

Study of the effect and cosmetic properties of a product through evaluations and instrumental analysis performed by professionals under medical supervision and consumer self-assessments.

Crystal srl

BLEND OF MOISTURIZING AND SOOTHING ACTIVES REF 2501221L

Report

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INTRODUCTION

The clinical trial protocols are audited and approved by the Technical Scientific Committee (TSC) of Bio Basic Europe S.r.l., whose functions, compositions and procedures are described in the document "Statute - Regulation" (Ann. C). The TSC ascertains the protocol's completeness, confirms the adequacy of the documentation and the conformity of the procedures and methodologies followed in designing and developing the research project, in compliance with the applicable legislation. The protocol is audited by at least the following mandatory members of the TSC:

a) The Chairman and/or the Vice Chairman of the TSC
b) The University of Pavia Director of Research
c) The Investigator/Medical Director of the CDC Dermo Clinical Research Institute
d) The expert of Bio Basic Europe S.r.l. depending on the issue on which the opinion is formulated

The final report is signed by the Investigator/Medical Director of the CDC Dermo Clinical Research Institute and, subsequently, by the Safety Assessor, who attests the document's validity, affixing a digital signature.

PERSONS RESPONSIBLE FOR SIGNING THE PROTOCOL

Safety Assessor
CLAUDIO ANGELINETTA, Vice Chairman of the Technical Scientific Committee, Chemist/Cosmetic Chemist, Degree in Chemistry, Specialisation in Cosmetic Sciences and Technologies, University of Milan.

Investigator
Dr. FERNANDO MARCO BIANCHI M.D., Bio Basic Europe S.r.l. CDC Dermo-Clinical Research Institute Health Director, medical surgeon specialist in dermatology and venereology.

LEGAL AND CONTRACTUAL INFORMATION

- *The protocols are drafted in accordance with the applicable legislation, the guidelines of the Technical Scientific Committee and the provisions of the research contracts in force between Bio Basic Europe S.r.l. and the University of Pavia (contract dated 01/09/2019 and further renewals with the L. Spallanzani Faculty of Biology and Biotechnologies).*
- *In accordance with the applicable regulatory framework and the Helsinki declaration* (Regulation (EC) no. 1223/2009 of the European Parliament and of the council of 30 November 2009 on cosmetic products)*, the volunteers are adequately informed of the purpose, the methods and the characteristics of the clinical study, the beneficial effects and the possible side effects. Each volunteer signs the informed consent form as a sign of acceptance, which is managed and archived in accordance with the internal procedures of the Quality Management System of Bio Basic Europe S.r.l.*
- *This clinical trial was conducted at the CDC Dermo Clinical Research Institute, in accordance with the guidelines dictated by the Technical Scientific Committee.*
- *All rights are reserved. This report is a technical scientific document protected by copyright. No part thereof may be reproduced by any means without the prior written authorisation of Bio Basic Europe S.r.l., including texts, images, logos, graphs, data, results, references to the persons involved in the study.*
- *Based on the experience of Bio Basic Europe, it is recommended to check, once every three years, its harmonisation with any regulatory update.*
- *This final technical report was drafted by: ANTONELLA PRATICO', Bio Basic Europe Clinical Test Reporting Coordinator, Master's Degree in Natural Sciences, University of Milan, II Level Master's Degree in Evaluation and control of the toxicological risk caused by environmental pollutants.*

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ABSTRACT

The primary objective of this clinical trial was to assess whether the cosmetic product BLEND OF MOISTURIZING AND SOOTHING ACTIVES REF 2501221L has a moisturizing and soothing effect. As erythema and TEWL increase in response to irritation, the soothing effect was assessed by evaluating the reduction in erythema and TEWL in the treated skin area compared with an untreated control area. The moisturizing effect was assessed by analyzing the increase in skin moisturization.

The trial also had the following secondary objective: to assess the perceived pleasantness and effect of the product.

