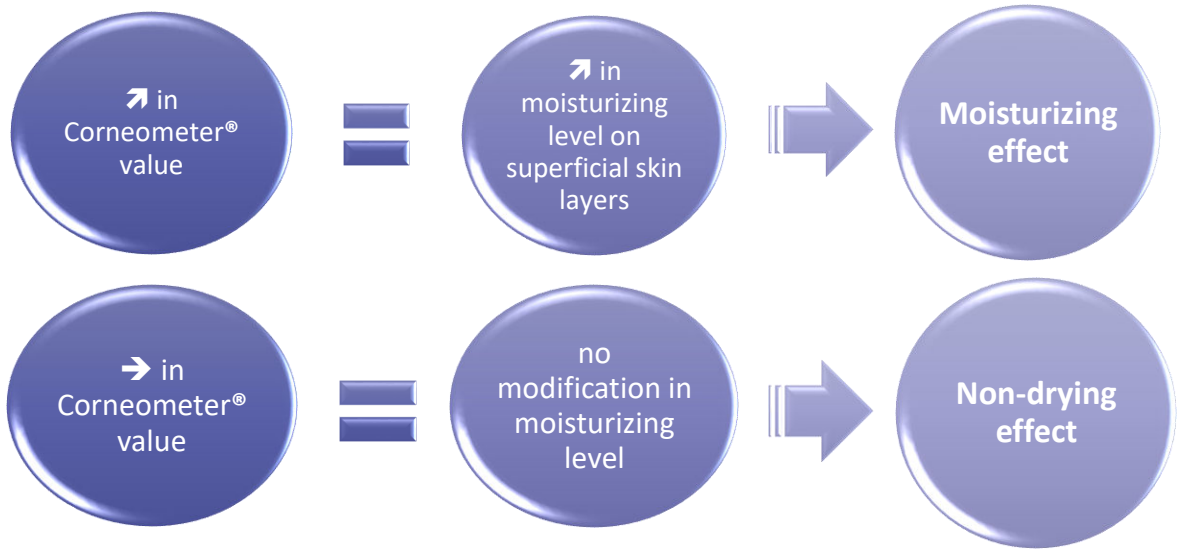
3 PRINCIPLES AND RESULTS

3.1 MOISTURIZING EFFECT

3.1.1 Principle

Cutaneous hydration measurements are performed with a **Corneometer® CM 825 (*COURAGE & KHAZAKA*)**. The measuring principle is based on capacitance measurement. The surface of the measurement head, in contact with the skin, modifies its electrical capacity according to the humidity level of the skin.

This technique is a well-established method to reproducibly and accurately determine the hydration level of the skin surface, i.e. the humidity level of the most external cutaneous layers of the *Stratum Corneum* (10-20 µm depth).



