CONFIRMATION IN HUMAN SUBJECTS OF A FACIAL COSMETIC PRODUCT AFTER APPLICATION UNDER NORMAL CONDITIONS OF USE

CHECKING OF ITS COMPATIBILITY AND ACCEPTABILITY
OBJECTIVE ASSESSMENT OF ITS QUALITIES AND EFFICACY

Test with clinical control by a dermatologist

Final Report	November 19th, 2018
Study Code	9171018.A
Product	DMC - SÉRUM ROSTO
Sponsor	DMC
Study monitor	Jorge Leal Barreto
Study Center	PhD Trials Rua das Murtas 1B, 1º andar. 1700-309 Lisboa
Scientific Manager / Principal Investigator	Pedro Contreiras Pinto, *PhD*

CONFIDENTIAL DOCUMENT

The present study was performed according the criteria of Good Clinical Practices, and the Quality procedures implemented in PhD Trials®.

This report has 48 pages

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CERTIFICADO DE CONTROLO DE QUALIDADE

Quality Inspection Certificate

Study number	9171018.A
Date of the beginning of the study	October 3rd, 2018
Date of the end of study	October 31st, 2018
Date of audit	October 31st, 2018

O estudo acima referenciado foi realizado de acordo com as regras das Boas Práticas Clínicas e com os procedimentos padronizados da PhD Trials.
The study above listed was performed according with the rules of Good Clinical Practices, and under the standardized procedures of PhD Trials.

O responsável pelo Sistema de Gestão da Qualidade atesta que o presente relatório está de acordo com os dados obtidos e que foi realizado de acordo com os procedimentos e regras acima referenciados.
The Quality System responsible certifies that this report is according with the obtained raw data and respects the procedures and rules above listed.

Name / Surname	Patrícia Costa, MsC *(Quality manager NP EN ISO 9001:2015;* *Quality internal auditor EN ISO 19011:2011)*
Date	November 19th, 2018
Signature	

STUDY SUMMARY REPORT

OBJECTIVE	This study intends to assess the **anti-ageing effects,** as well as to check the **compatibility** and **acceptability** and to assess the **qualities and efficacy** of a cosmetic product, after application under the normal conditions of use planned by the Sponsor.
STUDY DATES	**Beginning**: October 3rd, 2018 **End**: October 31st, 2018
NAME **REFERENCE** **BATCH NUMBER**	DMC - SÉRUM ROSTO 9900000292 830199
SUBJECT NUMBER	The test product was assessed in **fifteen** (15) subjects.
SPECIFIC INCLUSION CRITERIA	Age: 40 - 70 years old, Gender: women Type of skin: mixed to dry and very dry skin Skin with aging signs (spots, wrinkles, ridles)
CONCLUSION	According with the experimental conditions adopted, and considering the classification defined in the protocol, the product **DMC - SÉRUM ROSTO** did not show any reactions during the 28 days of application. Therefore, the product presented **very good skin acceptability and compatibility**. **Regarding the instrumental efficacy:** The application of product **DMC - SÉRUM ROSTO** presented a 35.3% decrease in Wrinkles count, after 28 days. This decrease capacity is statistically significant regarding D0**.** The application of product **DMC - SÉRUM ROSTO** presented a 10.9% decrease in Wrinkles volume, after 28 days. This decrease capacity is statistically significant regarding D0. The application of product **DMC - SÉRUM ROSTO** presented an 8.8% decrease in Ra roughness parameter after 28 days. This decrease capacity is statistically significant regarding D0. The application of product **DMC - SÉRUM ROSTO** presented a 38.8% increase in skin hydration after 28 days. This increase capacity is statistically significant regarding D0. **Regarding the Self-assessment of qualities and efficacy:** After 28 days of application the Product **DMC - SÉRUM ROSTO** was well appreciated regarding the following items:

	- Pleasant texture - Easiness to apply - Pleasnt fragrance - Product is easily absorbed - Wrinkles improvement - Skin's firmness - Skin´s moisturized - Skin's visible health - Skin´s softness - Skin´s radiance - The skin is visible youthfulness Also, 100% of the subjects have a positive general opinion about the product after 28 days of applicaton. The results suggest that product **DMC - SÉRUM ROSTO** has the capacity to reduce wrinkle, to improve skin aging appearance and to increase skin hydration**.**

STUDY SCHEDULE

Assessments	**Screening/ Admission**	**D0**	**D0-D27**	**D28**
Informed written consent	X			
Demographic data	X			
Medical history	X			
Medical history update	X[1]			
PRIMOS		X		X
Corneometer measurements		X		X
Specific questionnaire				X
Skin examination and questioning		X		X
Adverse events monitoring		X	X	X
Product application		X (after evaluations)	X	X

[1]if applicable

I . OBJECTIVE

This study intends to assess the **anti-ageing effects,** as well as to check the **compatibility** and **acceptability** and to assess the **qualities and efficacy** of a cosmetic product, after application under the normal conditions of use planned by the Sponsor.

The **anti-ageing efficacy** of the product was assessed:

- objectively and quantitatively**,** by instrumental measurements of the wrinkles and skin roughness obtained in the periocular area with a Fringe projection system (Primos 3D®).
- objectively and quantitatively**,** by instrumental measurements of the skin hydration obtained with a Corneometer® (Dual-Cutometer MPA 580®).

The **acceptability** was:

- controlled by the dermatologist or the technician, under his authority, and after questioning of the subjects, after product application.
- Checked every day by the subjects themselves at home.

The **compatibility** was:

- controlled after visual examination of the experimental area, by the dermatologist or the technician, under his authority, and after questioning of the subjects, after product application.

The subjective **qualities and efficacy** were assessed, at the end of the study (D28), using a self-assessement questionnaire.

II . STUDY RELEVANCE

II. 1. Methodological approach

The experimental conditions adopted (experimental area, quantity of product applied, frequency and duration of the applications…) reproduce the normal conditions of use advocated and the test performed on a “small scale”, reflects the application by the future consumers.

The observance of the experimental conditions by the subjects who take part in the study was assessed by a questionnaire during and at the end of the study and by a control of the products consumption.

The subjects’ opinion was taken into account since it can reflect that of the potential consumers.

II.2. Panel

The panel corresponded to the population likely to use the product. The main inclusion criteria: women with ages between 40-70 years old who have signs of ageing, correspond to the target market of the product.

The number of subjects defined in the protocol was sufficient to check acceptability and compatibility and to assess the efficacy of the product.

II.3. Results

II.3.1. Assessment of the efficacy

The efficacy of the product was assessed by the Technical Department Manager of the investigator center, who has an appropriate experience or by a qualified and experienced technician under his authority.

The method chose for the assessment of the **anti-ageing efficacy** uses several methodologies. Numerous publications support this methodology (see XII).

The instrumental efficacy data are expressed in numbered data and are submitted to a suitable statistical treatment (student-t or Wilkoxon Ranks Signs Test for all the continuous data comparisons between D0 and D28).

All the calculations were performed using SPSS 23 (IBM). A 95% level of significance was adopted.

The subjective data of efficacy was submitted to a suitable statistical treatment Binomial test.

II.3.2. Checking of the acceptability

The acceptability of the product was controlled by the dermatologist who has an appropriate experience or by the responsible technician under his authority. Numerous publications support this methodology, see XII).

The results were mainly expressed as descriptive data and did not require a statistical treatment.

If the test products are well accepted by the subjects, under these experimental conditions, by extrapolation it should be safe for human health when applied by a great panel of consumers.

II.4. Ethics

The study was performed according to the Declaration of Helsinki principles and subsequent amendments.

The object of the study consists in the application of the test product in accordance with its normal use, in order to reduce any possible risk to subjects that may be selected for the trial. There is a commitment between the particular objectives of the study and any potential risks and problems related to the protocol on trial.

The application of the product was carried out by the responsible Researcher, at the Research Centre. The study was conducted in the spirit of Good Clinical Practice Guidelines and general principles of Law 46/2004 of August 19th. The protocol and test conditions were reviewed by the Internal Review Board (**opinion nº 3925/2018**) and the standard protocol was submitted to the Ethical Commission of PhD Trials.

The risks incurred by subjects in the development of this study were minor and without any clinical implications. The study may come to reveal previously acquired allergies to some of the ingredients. However even in such cases, the reaction should be limited to the test area, and its manifestations confined and controlled.

The research centre was responsible for providing information and prior knowledge to all subjects selected.

All the data concerned subject health and clinical data during and after the study performance are subject to medical-patient relationship. The investigational centre cannot send to the sponsor the actual identity of the subjects. The investigational centre presented the data fully codified in respect to subject's data.

III . TYPE OF STUDY

This project is a single-center, blinded controlled study in healthy subjects.

The evaluation of the subjects was against the baseline evaluation.

It is performed according to the general conditions of PhD Trials®, established for the performance of Human test projects.

This study was conducted in accordance with the general conditions of PhD Trials, established for the development of a research project involving human subjects, summarised by protocol (MD.122/02 Protocol PT.06.01 final/01).