A clinical study was conducted on 20 enrolled subjects. For the evaluation of immediate soothing efficacy, slight skin irritation was induced on specific areas of the forearm; the areas were then either treated with the cosmetic product or left untreated. Specific endpoint variables were analyzed at baseline and after irritation and treatment. For the evaluation of the moisturizing action, the volunteers used the product on the forearm four times a day for 28 consecutive days. Specific endpoint variables were analyzed at baseline (before product use) and after 28 days of treatment.

The results demonstrated a moisturizing effect and soothing efficacy of the product, the primary objective of the study: after product use, improvement was observed in all primary endpoints studied. Along with this, good product pleasantness and effect were perceived.

Along with this phenomenon, it was also observed a good pleasantness and effect of the product were perceived.

OBJECTIVES

Primary objective

The aim of this study is to assess whether the cosmetic product BLEND OF MOISTURIZING AND SOOTHING ACTIVES REF 2501221L has a moisturizing and soothing effect. The evaluation was performed by comparison with an untreated area.

Primary endpoints:

- *skin moisturization (quantitative endpoint)*
- *erythema (quantitative endpoint)*
- *TEWL (quantitative endpoint)*

Secondary objectives

The secondary objectives were designed to substantiate and confirm the primary objective. Furthermore, a series of sensory self-evaluations were collected from the enrolled subjects in order to evaluate the effect and pleasantness of use of the product.

Secondary endpoints:

- *subjective evaluations (quantitative discrete endpoint)*

STUDY CHARACTERISTICS

Study design

The moisturizing effect of the product was evaluated by comparing the results obtained after the use with the baseline data.
The assessment of the soothing efficacy of the product was carried out by comparing the results obtained after the application of the product with the data collected immediately after skin irritation and with a control area.

The perceived pleasantness and effect were evaluated by analysing the results obtained after the use of the product.

Sample size

Based on Bio Basic Europe experience, by considering the type of product, the objectives of the trial and taking into account any possible drop-out, the sample size is composed of 20 subjects.

Eligibility criteria

The subjects participating in the study were screened under medical supervision and enrolled according to the following inclusion criteria:

- *female sex;*
- *age between 18 and 60 years;*
- *very dry skin*
- *historicity of atopic dermatitis and psoriasis*
- *good general health status/absence of psychological and/or cognitive disorders;*
- *absence of dermatological and allergological pathologies (cosmetological or to other specific excipients) or other pathologies (such as irritative reactions of unknown origin);*
- *absence of ongoing pharmacological treatments which may affect the outcome of the test;*
- *non-participation in other clinical trials in the previous 30 days;*
- *informed consent obtained.*