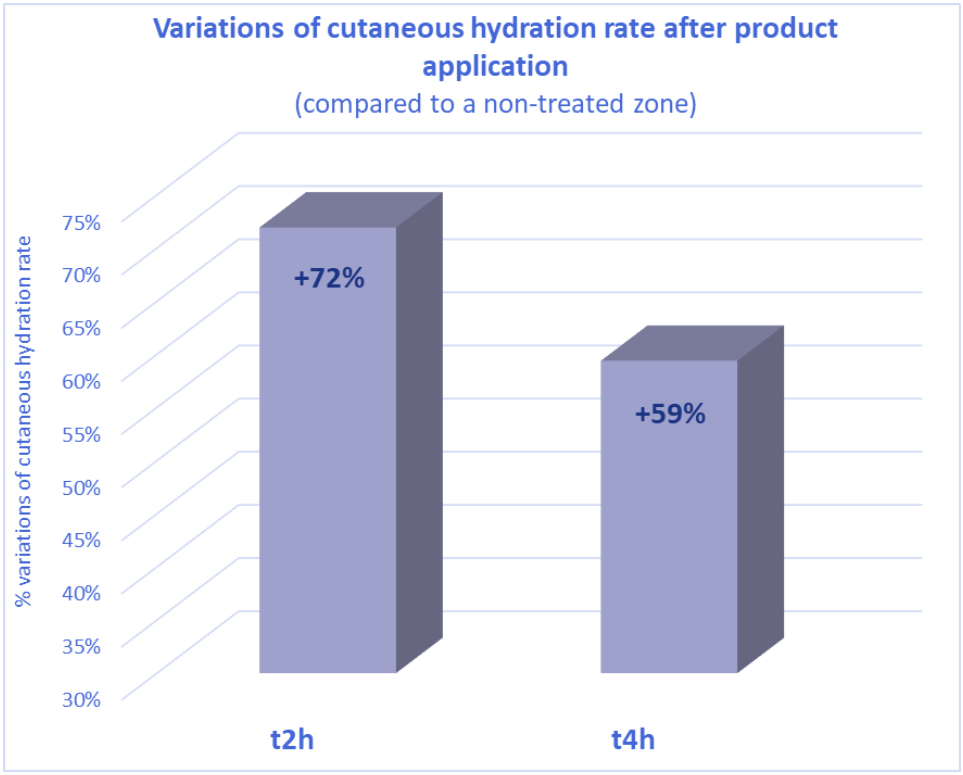
3.1.2 Summary of the results

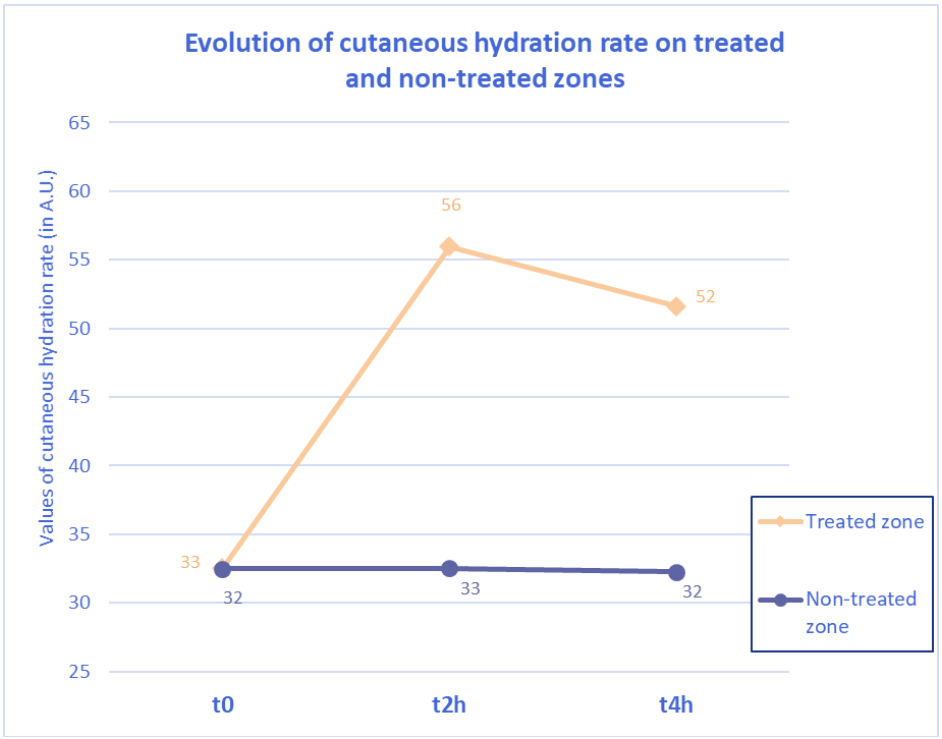
Individual results are presented in **Appendix 7.3.**
The synthesis of these results is presented in the table below:

Variation of the cutaneous hydration rate after a standardized application of the product (in comparison to a non-treated zone)

	Parameter	Kinetics	ΔΔ Tx-T0 (mean ± SEM)	Statistic p	Statistic Significativity	% of efficacy	% of subjects presenting an improvement
SERUM NOURRISSANT Ref. 3069.03 Batch #201106.002	Cutaneous hydration rate	Δ t2h	23 ± 1	<0.001	Yes	+72%	100%
		Δ t4h	19 ± 1	<0.001	Yes	+59%	100%

These results are presented in the graphs below:





Under these study conditions, in comparison to a non-treated zone, the product "SERUM NOURRISSANT Ref. 3069.03 Batch #201106.002" presented a significant moisturizing effect of epidermis superficial layers two and four hours after its standardized application: increase in cutaneous hydration rate of 72% at t2h and 59% at t4h.