IV . INVESTIGATION CENTER

IV.1. Study Center

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IV.2. Technical staff

Investigator (dermatologist): Leonor GIRÃO, *MD*
Scientific manager: Pedro CONTREIRAS PINTO, *PhD*
Quality manager: Patrícia COSTA, MsC
Administrative coordinator: António COSTA

V . DATES OF STUDY

Beginning: October 3rd, 2018

End: October 31st, 2018

VI . PRODUCT

VI.1. Identification of the test product

Denomination of the product	Batch Number	PhD Trials reference	Usual conditions of use	Quantity required for the study /number of samples
DMC - SÉRUM ROSTO	830199	9171018.A	Once a day	50ml / 15 samples

VI.2. Information concerning the test product

The documents related with the test product, supplied with the samples, were: Letter of Agreement, particularly concerning the conformity of the formulae to the established regulations and their safety, and the Order Form. The qualitative and quantitative formula of the product can be requested by the Investigator in a case by case situation, especially if there are some reactions noted.

VII . SUBJECTS

VII.1 . Number

The number of subjects whose data had to be exploitable at the end of the study was 15.

Fifteen (15) subjects were included in the study.

There were no withdrawals and no exclusions.

The compatibility and efficacy of the test product was therefore assessed on fifteen (15) subjects.

VII.2 . Specific inclusion criteria

The specific inclusion criteria, defined in the protocol, were the following ones:

Age: 40 - 70 years old,
Gender: women
Type of skin: Mixed to dry and very dry
Skin with aging signs (wrinkles, loss of firmness)

All the subjects corresponded to these specific inclusion criteria. Their typological characteristics are defined in **Appendix 1**

VII.3 . Specific non-inclusion criteria

The specific non-inclusion criteria are those defined for this kind of methodology in accordance with the corresponding procedure and the following ones for this study particularly:

- cutaneous marks on the experimental areas, which could interfere with the assessment of skin reactions (pigmentation troubles, scar elements, over-developed pilosity, ephelides and naevi in too great quantity, sunburn),
- allergy or reactivity to products of the same category than the tested one,
- with history of malignant melanomas (Dubreullh melanosis…)
- unbalanced hormonal treatment,
- forecast of initiation of an hormonal treatment or change of the usual hormonal treatment during the study,
- treatment with Vitamin A acid or its derivatives stopped less than 3 months before the beginning of the study,
- forecast of intensive sun or UVA exposure (UV lamps) during the test period,
- breast-feeding or pregnancy.
- no anti-ageing or aesthetic treatment: botox or botox like products, peelings, plastic surgery, hyaluronic acid treatment, Plasma Rich Platelets treatment, or any other specific treatments prone to change the skin aspect during the last 6 months.

- neither anti-allergic, anti-inflammatory treatment nor treatment with patent medicines containing Vitamin A acid or its derivatives before and during the study (if therapeutic requirement : exclusion foreseen),

- systemic disorders: Cardiovascular, pulmonary, digestive, neurologic, psychiatric, genital, urinary, haematological, endocrine

- individuals who have undergone a bilateral mastectomy with lymph node removal, a unilateral mastectomy with lymph node removal within the last year, or a bilateral axillary lymph node removal,

- individuals with a history of immune deficiency or auto-immune disease, treated for malignancy within 6 months prior to enrollment or who are currently under treatment for asthma or diabetes,

- forecast of vaccination during the test period or last vaccination within 3 weeks before the study.

All the subjects corresponded to these specific non-inclusion criteria.

VIII. METHODOLOGY

VIII.1. Experimental conditions of application of the test products

The experimental conditions, defined by protocol, were the following ones:

Experimental area(s)	Product directions of use	Application(s) at the Institute	Application(s) at home Frequency/duration	Quantity
Face	Application, **by the subject herself**, on clean skin by gentle digital massage until complete absorption.	First application (Volunteers' education and trainee application)	**From D1 to D27** Application, **once a day** for 27 +/- 2 consecutive days **(4 weeks)**	As much as necessary

VIII.2 . Constraints of the study

The constraints imposed on the subjects were those defined in the corresponding protocol:

- no application of products on the experimental area (except the tested products),

- full respect for the test product conditions of use,
- no application of hydrating products on the experimental areas,
- no change in hygiene habits,
- no application of makeup on face and lips, on the day of the evaluations
- no change in the way of life or in the physical activity,
- no exfoliating treatment on the experimental areas,
- coming to the investigator centre at each control **at the defined day and hour**,
- description of any treatment undertaken during the study and all eventual deviations.
- no application of the tested products on the day of measurements.

VIII.3. Control of the observance of the modalities of the protocol

The investigator checked about the respect of the **constraints**.

The subjects were questioned during and at the end of the study. The Investigator assessed the importance of the possible deviations in comparison with the experimental conditions required at the beginning of the study.

The synthesis of the answers obtained was enclosed in **Appendices 2/1 and 2/2**.

All the deviations from the protocol were analyzed and the investigator assessed their effect on the validity of the results.

All the constraints of the study, defined in the protocol, were respected by the subjects.

A product consumption control was performed at the end of the study. The sample(s) supplied to each subject was (were) weight in the beginning of the study and at the end after the last application.

The mean consumption by application was **1.17g ± 0.44g**. The results are presented at **Appendix 3**.

VIII.4 . Specific information regarding concomitant medication

The subjects provided information about any anti-ageing, anti-wrinkle or aesthetic treatment before the study inclusion. They also provided information about the concomitant medication that were undertaken during the study. No concomitant or specific medication or treatments were performed during the study by the subjects.

VIII.5 . Checking of the acceptability

VIII.5.1. Frequency of the examinations

The subjects were requested to note every day any reaction observed and sensation of discomfort felt on the **individual observation sheet** they were given at the beginning of the study.

A skin examination of the experimental areas was performed by the dermatologist or the responsible technician.

This examination was performed visually under standard "daylight" source, before then after 28 ± 2 consecutive days of use.

Concurrently with the clinical examination(s) performed after use of the product, each subject was questioned about the possible sensations of discomfort she felt.

All the examinations were performed in accordance with the conditions defined in the protocol.

VIII.5.2. Expression of the results of the skin examination and questioning

The information gathered during the questioning is compared to that noted every day by the subject on her individual observation sheet.

The expression of the results of the skin examination and questioning was that defined for this type of study in accordance with the corresponding procedure.

VIII.5.3. Expression of the data gathered in the individual observation sheet

The subject had noted any reaction or sensation of discomfort on the individual observation sheet reserved for that effect, using hers own words to express what they had felt.

VIII.5.4. Expression of the results of the questioning and skin examination

In the case of reactivity:

- **The main visible signs are noted, i.e.**:

Erythema, Oedema, Vesicle, Bulla, Papule, Scab, Dryness, Coloration, Soap effect.

The intensity of the **erythema and oedema** is assessed according to an ordinal scale: slight, moderate, severe.

The appearance of the **erythema** is specified: diffuse, punctuated, peripheral (around the application site).

The importance of the number of **vesicles and papules** is assessed according to an ordinal scale: 1 to 2 vesicles or papules, more than 2 vesicles or papules.

Bulla, scab, dryness, coloration and soap effect are described.

The importance of the **dryness and coloration** is assessed according to an ordinal scale: slight, moderate, severe.

- **The main sensations of discomfort are described, i.e.:**

Heating, Stinging, Pruritus (itching), others.

VIII.5.5. Interpretation of the results of the questioning and skin examination

The dermatologist or the responsible technician notes for any clinical sign or sensation of discomfort described its location, duration, date of occurrence after application of the product, frequency, intensity, evolution, medical treatment possibly undertaken, accountability of the product: **excluded, doubtful, not clearly attributable, likely, very likely**.

He also notes the usual or unusual characteristic of the clinical sign or sensation of discomfort described, by questioning the subjects about the effects observed when applying similar products.

The results are expressed in a descriptive manner for the visible signs or the sensations of discomfort and the percentage of "reactive" subjects is calculated.

All the subjects included in the study are taken into account to check the acceptability of the test product as long as they are submitted at least to one post application examination at the defined time or else.

The interpretation of the results of the questioning and skin examination and of the data gathered in the individual observation sheet is that defined for this type of study in accordance with the corresponding procedure.

This interpretation, performed by the dermatologist is absolute, referring to the following grading scale, which takes into account the sensations of discomfort described by the subjects and the visible reactions of irritation (clinical signs). The test product can therefore have a **very good, good, moderate or bad compatibility and acceptability.**

Compatibility and Acceptability	% of subjects exhibiting clinical signs ascribable to the test product (compatibility)	% of subjects exhibiting sensations of discomfort ascribable to the test product (acceptability)
Very good	0 %	0 %
Good	0 %	< 25 %
Moderate	< 10 %	whatever
	0 %	25 to 50 %
Bad	≥ 10%	whatever
	0 %	> 50 %

According to the nature and intensity of the clinical signs or sensations of discomfort, the dermatologist can have to under-class or over-class the product in relation to the grading scale.

If an **allergy** to the test product **is suspected**, an additional study can be required and performed after agreement by the Sponsor; for example, allergologic inquiry (patch test) to search for the responsible ingredient(s) or confirmation of the reactivity of the skin to the product concerned (open test). The modalities of the additional study are defined by the dermatologist.