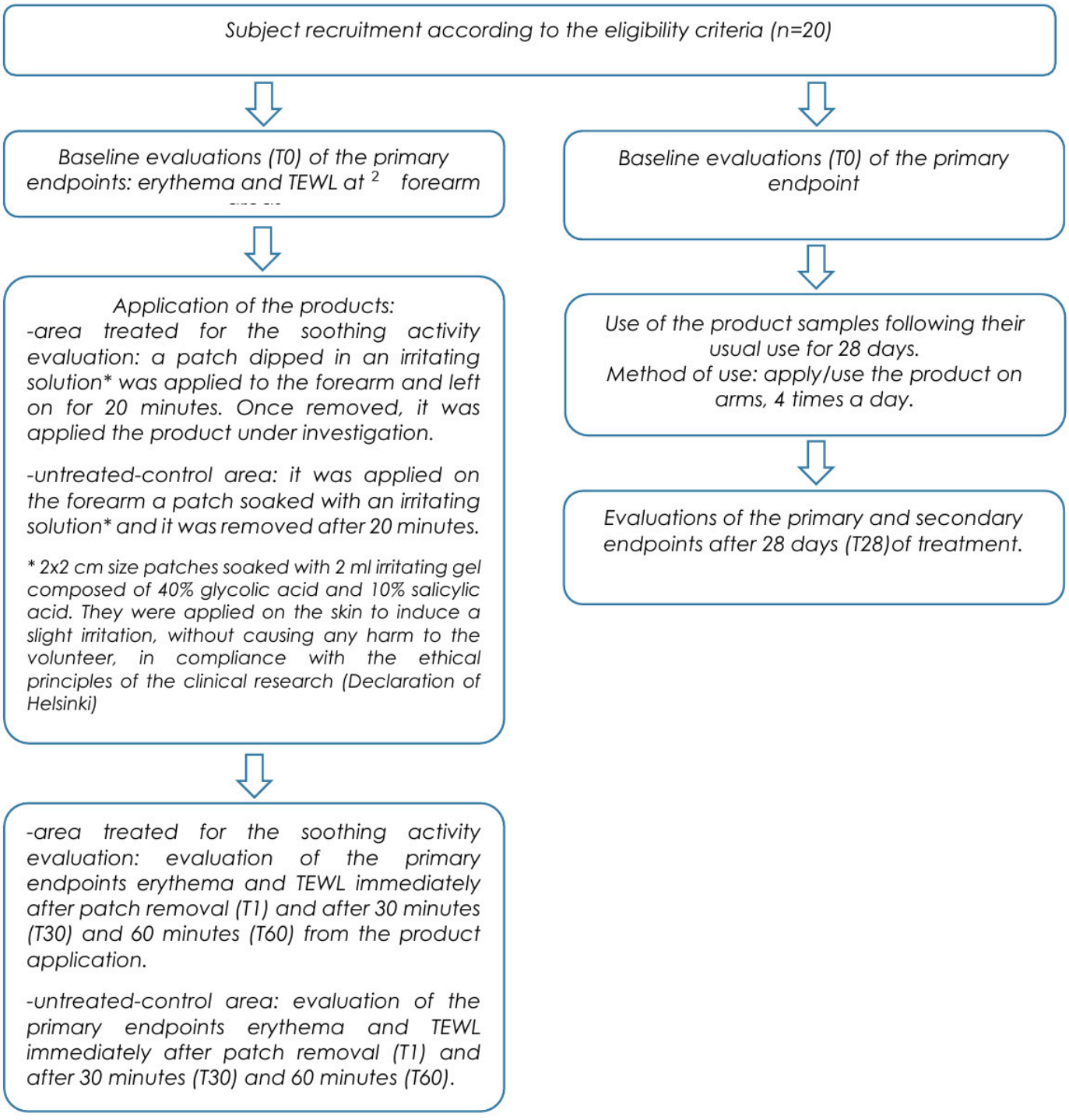
Randomization

Not applicable.

Blindness

The subjects received the product without packaging or indications regarding the manufacturer's brand in order to avoid the distortions caused by the conditioning effect of the awareness of the product.

Trial scheme



Criteria for the subject withdrawal

The following rules were imposed on a possible subject withdrawal which may occur during the trial:

- *breach of one of the inclusion/exclusion criteria;*
- *development of adverse effects.*

Endpoints

- *Quantitative endpoints*

- Skin moisturisation (instrumental analysis)
  Measured by CORNEOMETER CM 825 (A.U. arbitrary units)

  The instrument measures the skin capacitance (quantification of the ability of the skin to collect electrical charge) by application of a high frequency electrical field.
  The measurement is based on the principle that skin capacitance depends on the changes in dielectric constant, which are proportional to the water content in skin. With increasing hydration in the stratum corneum, its dielectric constant grows and therefore its capacitance; to clarify, the more the skin is hydrated, the more the stratum corneum becomes a good electric conductor.
  Hence the instrument can indirectly detect skin hydration level, using arbitrary units.

- EWL trans epidermal water loss (instrumental analysis)
  Measured by TEWAMETER TM 300 (g/m^2 h)

  The instrument measures trans epidermal water loss, or the quantity of water lost from the dermis and epidermis through the stratum corneum, in the form of water vapour. The result is expressed in grams per unit area per hour. The method gives indication about the integrity of the stratum corneum and thus on the efficacy of the barrier function of the skin. A barrier which is intact is related to low TEWL values, high TEWL values show on the other hand a higher water loss hence a low protective function of the skin.