4 CONCLUSION

Under these study conditions:

After a standardized application and compared to a non-treated zone, the product "SERUM NOURRISSANT Ref. 3069.03 Batch #201106.002" presented a significant moisturizing effect until t4h:

T2h	**+72%** of hydration level (↗ significant)	**100% of subjects presenting an improvement**	**Moisturizing effect**
T4h	**+59%** of hydration level (↗ significant)	**100% of subjects presenting an improvement**	**Moisturizing effect**

Nevertheless, it should be noted that the galenic form of the product (greasy substance) takes part in the water concentration of the superficial layers of the epidermis by its occlusive effect.

5 CERTIFICATION

The study is conducted according to Helsinki Declaration (1964) and its successive updates. Data are obtained using the study protocol, current internal procedures and as closely as possible to the guidance on Good Clinical Practice CPMP / ICH / 135 / 95 (R2).

This study is totally performed under the responsibility of EUROFINS Dermscan/Pharmascan.

All the observations and numerical data collected throughout the study are reported in this document and are in accordance with the obtained results.

	PROJECT MANAGER ASSISTANT
Name	**Olga CZECHOWSKA**
Date	**September 29, 2021**
Signature	

Any modifications are the sole responsibility of the author of the modification, whether he/she is acting for the Sponsor or independently.

The on-line publishing, on the Internet, of this study report with the names and signatures is strictly prohibited.

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Data analysis

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APPENDICES:

STUDY DOCUMENTS, DETAILED RESULTS & ETHICAL REQUIREMENTS AND REGULATORY STANDARDS

7 APPENDICES – STUDY DOCUMENTS

7.1 SUBJECTS CHARACTERISTICS

Subject #	Last name	First name	Age	Sex	Skin type on the legs	Phototype	Comments	Study date
1	ZW	M	43	F	D	II	None	September 15, 2021
2	MI	A	30	F	VD	III	None	September 15, 2021
3	MI	M	33	F	VD	II	None	September 15, 2021
4	WI	M	52	F	D	II	None	September 15, 2021
5	WO	U	64	F	VD	II	None	September 15, 2021
6	RO	T	60	F	VD	II	None	September 15, 2021
7	BI	K	22	F	D	II	None	September 15, 2021
8	KO	J	45	F	D	II	None	September 15, 2021
9	DO	K	59	F	VD	III	None	September 15, 2021
10	KI	E	45	F	D	II	None	September 15, 2021
11	WE	D	34	F	VD	II	None	September 15, 2021

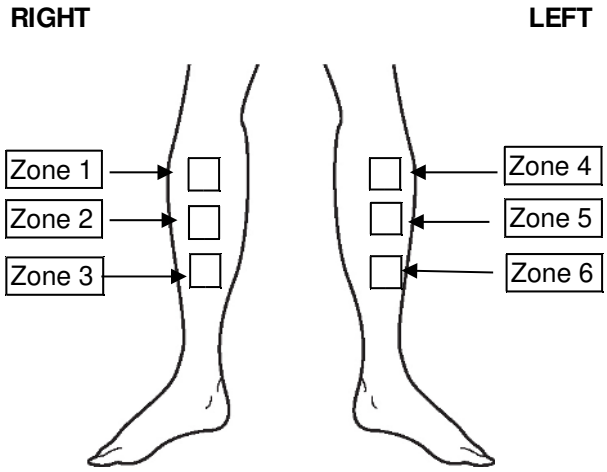
Mean	**44**	**F**	11	**VD**	6	**I**	0
Median	45			**D**	5	**II**	9
Minimum	*22*					**III**	2
Maximum	*64*					**IV**	0
SEM	**4**						
95% CI	9						

Legend: F: female
VD: very dry skin
D: dry skin

7.2 RANDOMIZATION LIST

Subject #	Measurment zones : legs					
	Right leg			Left leg		
	Zone 1	Zone 2	Zone 3	Zone 4	Zone 5	Zone 6
1	F	/	/	/	NT	/
2	/	F	/	/	/	NT
3	NT	/	F	/	/	/
4	/	NT	/	F	/	/
5	/	/	NT	/	F	/
6	/	/	/	NT	/	F
7	F	/	/	/	NT	/
8	/	F	/	/	/	NT
9	NT	/	F	/	/	/
10	/	NT	/	F	/	/
11	/	/	NT	/	F	/

Legend:
F: SERUM NOURRISSANT Ref. 3069.03 Batch #201106.002
NT: non-treated zone



7.3 INDIVIDUAL RESULTS

Cutaneous hydration rate evaluation: Corneometer® measurements (in arbitrary units)
A significant increase in the values characterizes a moisturizing effect of the product.