The interpretation of the results is also relative referring to the internal data base of the investigator center.

VIII.6. Assessment of the efficacy

VIII.6.1. General conditions of the study

VIII.6.1.1 Standardization of the room conditions

All the evaluations were performed in a fully controlled room and after an initial acclimatization process of at least 15 min in a fully controlled and acclimatized room (Controlled temperature: T = 21°C ± 2°C; Controlled relative humidity: RH = 55% ± 10%). A summary of the room conditions during the evaluation days is presented in **Appendix 4**.

VIII.6.1.2 Standardization of the period of the day

To avoid circadian changes, 2 evaluation periods were defined (Morning: 9h-13h00m; Afternoon: 13h00m-19h00). Each subject chose, on the first day, the best hour to be evaluated. All the evaluations were performed on the same period of the day.

VIII. 6.2. Assessment of the wrinkles.

VIII. 6.2.1 Principle

3D images of the skin topography are obtained by a digital fringe projection using DLP® micro mirror displays. A fringe standard is projected on the skin and detected by the CCD camera of the optical system. The 3D effect is calculated by the deflection in the fringes which represent qualitative and quantitative the skin profile.

VIII. 6.2.2 Equipment

A Phase Shifting Rapid In-vivo Measurement of Skin system will going to be used (PRIMOS 3D 40x30 mm evaluation area, Gfm, Germany).

VIII. 6.2.3 Measurement area

The measuring area was the periocular area (left or right), randomly selected. The same area was evaluated at D0, D28.

VIII. 6.2.4 Frequency of measurements

The measurements were performed on **D0, D28.**

VIII. 6.2.5 Expression and interpretation of the results

At each experimental time, the wrinkle parameters and standard roughness is calculated in the full aligned image.

The parameters defined are:

Wrinkle count and volume
Ra = Arithmetic mean of the skin surface
Rz = Mean of the 5 biggest peaks and the 5 lowest valleys in the image area

All the subjects included in the study are taken into account to assess the efficacy of the test product as long as they are submitted to all the examinations, at the defined times.

The individual results are expressed:

- in absolute values of the parameter for each experimental time,
- in variation of the parameter against D0 for each experimental time.
- In % change of the parameter values and area variation of D28 against D0.

VIII. 6.3. Assessment of the hydration

VIII. 6.3.1 Principle

Hydration content is obtained by an electrometric system which is based in the "Capacitance" measurement, allowing the calculation of the water dielectric constant. The measuring probe has an interdigital grid of gold-covered electrodes. The interdigital electrode is covered by a low dielectric vitrified material. Therefore there is no galvanic contact between the electrode and skin surface. A constant application pressure is applied on the skin surface through a spring system. As a consequence of the probe design, the system (electrode, superficial parts of the stratum corneum and epidermis) behaves a capacitor. Measurements are obtained in Arbitrary Units as reference to a Factory standard.

VIII. 6.2.2 Equipment

The measurements are performed with a Corneometer CM825 probe connected to a Cutometer dual MPA 580 (Courage & Khazaka, Germany).

VIII. 6.2.3 Measurement area

The measuring area is in the face (malar) left or right.

VIII. 6.2.4 Frequency of measurements

The measurements were performed on **D0, D28.**

VIII. 6.2.5 Expression and interpretation of the results

All the subjects included in the study are taken into account to assess the efficacy of the test product as long as they are submitted to all the examinations, at the defined times.

The individual results are expressed:

- in absolute values of the parameter for each experimental time,
- in variation of the parameter against D0 for each experimental time.
- in % change of the parameter values and area variation, for each intermediate day and against D0.

VIII.7. Self-Assessment evaluation

The subjects answered a questionnaire at the end of the study (D28) which gathers the items concerning the efficacy of the product, defined with the Sponsor according to the category and target market of the test product.

All the subjects included in the study are taken into account to assess the efficacy of the procedure.

For each item, the subjects answer according to a defined grading scale and the results are expressed in percentage of satisfied subjects.

IX . RESULTS

IX.1. Acceptability results

The results related with skin acceptability and compatibility are presented in the **Appendix 5**. No skin reaction was noted after the application of the product. No subject experienced any discomfort during the study. Therefore, the products presented **very good** skin compatibility and acceptability during the study.

IX.2. Assessment of the wrinkles.

Wrinkles were evaluated by a PRIMOS® system, before and after the application of the product. All individual data is presented in **Appendices 6/1 to 6/4**.

Statistical outputs are presented in **Appendix 9**.

IX.2.1 – Assessment of the wrinkles count

Figure 1 shows the wrinkles evolution during the study.

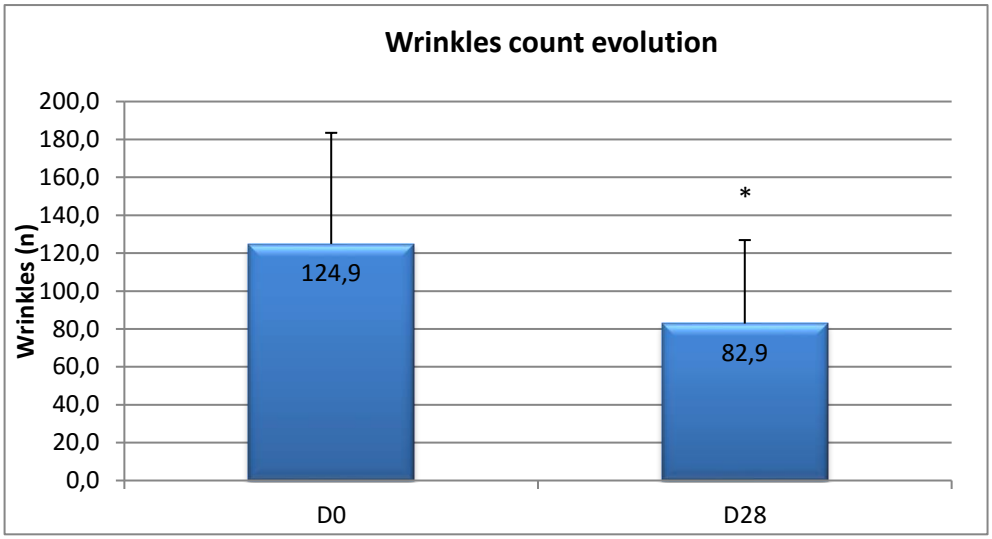

Figure 1 – Wrinkles count evolution during the study. Mean + sd values of all the subjects (n=15). Also shown is the statistical comparison against the D0 (*: p<0,05; N.S.: Non-significant)

In summary, after 28 days, as a result of the application, there is a significant decrease in wrinkles count in the measured area.

To evaluate the true wrinkles effect of the product after 28 days, a relative transformation in relation with D0 was performed. The results are summarized in **Figure 2**.

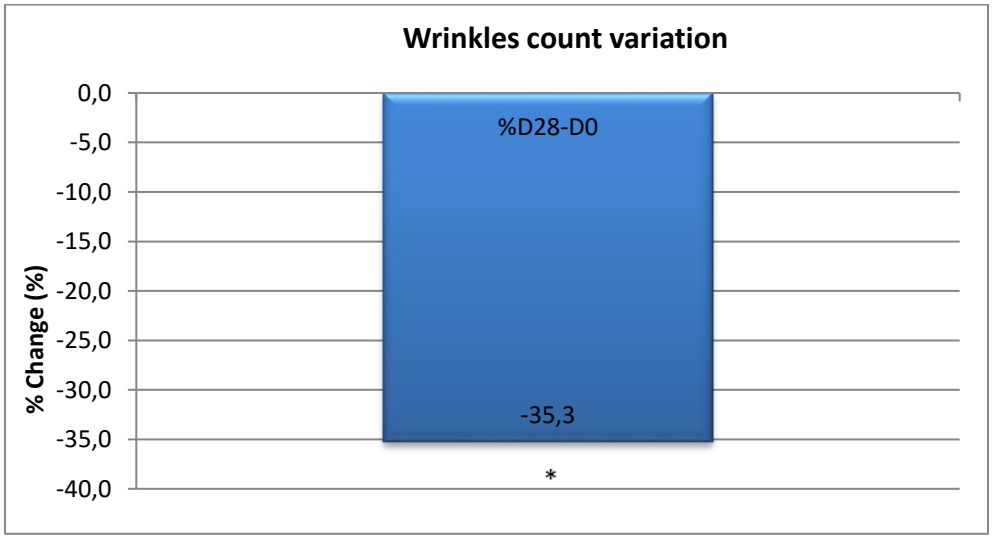

Figure 2 – Wrinkles count % change during the study. Mean values of all the subjects (n=15). Also shown is the statistical comparison against the D0 (*: p<0,05; N.S.: Non-significant)

Regarding wrinkles count, the product presented a 35.3% decrease in the measured area, after 28 days of application.

In conclusion the product has the capacity to decrease wrinkles after 28 days of product application.

IX.2.2 – Assessment of the wrinkles volume

Figure 3 shows the wrinkles volume evolution during the study.