- *Erythema index (instrumental analysis)*
  Measured by MEXAMETER MX 18 (A.U. arbitrary units)

  The instrument can detect the quantity of skin pigments through reflectance spectroscopy. The measurement is based on absorption/reflection principles: a probe emits light with different wavelengths which are absorbed by the pigment and a receiver measures the quantity of light reflected by the skin. Therefore, the instrument can calculate the quantity of light absorbed by the skin and thus estimating the quantity of pigment, to which the test refers. Melanin index is measured by two specific wavelengths: one is related to the spectral absorption peak of haemoglobin and the other helps avoiding colorimetric influences of other pigments (e.g., bilirubin).

Data analysis and statistical analysis

- *Quantitative endpoints*

Skin moisturization

The data on the quantitative endpoints were described using the normal position and dispersion measurements: mean and standard deviation/median and interquartile range.

For each quantitative end-point variable a Shapiro-Wilk test was used to verify the normality of the distribution of the differences between the paired measurements. Furthermore, it was checked the independence of the observations.

When assumptions were fulfilled, a paired samples Student t-test was used for comparing the data obtained at the two observation times.

When assumptions were violated, a non-parametric approach was applied.

The symmetry of the distribution of the differences between the paired evaluations was verified and the most appropriate paired samples non-parametric test (Wilcoxon signed rank test/Sign test) was used for comparing the data obtained at the two observation times.

A significance level of <0.05 was considered.

Analyses were performed using RStudio Version 1.4.1106 © 2009-2021 RStudio, PBC.

Erythema, Tewl

The data on the quantitative endpoints *were described using the normal position and dispersion measurements: mean and standard deviation/median and interquartile range.*

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When a significant interaction between treatment and time variables occurred, the results of the two main effects (treatment and time) were not taken into account and the considerations regarding the outcome of the analysis were drawn.

When a significant effect of the time variable and no significant interaction between treatment and time variables occurred, a Student's t test with Bonferroni corrections was used to compare the different observation times.

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- *Quantitative discrete endpoints*

The data on the quantitative discrete endpoints were described using the median. For each self-evaluation question, the percentage frequencies of each score were calculated.

Finally, the percentage frequencies of the responses were summarized: responses ≥7 and ≥6 were considered respectively as fully positive and positive.

The conclusions about the self-assessment test were drawn from an overall analysis of the medians of responses to all the questions, as shown in the table below:

Overall median	Conclusion
<6	Insufficient pleasantness and perceived effect
6-6.5	Sufficient pleasantness and perceived effect
7-7.5	Moderate pleasantness and perceived effect
8-8.5	Good pleasantness and perceived effect
9-10	Excellent pleasantness and perceived effect