	Treated zone					Non treated zone					ΔΔ ZT / ZNT	
Subject	t0	t2h	t4h	Δ t2h	Δ t4h	t0	t2h	t4h	Δ t2h	Δ t4h	ΔΔ t2h	ΔΔ t4h
1	39	64	60	25	21	39	39	39	0	0	25	21
2	23	46	40	22	17	23	23	24	0	0	22	17
3	28	55	50	27	22	30	30	29	0	-1	27	23
4	33	52	49	19	15	37	38	38	1	1	18	15
5	26	53	49	27	23	25	25	25	0	0	27	24
6	26	59	54	33	28	25	24	24	0	0	33	28
7	40	57	54	18	14	38	39	39	0	0	17	14
8	39	62	59	24	20	43	44	43	0	-1	23	21
9	30	56	50	25	19	30	30	29	0	-1	25	20
10	44	65	61	21	17	40	40	40	0	0	22	17
11	30	48	43	18	13	27	26	26	-1	-1	18	14
Mean	**33**	**56**	**52**	**23**	**19**	**32**	**33**	**32**	**0**	**0**	**23**	**19**
Median	30	56	50	24	19	30	30	29	0	0	23	20
Minimum	*23*	*46*	*40*	*18*	*13*	*23*	*23*	*24*	*-1*	*-1*	*17*	*14*
Maximum	*44*	*65*	*61*	*33*	*28*	*43*	*44*	*43*	*1*	*1*	*33*	*28*
SEM	**2**	**2**	**2**	**1**	**1**	**2**	**2**	**2**	**0**	**0**	**1**	**1**
CI 95%	5	4	4	3	3	5	5	5	0	0	3	3

p	**<0.001**	
% of variation of cutaneous hydration	**72%**	**59%**
% subjects presenting an improvement	**100%**	**100%**

8 APPENDICES - ETHICAL REQUIREMENTS AND REGULATORY STANDARDS

8.1 ADVERSE EVENT

8.1.1 Adverse Event (AE)

Any noxious symptom, occurring in a subject taking part in a clinical trial, whether or not this symptom is related to the study or the study product(s) (e.g. flu, headache, abnormal biological analysis…).

8.1.2 Undesirable Effect (UE) / Adverse Reaction (AR)

For a cosmetic product, an **undesirable effect** is defined as an adverse reaction for human health attributable to the normal or reasonably foreseeable use of the cosmetic product(s).
There are 5 levels of imputability: very likely, likely, not clearly attributable, unlikely and excluded (ANSM methodology).

The severity/intensity of undesirable effects/adverse events can be graded on a three-point scale:
- **mild**: discomfort noted, that does not disturb normal daily activities;
- **moderate**: discomfort sufficient to reduce or affect normal daily activities;
- **severe**: inability to work or have normal daily activities.

8.1.3 Serious Adverse Event (SAE) / Serious Undesirable Effect (SUE)

Any event that:
- results in death (note: death is the outcome, not the event);
- is life threatening;
- requires in-patient hospitalization (at least one night) or prolongation of existing hospitalization (does not include hospitalization scheduled before the inclusion);
- results in temporary or permanent functional incapacity or disability;
- is a congenital anomaly;
- is considered like by the investigator.

8.1.4 Documentation

All concomitant treatments are reported in the CRF (Case Report Form); only those started after the beginning of the study are reported in the study report.

All Undesirable Effects are reported in the CRF and the study report.
If it requires the temporary or definitive termination of the study product, the need for a corrective treatment or the withdrawal of the subject, an Adverse Event form is completed.

All SAE/SUE are reported in the CRF and the study report.

8.1.5 Notification

The investigator declares to the Sponsor, by e-mail, the occurrence of adverse reactions according to their severity and their unexpectedness (according to the investigator's advice).

All SAE/SUE are transmitted by e-mail to the Sponsor without delay, at the latest 24 hours after knowledge of their occurrence.
A SAE/SUE declaration form signed by a physician is sent, within 48 hours, by e-mail with acknowledgement of receipt.

8.1.6 Follow-up

When an adverse event linked to the investigational product or the protocol persists at the end of the study, the Investigator ensures that the subject is followed up until total resolution of the event or stabilization of the symptoms without releasing the Sponsor of any obligation or responsibility.