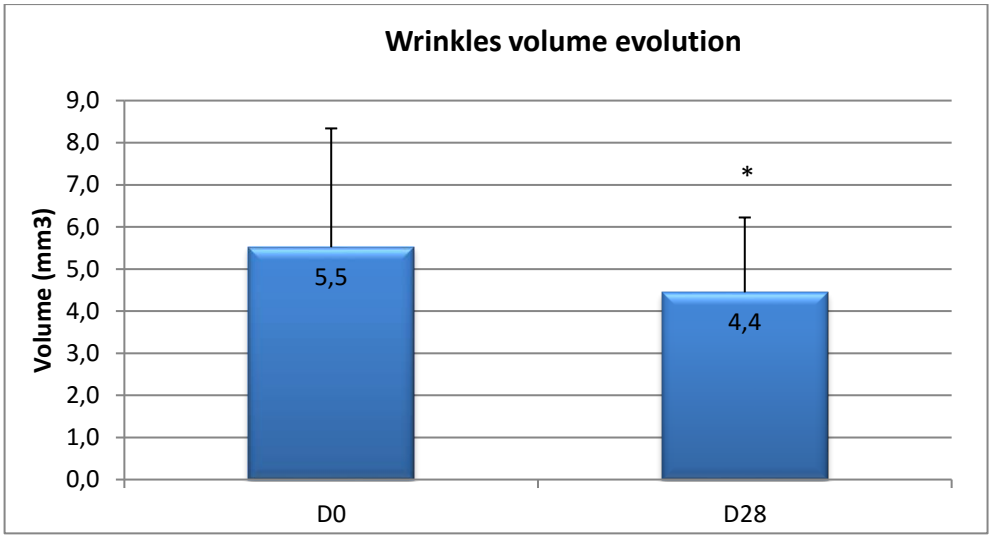

Figure 3 – Wrinkles volume evolution during the study. Mean + sd values of all the subjects (n=15). Also shown is the statistical comparison against the D0 (*: p<0,05; N.S.: Non-significant)

In summary, after 28 days, as a result of the application, there is a significant decrease in wrinkles volume in the measured area.

To evaluate the true wrinkles effect of the product after 28 days, a relative transformation in relation with D0 was performed. The results are summarized in **Figure 4**.

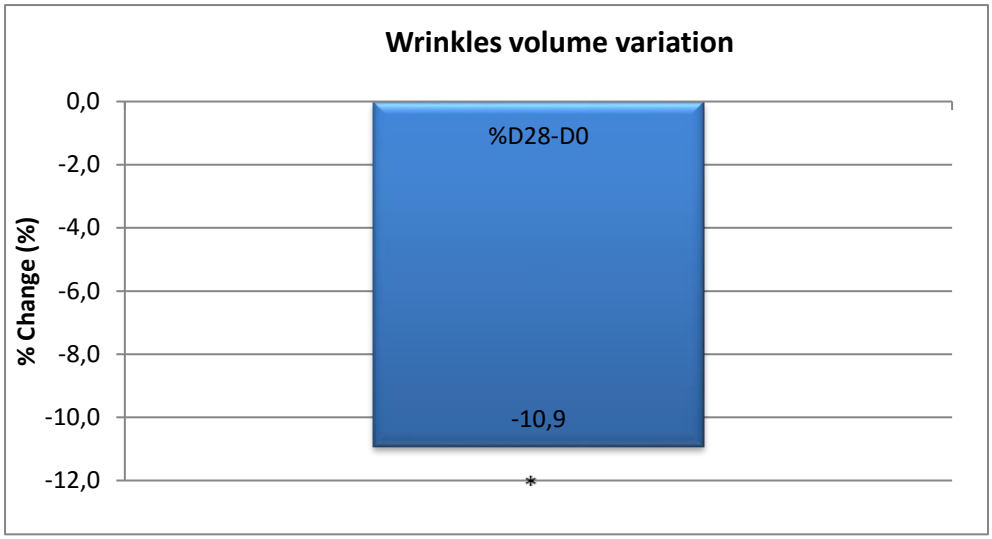

Figure 4 – Wrinkles volume % change during the study. Mean values of all the subjects (n=15). Also shown is the statistical comparison against the D0 (*: p<0,05; N.S.: Non-significant).

Regarding wrinkles count, the product presented a 10.9% decrease in the measured area, after 28 days of application.

In conclusion the product has the capacity to decrease wrinkles volume after 28 days of product application.

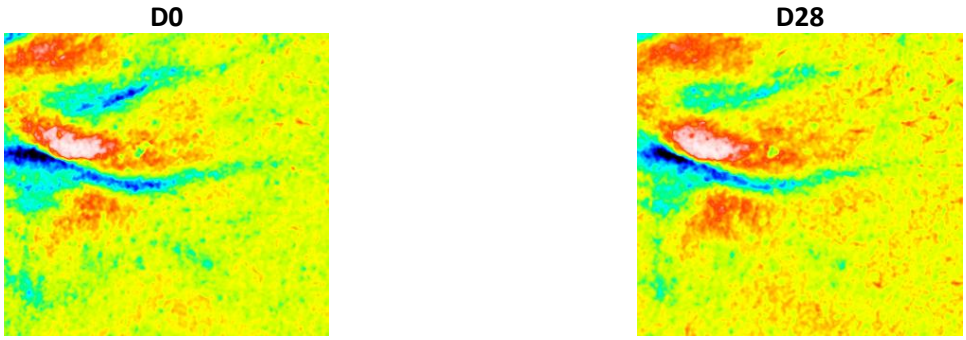

Figure 4a – Wrinkles evolution images of product application area from subject #02.

IX.2.3 – Assessment of the roughness (Ra and Rz)

Figure 5 shows the roughness evolution during the study.

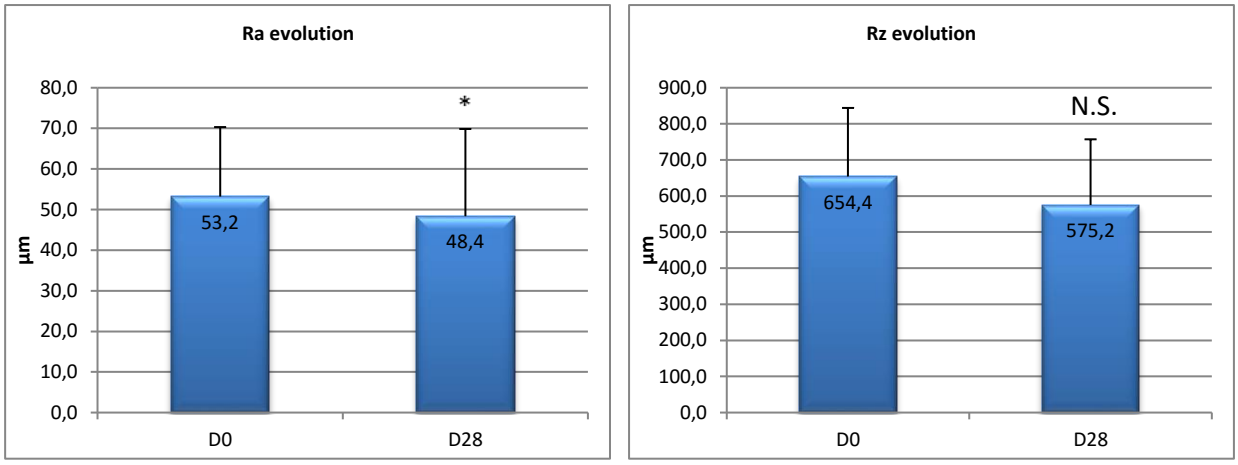

Figure 5 – Ra and Rz parameters evolution during the study. Mean + sd values of all the subjects (n=15). Also shown is the statistical comparison against the D0 (*: p<0,05; N.S.: Non-significant)

In summary, after 28 days, as a result of the application, there is a significant change in Ra roughness parameter in the measured area.

To evaluate the true roughness effect of the product after 28 days, a relative transformation in relation with D0 was performed. The results are summarized in **Figure 6**.

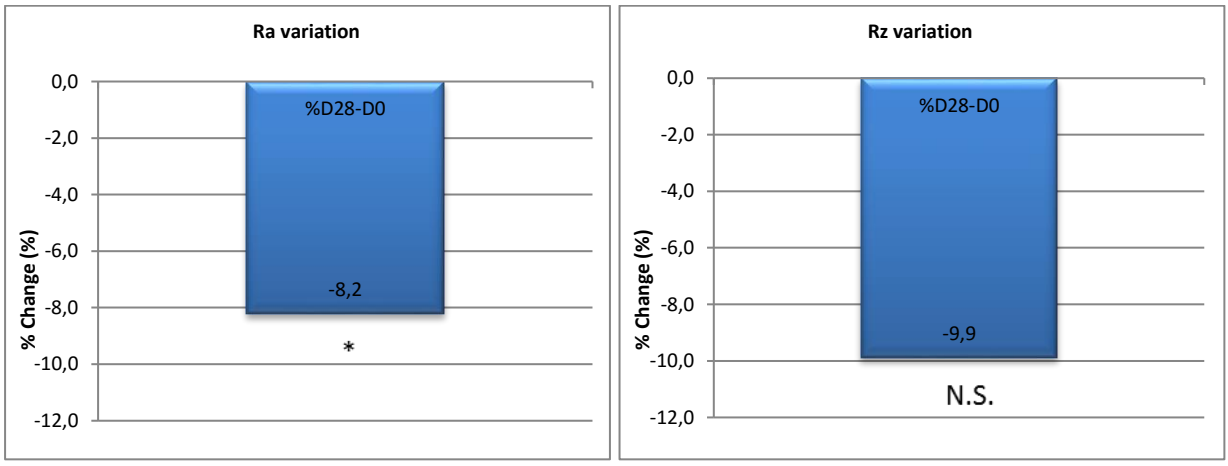

Figure 6 – Ra and Rz % change during the study. Mean values of all the subjects (n=15). Also shown is the statistical comparison against the D0 (*: p<0,05; N.S.: Non-significant)

Regarding roughness, the product presented an 8.2% and 9.9% decrease on Ra and Rz parameters in the measured area, after 28 days of application. This change on Ra parameter is statistically significant.