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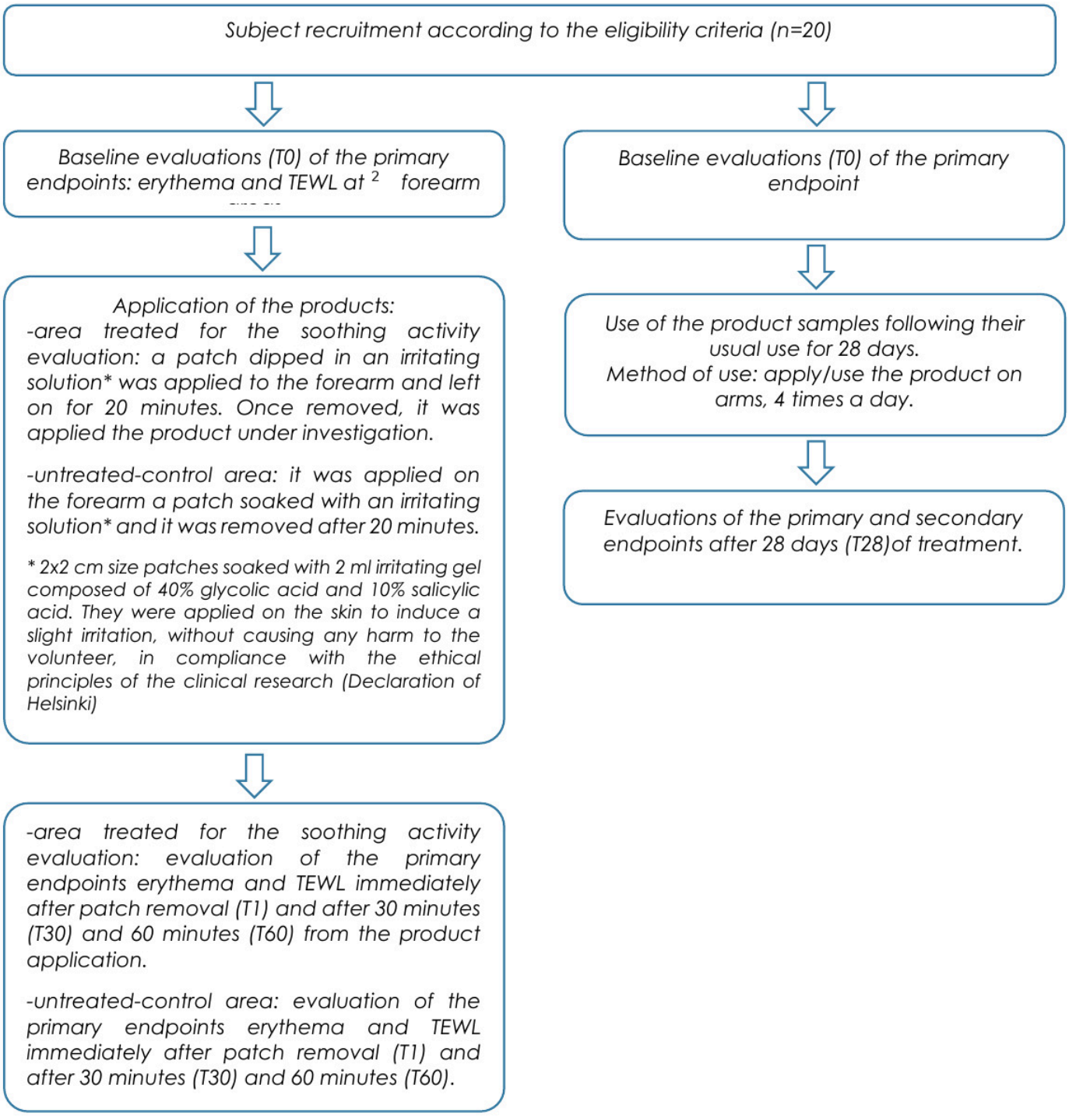
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The measurements are carried out in the treatment sites following a rest period of at least 20 minutes in an air-conditioned room with controlled and regulated temperature and humidity (temperature = 21°C +/- 2°C and humidity 40%-60%).

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Skin moisturization

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RESULTS

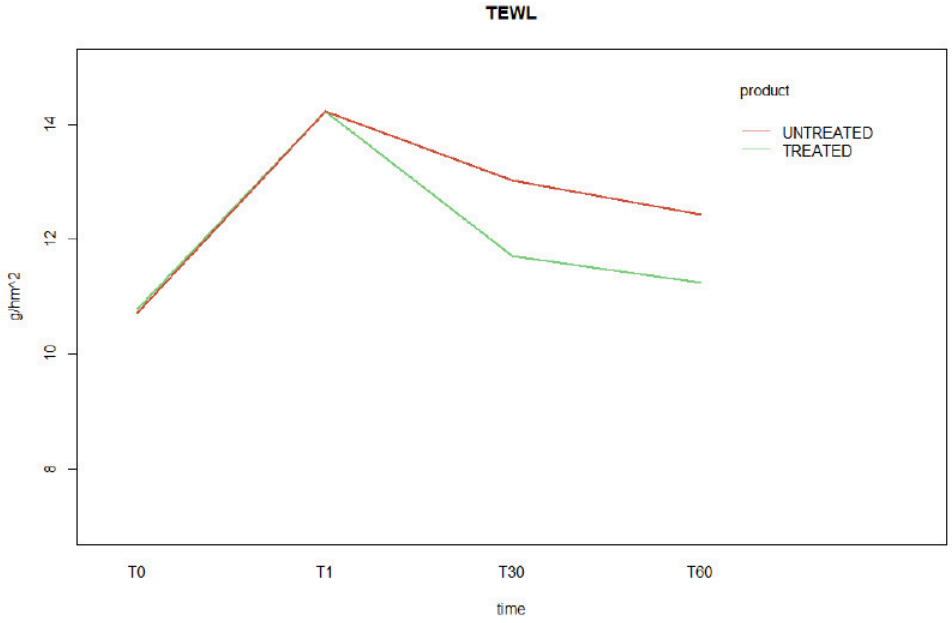
During the trial, no subject developed undesirable effects or breached the established inclusion/exclusion criteria. Furthermore, there were no cases of drop-out. Therefore, the analysis refers to a sample of 20 subjects.