8.2 PREMATURE TERMINATION OF SUBJECT PARTICIPATION

In compliance with the Helsinki Declaration (1964) and its successive updates, subjects have the right to exit from the study at any time and for any motive.

The investigator can also interrupt the subject participation in the study prematurely in the case of a disease occurrence, a pregnancy or the occurrence of an adverse reaction.

The Sponsor can demand that any subject be excluded from the study for major infringements to the protocol, for administrative reasons or any other motive however this would need to be clearly documented with a rationale as to why.

Nevertheless, premature removal of a high percentage of subjects from the study can make it difficult or impossible to interpret. Consequently, any premature exit without valid motives should be avoided as much as possible and is carefully documented in the case report form, the final report and, if necessary, in the Adverse Event form.

Every premature exit must be classified under one of the following headings:
- presence of a non-inclusion criteria;
- Undesirable Effect / Adverse Event occurrence;
- Serious Adverse Event / Serious Adverse Effect occurrence;
- withdrawal of consent;
- lost to follow-up;
- appearance of non-inclusion criteria;
- non-adherence to the protocol;
- other reason.

No replacement is foreseen as 10% additional subjects are planned to be included in the study.

8.3 CONFIDENTIALITY AND GENERAL DATA PROTECTION REGULATION

In this study, EUROFINS Dermscan/Pharmascan processes personal data of subjects on behalf of the Sponsor, in accordance with the rules on the protection of personal data and, in particular, the Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data. For this purpose, EUROFINS Dermscan/Pharmascan limits the collection and use of personal data to that which is needed for analysis and control purposes, by ensuring their security and integrity and by guaranteeing their confidentiality.
EUROFINS Dermscan/Pharmascan makes sure beforehand and throughout the duration of the data-processing:
- of the compliance with the obligations of the applicable data protection law,
- to inform subjects of their personal data-processing after obtaining their consent,
- to implement and maintain appropriate technical and organisational measures.

An identification code is attributed to each subject for the purpose to keep his/her identity confidential. This code consists of the first two letters/first letter of the subject's name and the first letter of his/her first name.

According to Article 14 of GDPR, the concerned subject must be informed of the identity and the contact details of the Controller and, where applicable, of the controller's representative. However, considering the objective of the study, to avoid any bias in the investigational product evaluation, the identity of the Sponsor is not revealed to the subject participating.

8.4 DATA COLLECTION AND VALIDATION

The personnel in charge of the study collects data into individual case report forms in electronic (e-CRF CleanWEB™ internet platform) or paper format and/or directly from measurement software.
When information is collected in paper format, the simple/double data entry is then done from these supports by the designed operator(s), without any interpretation, in specific MS EXCEL databases.
The Project Manager or assistant checks the double data entry by comparing both databases.

Then the coherence of the whole data set is checked as well as formulas used in the EXCEL tables (calculation formulas, selected data…).
When all the controls are done, the database is locked.

8.5 QUALITY MANAGEMENT

In order to ensure that the clinical trials are in compliance with the Sponsor's requirement, EUROFINS Dermscan/Pharmascan has implemented a quality management system which has been certified ISO 9001: 2015.
This quality assurance system includes appropriate Good Clinical Practices (GCP) and regulation requirements.

Each study report is subjected to a quality inspection by a member of the EUROFINS Dermscan/Pharmascan Proofreading Committee. The proofreader is chosen because he(she) is not involved in the audited study. The inspection of the study report allows to confirm that the results reflect exactly the study raw data and that the study fulfils any standard and regulatory requirements.
A certificate of quality inspection signed by the person who checked the report is enclosed in each study.

8.6 ARCHIVES OF STUDY DOCUMENTS

<table>
<tr><td rowspan="2">STUDY DOCUMENTS AND DATA</td><td colspan="3">TIME AFTER DISPATCH OF THE FINAL REPORT:
investiga-tion center → service provider → destruction
0 1 (maximum) 10 YEARS</td></tr>
<tr><td>Paper</td><td>Stored at the investigation center</td><td>Securely archived at an approved service provider</td><td rowspan="2">Destruction of the archives unless otherwise stipulated in writing by the Sponsor</td></tr>
<tr><td>Digital</td><td colspan="2">Securely archived</td></tr>
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