These results show that product has the capacity to induce a decrease in skin roughness.

IX.3. Assessment of the hydration.

Hydration was evaluated by a Corneometer® system (capacitance parameter), before and after the application of the product. All individual data is presented in **Appendix 7**.

Statistical outputs are presented in **Appendix 9**.

IX.3.1 – Assessment of the hydration

Figure 7 shows the capacitance evolution during the study.

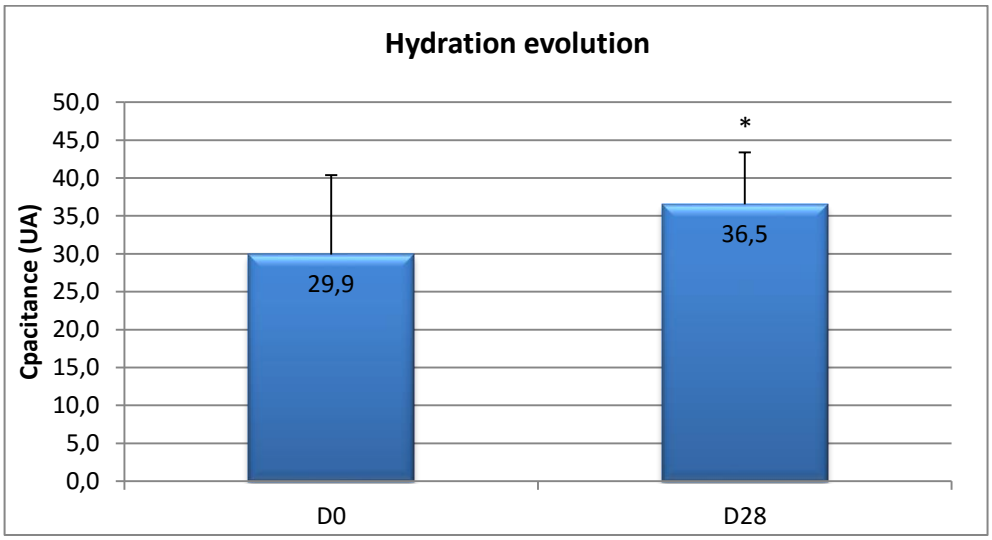

Figure 7 – Capacitance evolution during the study. Mean + sd values of all the subjects (n=15). Also shown is the statistical comparison against the D0 (*: p<0,05; N.S.: Non-significant)

In summary, after 28 days, as a result of the application, there is a significant increase in skin hydration in the measured area.

To evaluate the true hydration effect of the product after 28 days, a relative transformation in relation with D0 was performed. The results are summarized in **Figure 8**.

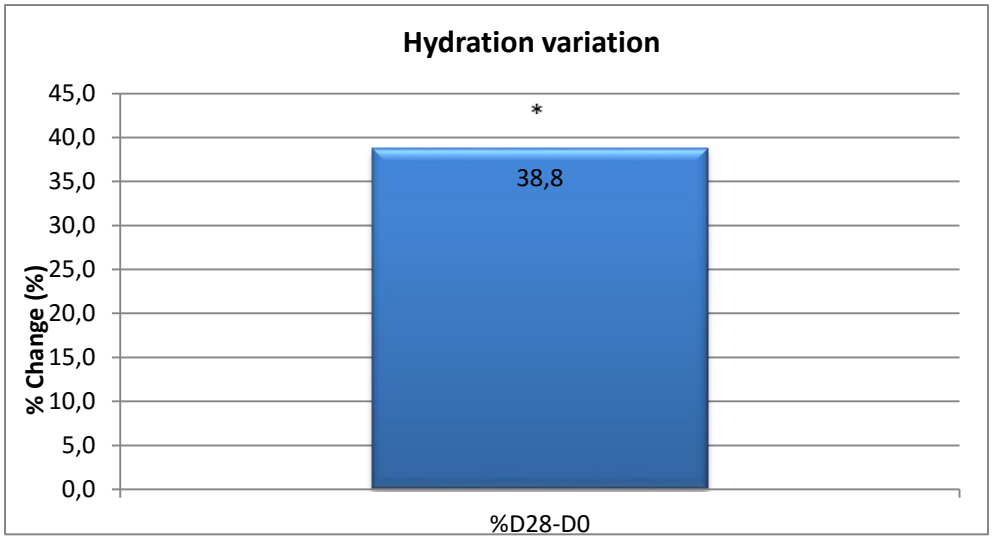

Figure 8 – Capacitance % change during the study. Mean values of all the subjects (n=15). Also shown is the statistical comparison against the D0 (*: p<0,05; N.S.: Non-significant)

Regarding hydration, the product presented a 38.8% increase in the measured area, after 28 days of application.

In conclusion the product has the capacity to increase skin hydration after 28 days of product application.

IX.4. Assessment of qualities and efficacy (self-assessment) of the product

Self-assessment of the skin condition was performed by the subjects at D28. All individual data and the complete questionnaire was presented in **Appendix 8.**

Statistical outputs are presented in **Appendix 9.**

Figure 9 and **table I** presented the results for all answers obtained from the subjects.

Table I – Summary of results evolution obtained in the self-assessment performed by the subjects (n=15)

		Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12
D28	Satisfied subjects (grade>=5)	15	15	15	14	15	13	13	14	14	15	14	14
	%	100,0	100,0	100,0	93,3	100,0	86,7	86,7	93,3	93,3	100,0	93,3	93,3
	Median	9,00	9,00	9,00	9,00	9,00	8,00	8,00	9,00	9,00	8,00	8,00	8,00

Figure 9 present the distribution of answers to the questions 1 to 12 at D28.

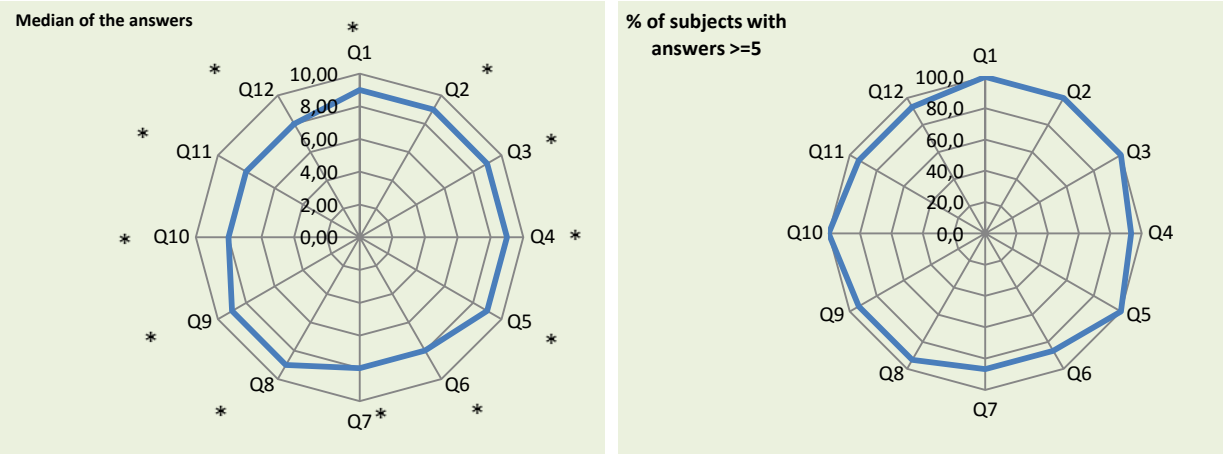

Figure 7 – Median and % of positive answers to Question 1 to 12 after 28 days. Mean values of all the subjects (n=15). The complete description of the questions is in Appendix 8 and in the text. Also shown is the statistical significance of positive responses (*: p<0,05; N.S.: Non-significant)

In brief, after 28 days of application the subjects refer that product was well appreciated regarding the following items:

- Pleasant texture (Q2)
- Easiness to apply (Q3)
- Pleasnt fragrance (Q4)
- Product is easily absorbed (Q5)
- Wrinkles improvement (Q6)
- Skin's firmness (Q7)
- Skin´s moisturized (Q8)
- Skin's visible health (Q9)
- Skin´s softness (Q10)
- Skin´s radiance (Q11)
- The skin is visible youthfulness (Q12)

Also, 100% of the subjects have a positive general opinion about the product after 28 days of applicaton.

X. CONCLUSION

According with the experimental conditions adopted, and considering the classification defined in the protocol, the product **DMC - SÉRUM ROSTO** did not show any reactions during the 28 days of application. Therefore, the product presented **very good skin acceptability and compatibility**.

Regarding the instrumental efficacy:

The application of product **DMC - SÉRUM ROSTO** presented a 35.3% decrease in Wrinkles count, after 28 days. This decrease capacity is statistically significant regarding D0**.**

The application of product **DMC - SÉRUM ROSTO** presented a 10.9% decrease in Wrinkles volume, after 28 days. This decrease capacity is statistically significant regarding D0.

The application of product **DMC - SÉRUM ROSTO** presented an 8.8% decrease in Ra roughness parameter after 28 days. This decrease capacity is statistically significant regarding D0.

The application of product **DMC - SÉRUM ROSTO** presented a 38.8% increase in skin hydration after 28 days. This increase capacity is statistically significant regarding D0.

Regarding the Self-assessment of qualities and efficacy:

After 28 days of application the Product **DMC - SÉRUM ROSTO** was well appreciated regarding the following items:

- Pleasant texture
- Easiness to apply
- Pleasnt fragrance
- Product is easily absorbed
- Wrinkles improvement
- Skin’s firmness
- Skin´s moisturized
- Skin’s visible health
- Skin´s softness
- Skin´s radiance
- The skin is visible youthfulness

Also, 100% of the subjects have a positive general opinion about the product after 28 days of applicaton.

The results suggest that product **DMC - SÉRUM ROSTO** has the capacity to reduce wrinkle, to improve skin aging appearance and to increase skin hydration**.**

XI . DATE AND SIGNATURES

Investigator / Scientific Manager: Pedro CONTREIRAS PINTO

I the undersigned, Pedro CONTREIRAS PINTO, declare that the overall conduct of the study was carried out under my responsibility having in mind the basic principles and spirit of Good Clinical Practices ("Avis aux promoteurs et aux investigateurs pour les essais cliniques des médicaments" : principes généraux – FR.OB – 1987, international recommendations ICH E 6, step 4, of 1/5/1996 and general principals of the Portuguese law 46/2004 from August 19th).

Investigator : Leonor GIRÃO (dermatologist)

I the undersigned, Leonor GIRÃO, declare that the overall conduct of the study was carried out under my responsibility having in mind the basic principles and spirit of Good Clinical Practices ("Avis aux promoteurs et aux investigateurs pour les essais cliniques des médicaments" : principes généraux – FR.OB – 1987, international recommendations ICH E 6, step 4, of 1/5/1996 and general principals of the Portuguese law 46/2004 from August 19th).

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APPENDICES

Appendix 1/1

TYPOLOGICAL CHARACTERISTICS OF THE SUBJECTS

Subjects		Age (years)	Sex F=female M=male	Phototype[1]
Ref.	Codification			
1	SILV.MA	54	F	III
2	MART.MA	60	F	III
3	ROCH.DE	59	F	III
4	DANT.MA	52	F	III
5	BARR.MA	45	F	III
6	ENFE.AN	55	F	III
7	MORE.CA	44	F	III
8	BRIT.EL	48	F	III
9	ALBU.PA	49	F	III
10	GABO.EL	57	F	III
11	DIAS.CU	58	F	II
12	LAMO.LE	52	F	III
13	PINH.SI	42	F	III
14	SOAR.MA	54	F	III
15	PERE.TA	41	F	III

[1] ***phototype according to Fitzpatrick***, *established on the principle of a first 30 to 40-minute sun exposure after the winter or a period without exposure of an equivalent duration:*

Type I *: Always burns easily, never tans*
Type II *: Always burns easily, tans minimally*
Type III *: Burns moderately, tans gradually*
Type IV *: Burns slightly, always tans easily*
Type V *: Burns rarely, tans intensely*
Type VI *: Never burns, strongly pigmented*

Appendix 2/1

CONTROL OF THE OBSERVANCE - Constraints

Constraints **(15 exploitable results)**	**Number** of volunteers who respected the constraints	**Percentage** of volunteers who respected the constraints
Application area: Face **Deviation: none**	15	100%
Experimental conditions: Apply on clean skin by gentle digital massage until complete absorption. **Deviation: none**	15	100%
Frequency of application: Once a day **Deviation: none**	15	100%
Application at home: 27 consecutive days **Deviation: none**	15	100%
Exclusive application by the volunteer **Deviation: none**	15	100%
No application of products on the experimental area (except the tested one) **Deviation: none**	15	100%
Full respect of the test product conditions of use **Deviation: none**	15	100%
No application of hydrating products on the experimental areas **Deviation: none**	15	100%
No change in hygiene habits **Deviation: none**	15	100%
No application of makeup on face and lips, on the day of the evaluations **Deviation: none**	15	100%
No anti-ageing or aesthetic treatment: botox or botox like products, peelings, plastic surgery, hyaluronic acid treatment, Plasma Rich Platelets treatment, or any other specific treatments prone to change the skin aspect during the last 6 months **Deviation: none**	15	100%

Appendix 2/2

CONTROL OF THE OBSERVANCE - Constraints

Constraints **(15 exploitable results)**	**Number** of volunteers who respected the constraints	**Percentage** of volunteers who respected the constraints
No change in the way of life or in the physical activity **Deviation: none**	15	100%
No exfoliating treatment on the experimental areas **Deviation: none**	15	100%
Coming to the investigator centre at each control at the defined day and hour **Deviation: none**	15	100%
Description of any treatment undertaken during the study and all eventual deviations **Deviation: none**	15	100%
No application of the tested products on the day of measurements **Deviation: none**	15	100%

Appendix 3

CONSUMPTION CONTROL – Product DMC - SÉRUM ROSTO

Subject		Weight D0 A (g)	Weight D28 B (g)	Product Consumption A-B = C in (g)	Number of applications N	Consumption by application C/N in (g)
Ref.	Codification					
1	SILV.MA	80,85	33,62	47,23	28	1,69
2	MART.MA	80,88	37,93	42,95	28	1,53
3	ROCH.DE	81,36	62,27	19,09	28	0,68
4	DANT.MA	80,75	32,94	47,81	28	1,71
5	BARR.MA	81,40	60,37	21,03	28	0,75
6	ENFE.AN	81,26	40,88	40,38	28	1,44
7	MORE.CA	81,20	34,21	46,99	28	1,68
8	BRIT.EL	81,42	63,06	18,36	28	0,66
9	ALBU.PA	81,38	33,26	48,12	28	1,72
10	GABO.EL	81,59	44,46	37,13	28	1,33
11	DIAS.CU	81,27	60,85	20,42	28	0,73
12	LAMO.LE	81,40	65,59	15,81	28	0,56
13	PINH.SI	81,32	45,63	35,69	28	1,27
14	SOAR.MA	81,59	56,98	24,61	28	0,88
15	PERE.TA	81,30	53,81	27,49	28	0,98
Mean consumption by application (± sd)		**1.17g ± 0,44g**				

Appendix 4

ROOM CONDITIONS

DATE	TIME	RELATIVE AIR HUMIDITY (%)	TEMPERATURE (ºC)
03/10/2018	08:37:25	49,4	21,8
	13:37:25	46,9	21,1
	18:37:25	49,8	20,9
31/10/2018	08:38:15	60,0	19,3
	13:38:15	60,3	19,8
	18:38:15	62,8	20,4

Appendix 5/1

ACCEPTABILITY – Sensations of discomfort

Volunteers		Summary of the questionnaire performed to the volunteers at the end of the study and the comments noted in the individual observation sheet *All sensations not related with the product were not included in this table.*
Ref.	**Codification**	
1	SILV.MA	/
2	MART.MA	/
3	ROCH.DE	/
4	DANT.MA	/
5	BARR.MA	/
6	ENFE.AN	/
7	MORE.CA	/
8	BRIT.EL	/
9	ALBU.PA	/
10	GABO.EL	/
11	DIAS.CU	/
12	LAMO.LE	/
13	PINH.SI	/
14	SOAR.MA	/
15	PERE.TA	/

Legend:

/: nothing to report
Hea: Heat
Sti: Stinging
Pr: Pruritus
Bur: Burning
Pu: Pulling

1: Slight intensity
2: Moderate intensity
3: Severe intensity

Appendix 5/2

Compatibility – Cutaneous examination: Clinical signs

Volunteers		Clinical signs noted during the study *All signs not related with the products were not included in this table*
Ref.	**Codification**	
1	SILV.MA	/
2	MART.MA	/
3	ROCH.DE	/
4	DANT.MA	/
5	BARR.MA	/
6	ENFE.AN	/
7	MORE.CA	/
8	BRIT.EL	/
9	ALBU.PA	/
10	GABO.EL	/
11	DIAS.CU	/
12	LAMO.LE	/
13	PINH.SI	/
14	SOAR.MA	/
15	PERE.TA	/

Appendix 6/1

PRIMOS 3D EVALUATION – WRINKLES COUNT (n) – PRODUCT DMC - SÉRUM ROSTO

Ref.	Codification	D0	D28	D28-D0	% change D28(%)
1	SILV.MA	57,0	33,0	-24,0	-42,1
2	MART.MA	80,0	53,0	-27,0	-33,8
3	ROCH.DE	45,0	25,0	-20,0	-44,4
4	DANT.MA	118,0	78,0	-40,0	-33,9
5	BARR.MA	182,0	132,0	-50,0	-27,5
6	ENFE.AN	202,0	124,0	-78,0	-38,6
7	MORE.CA	198,0	133,0	-65,0	-32,8
8	BRIT.EL	245,0	186,0	-59,0	-24,1
9	ALBU.PA	143,0	85,0	-58,0	-40,6
10	GABO.EL	61,0	34,0	-27,0	-44,3
11	DIAS.CU	107,0	64,0	-43,0	-40,2
12	LAMO.LE	112,0	81,0	-31,0	-27,7
13	PINH.SI	96,0	70,0	-26,0	-27,1
14	SOAR.MA	120,0	73,0	-47,0	-39,2
15	PERE.TA	107,0	72,0	-35,0	-32,7
Mean		124,9	82,9	-42,0	-35,3
SD		58,6	44,0	17,2	6,6
Median		112,0	73,0	-40,0	-33,9
Minimum		45,0	25,0	-78,0	-44,4
Maximum		245,0	186,0	-20,0	-24,1

Appendix 6/2

PRIMOS 3D EVALUATION – WRINKLES VOLUME (mm^3) – PRODUCT DMC - SÉRUM ROSTO

Ref.	Codification	D0	D28	D28-D0	% change D28(%)
1	SILV.MA	4,6	8,3	3,6	78,2
2	MART.MA	9,6	8,0	-1,6	-16,9
3	ROCH.DE	3,0	3,7	0,7	23,9
4	DANT.MA	6,1	5,2	-0,9	-14,8
5	BARR.MA	4,0	3,5	-0,5	-12,4
6	ENFE.AN	5,9	5,7	-0,3	-4,7
7	MORE.CA	5,3	4,2	-1,2	-21,7
8	BRIT.EL	6,9	5,6	-1,3	-19,1
9	ALBU.PA	6,3	3,8	-2,4	-38,6
10	GABO.EL	13,2	3,7	-9,5	-71,9
11	DIAS.CU	4,9	3,4	-1,5	-30,1
12	LAMO.LE	4,0	3,0	-1,0	-24,3
13	PINH.SI	2,1	2,0	-0,1	-6,1
14	SOAR.MA	3,4	3,3	-0,1	-2,4
15	PERE.TA	3,5	3,4	-0,1	-2,9
Mean		5,5	4,4	-1,1	-10,9
SD		2,8	1,8	2,7	32,3
Median		4,9	3,7	-0,9	-14,8
Minimum		2,1	2,0	-9,5	-71,9
Maximum		13,2	8,3	3,6	78,2

Appendix 6/3

PRIMOS 3D EVALUATION – ROUGHNESS Ra (µm) – PRODUCT DMC - SÉRUM ROSTO

Ref.	Codification	D0	D28	D28-D0	% change D28(%)
1	SILV.MA	94,2	121,0	26,8	28,5
2	MART.MA	69,0	60,5	-8,5	-12,3
3	ROCH.DE	38,0	44,2	6,2	16,3
4	DANT.MA	47,6	46,5	-1,1	-2,3
5	BARR.MA	37,0	32,2	-4,8	-13,0
6	ENFE.AN	48,9	45,4	-3,5	-7,2
7	MORE.CA	42,8	40,3	-2,5	-5,8
8	BRIT.EL	47,2	45,1	-2,1	-4,4
9	ALBU.PA	52,2	39,6	-12,6	-24,1
10	GABO.EL	85,4	33,8	-51,6	-60,4
11	DIAS.CU	54,2	44,4	-9,8	-18,1
12	LAMO.LE	45,6	38,1	-7,5	-16,4
13	PINH.SI	54,0	53,6	-0,4	-0,7
14	SOAR.MA	34,7	33,7	-1,0	-2,9
15	PERE.TA	47,6	47,5	-0,1	-0,2
Mean		53,2	48,4	-4,8	-8,2
SD		17,1	21,5	15,8	19,5
Median		47,6	44,4	-2,5	-5,8
Minimum		34,7	32,2	-51,6	-60,4
Maximum		94,2	121,0	26,8	28,5

Appendix 6/4

PRIMOS 3D EVALUATION – ROUGHNESS Rz (µm) – PRODUCT DMC - SÉRUM ROSTO

Ref.	Codification	D0	D28	D28-D0	% change D28(%)
1	SILV.MA	1147,5	1132,8	-14,7	-1,3
2	MART.MA	793,9	694,4	-99,5	-12,5
3	ROCH.DE	424,3	474,6	50,3	11,9
4	DANT.MA	606,1	601,0	-5,1	-0,8
5	BARR.MA	469,5	415,5	-54,0	-11,5
6	ENFE.AN	694,6	660,8	-33,8	-4,9
7	MORE.CA	488,6	485,6	-3,0	-0,6
8	BRIT.EL	580,7	559,4	-21,3	-3,7
9	ALBU.PA	658,7	511,6	-147,1	-22,3
10	GABO.EL	842,6	376,8	-465,8	-55,3
11	DIAS.CU	809,4	511,8	-297,6	-36,8
12	LAMO.LE	577,5	438,1	-139,4	-24,1
13	PINH.SI	720,0	627,4	-92,6	-12,9
14	SOAR.MA	514,5	662,0	147,5	28,7
15	PERE.TA	488,1	476,8	-11,3	-2,3
Mean		654,4	575,2	-79,2	-9,9
SD		189,6	181,9	146,4	19,8
Median		606,1	511,8	-33,8	-4,9
Minimum		424,3	376,8	-465,8	-55,3
Maximum		1147,5	1132,8	147,5	28,7

Appendix 7

CORNEOMETER EVALUATION – CAPACITANCE (AU) – PRODUCT DMC - SÉRUM ROSTO

Ref.	Codification	D0	D28	D28-D0	% change D28(%)
1	SILV.MA	41,6	45,0	3,4	8,3
2	MART.MA	43,8	44,4	0,6	1,4
3	ROCH.DE	40,0	39,8	-0,2	-0,5
4	DANT.MA	28,4	23,1	-5,4	-18,9
5	BARR.MA	32,7	46,4	13,7	41,8
6	ENFE.AN	33,8	32,6	-1,2	-3,5
7	MORE.CA	30,2	38,9	8,7	28,9
8	BRIT.EL	46,0	34,0	-12,0	-26,1
9	ALBU.PA	25,1	29,0	3,8	15,3
10	GABO.EL	27,4	40,0	12,6	45,8
11	DIAS.CU	15,9	37,1	21,2	133,1
12	LAMO.LE	26,4	39,8	13,4	50,8
13	PINH.SI	31,1	38,9	7,7	24,9
14	SOAR.MA	15,8	26,5	10,7	67,7
15	PERE.TA	10,5	32,8	22,3	212,4
Mean		29,9	36,5	6,6	38,8
SD		10,5	6,8	9,5	62,2
Median		30,2	38,9	7,7	24,9
Minimum		10,5	23,1	-12,0	-26,1
Maximum		46,0	46,4	22,3	212,4

Appendix 8

SELF-ASSESSMENT: Q1 – Q12: ON THE SCALE PRESENTED BELOW, HOW COULD YOU QUALIFY YOUR …? – D28
PRODUCT DMC - SÉRUM ROSTO

Ref.	Codification	Q1 General opinion	Q2 The product has a pleasant texture	Q3 The product is easy to apply	Q4 The product has a pleasant fragrance	Q5 the product is easily absorbed	Q6 Improvement on skin wrinkles	Q7 The skin is firmer	Q8 Skin´s moisturized	Q9 Skin has an healthier aspect	Q10 Skin is softer	Q11 Skin is more radiant	Q12 Skin is visible youthfulness
1	SILV.MA	9	9	10	8	10	9	9	10	10	9	10	9
2	MART.MA	6	6	9	9	9	8	8	8	8	8	8	8
3	ROCH.DE	9	9	9	0	9	4	4	9	4	9	4	1
4	DANT.MA	7	9	10	6	9	7	4	4	6	5	6	6
5	BARR.MA	9	9	9	10	10	8	8	9	9	9	9	8
6	ENFE.AN	8	9	9	7	9	3	5	5	7	7	9	7
7	MORE.CA	9	9	9	9	8	7	7	9	9	8	8	8
8	BRIT.EL	7	9	9	6	6	7	7	7	7	7	6	6
9	ALBU.PA	6	6	8	8	7	7	8	8	8	8	8	8
10	GABO.EL	10	10	10	10	8	9	10	10	10	10	9	9
11	DIAS.CU	10	9	10	10	10	10	10	10	10	10	10	10
12	LAMO.LE	10	10	10	10	10	10	10	10	10	10	10	10
13	PINH.SI	9	9	9	9	9	8	9	9	9	9	9	8
14	SOAR.MA	7	7	8	8	8	7	7	7	6	7	6	6
15	PERE.TA	10	10	10	10	10	10	10	7	9	8	8	9
Mean		8,4	8,7	9,3	8,0	8,8	7,6	7,7	8,1	8,1	8,3	8,0	7,5
SD		1,5	1,3	0,7	2,6	1,2	2,0	2,1	1,8	1,8	1,4	1,8	2,2
Median		9,0	9,0	9,0	9,0	9,0	8,0	8,0	9,0	9,0	8,0	8,0	8,0
Maximum		10,0	10,0	10,0	10,0	10,0	10,0	10,0	10,0	10,0	10,0	10,0	10,0
Minimum		6,0	6,0	8,0	0,0	6,0	3,0	4,0	4,0	4,0	5,0	4,0	1,0

Appendix 9

Statistical Data

Wrinkle Count

Normality

Testes de Normalidade

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Estatística	gl	Sig.	Estatística	gl	Sig.
WrinkleCount_D0	,200	15	,110	,936	15	,339
WrinkleCount_D28	,214	15	,063	,918	15	,177

a. Correlação de Significância de Lilliefors

Evolution

Teste de amostras emparelhadas

		Diferenças emparelhadas					t	gl	Sig. (bilateral)
		Média	Desvio Padrão	Erro Padrão da Média	95% Intervalo de Confiança da Diferença				
					Inferior	Superior			
Par 1	WrinkleCount_D28 - WrinkleCount_D0	-42,000000	17,212952	4,444365	-51,532215	-32,467785	-9,450	14	,000

Wrinkle Volume
Normality

Testes de Normalidade

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Estatística	gl	Sig.	Estatística	gl	Sig.
WrinkleVolume_D0	,191	15	,146	,861	15	,025
WrinkleVolume_D28	,242	15	,018	,859	15	,024

a. Correlação de Significância de Lilliefors

Evolution

Estatísticas de teste[a]

	WrinkleVolume_D28 - WrinkleVolume_D0
Z	-2,274[b]
Significância Assint. (Bilateral)	,023

a. Teste de Postos Assinados por Wilcoxon

b. Com base em postos positivos.

Ra
Normality

Testes de Normalidade

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Estatística	gl	Sig.	Estatística	gl	Sig.
Ra_D0	,277	15	,003	,827	15	,008
Ra_D28	,317	15	,000	,610	15	,000

a. Correlação de Significância de Lilliefors

Evolution

Estatísticas de teste[a]

	Ra_D28 - Ra_D0
Z	-2,101[b]
Significância Assint. (Bilateral)	,036

a. Teste de Postos Assinados por Wilcoxon

b. Com base em postos positivos.

Rz
Normality

Testes de Normalidade

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Estatística	gl	Sig.	Estatística	gl	Sig.
Rz_D0	,134	15	,200*	,904	15	,111
Rz_D28	,190	15	,153	,790	15	,003

*. Este é um limite inferior da significância verdadeira.

a. Correlação de Significância de Lilliefors

Evolution

Teste de amostras emparelhadas

		Diferenças emparelhadas					t	gl	Sig. (bilateral)
		Média	Desvio Padrão	Erro Padrão da Média	95% Intervalo de Confiança da Diferença				
					Inferior	Superior			
Par 1	Rz_D28 - Rz_D0	-79,16000	146,44937	37,81307	-160,26096	1,94096	-2,093	14	,055

Corneometer

Normality

Testes de Normalidade

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Estatística	gl	Sig.	Estatística	gl	Sig.
Corneometer_D0	,123	15	,200*	,960	15	,689
Corneometer_D28	,168	15	,200*	,953	15	,578

*. Este é um limite inferior da significância verdadeira.

a. Correlação de Significância de Lilliefors

Evolution

Teste de amostras emparelhadas

	Diferenças emparelhadas	t	gl	

		Média	Desvio Padrão	Erro Padrão da Média	95% Intervalo de Confiança da Diferença				Sig. (bilateral)
					Inferior	Superior			
Par 1	Corneometer_D28 - Corneometer_D0	6,640000	9,498556	2,452517	1,379875	11,900125	2,707	14	,017

Questionnaire

Teste binomial

		Categoria	N	Proporção observada	Proporção de teste	Sig exata (bilateral)
Q1	Grupo 1	<= 4	0	,00	,50	,000
	Grupo 2	> 4	15	1,00		
	Total		15	1,00		
Q2	Grupo 1	<= 4	0	,00	,50	,000
	Grupo 2	> 4	15	1,00		
	Total		15	1,00		
Q3	Grupo 1	<= 4	0	,00	,50	,000
	Grupo 2	> 4	15	1,00		
	Total		15	1,00		
Q4	Grupo 1	<= 4	1	,07	,50	,001
	Grupo 2	> 4	14	,93		
	Total		15	1,00		
Q5	Grupo 1	<= 4	0	,00	,50	,000
	Grupo 2	> 4	15	1,00		
	Total		15	1,00		
Q6	Grupo 1	<= 4	2	,13	,50	,007
	Grupo 2	> 4	13	,87		
	Total		15	1,00		
Q7	Grupo 1	<= 4	2	,13	,50	,007
	Grupo 2	> 4	13	,87		
	Total		15	1,00		
Q8	Grupo 1	<= 4	1	,07	,50	,001
	Grupo 2	> 4	14	,93		
	Total		15	1,00		
Q9	Grupo 1	<= 4	1	,07	,50	,001

	Grupo 2	> 4	14	,93		
	Total		15	1,00		
Q10	Grupo 1	<= 4	0	,00	,50	,000
	Grupo 2	> 4	15	1,00		
	Total		15	1,00		
Q11	Grupo 1	<= 4	1	,07	,50	,001
	Grupo 2	> 4	14	,93		
	Total		15	1,00		
Q12	Grupo 1	<= 4	1	,07	,50	,001
	Grupo 2	> 4	14	,93		
	Total		15	1,00		

Appendix 10

Statistical Data

Comissão de Ética Independente

Independent Ethics Committee
Comissão de Ética para a Saúde homologada pela Ordem dos Médicos (ms/ 2017 / 4457 / P22315)

17 de Março de 2018

Exmo. Prof. Dr. Pedro Pinto
Director da PhDTrials
Rua das Murtas, nº1B – 1º
1700-309 Lisboa, Portugal

Código do Protocolo de estudo PhD Trials:
PT.06.01
Data: 9 de Março de 2018
Versão: 1.0

Promotor/*Sponsor*:
Vários promotores

Titulo do Protocolo do Estudo
Protocol Study Title

March 17th, 2018

Dear Prof. Dr. Pedro Pinto
Head of PhDTrials
Rua das Murtas, nº1B – 1º
1700-309 Lisboa, Portugal

PhDTrials Protocol Study Code: PT.06.01
Date: *March 9th, 2018*
Version: *1.0*

CONFIRMATION IN HUMAN SUBJECTS OF A FACIAL COSMETIC PRODUCT AFTER APPLICATION UNDER NORMAL CONDITIONS OF USE

CHECKING OF ITS COMPATIBILITY AND ACCEPTABILITY OBJECTIVE ASSESSMENT OF ITS QUALITIES AND EFFICACY

Test under dermatological control

A Comissão de Ética Independente reviu o Protocolo do Estudo acima referido / *The Independent Ethics Committee reviewed the above referred Study Protocol*:

Tipo de Estudo: / Type of Study:	**Estudo de eficácia / In Use Efficacy Study**
Documentos revistos / *Reviewed Documents*	☒ **Protocolo do estudo / Study protocol**
	☒ **Declaração de Consentimento Informado / Informed Consent Form**
	☒ **Formulário de Submissão / Submission form**

Decisão / *Decision*:
Após o cumprimento dos requisitos processuais e outras condições impostas por esta comissão, o Protocolo do estudo e a Declaração de Consentimento Informado foram por unanimidade:

Subsequent to the fulfillment of the procedural requirements and other conditions imposed by the committee, Study Protocol and Informed Consent Form were unanimously:

Aprovados / *Approved*	✓
Aprovados com modificações / *Approved with modifications*	
Rejeitados / *Rejected*	

Justificação da rejeição / *Rejection justification*

O investigador principal e os promotores do estudo deverão ler e cumprir com o seguinte:

- A Comissão examinou os procedimentos para o trabalho aqui proposto. Estes não apresentam impedimentos éticos à sua realização pelo os aprova neste estrito sentido. Todos os outros requisitos relacionados com o trabalho (p.ex. científicos, processuais, legais, financeiros e regulamentares, etc) mantêm-se da única responsabilidade do investigador principal e/ou do promotor(es).

The principal investigator and the sponsors are required to read and comply with the following:

- *The Committee examined the proceedings for the work proposed concerning the ethical aspects and did not found any impeachment for their execution, therefore, approved them in this strict sense. All other concerns related to the work (e.g. scientific, procedural, legal, financial and regulatory etc) remain the sole responsibility of the principal investigator and/or the sponsor(s).*

Assinatura e data **Date and Signature**	Lousado, 17 de Março de 2018
Responsible for the review	**Carmen Lídia Vilela Assunção Pereira Ramos** Presidente da Comissão de Ética Chairman of the Independent Ethical Committee

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