TEWL

Descriptive analysis

	Treated			Untreated		
Survey times	Mean	±	Standard deviation	Mean	±	Standard deviation
T0	10,8	±	1,5	10,7	±	1,8
T1	14,2	±	1,7	14,2	±	1,8
T30'	11,7	±	2,1	13,0	±	1,8
T60'	11,3	±	1,5	12,4	±	1,5

Description of the tewl variable at different observation times in the two areas.



Trend of the variable TEWL at follow-up time points stratified by type of treatment

*In the **untreated area**, compared to the baseline value (T0), it is observed a decrease of TEWL:*

- *of 8%* after 30 minutes;*
- *of 13%* after 60 minutes.*

** Comparing to the value obtained at [T0'] (soon after the irritation induction)*

*In the **treated area**, compared to the baseline value (T0), it is observed a decrease of TEWL:*

- *of 18%* after 30 minutes from product application;*
- *of 21%* after 60 minutes from product application.*

** Comparing to the value obtained at [T0'] (soon after the irritation induction)*

Two-Way Repeated Measures ANOVA

Variability	F	df	p-value	significance
time	47,95	3;57	<0,001	yes
product	17,98	1;19	0,002	yes
time*product	**13,19**	**3;57**	**0,003**	**yes**

2-way repeated measures ANOVA test to evaluate the effect of the treatment and time on TEWL variable.

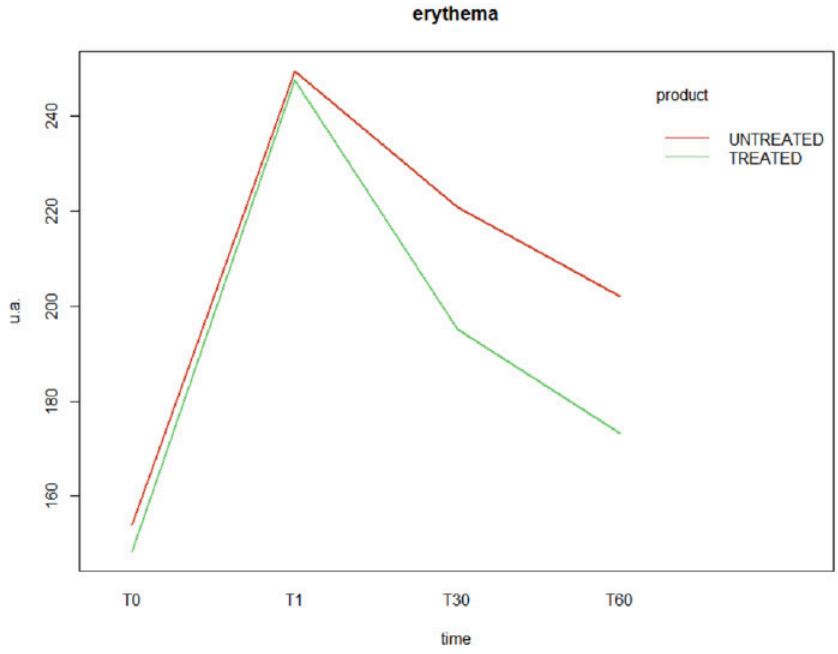
The table representing the result of the analysis of variance shows a statistically significant effect of the interaction between the product and time; therefore, it is possible to state that the evolution over time of TEWL is different between the area treated with the product compared to the untreated area.
In particular, as we can see in the graph, a more marked reduction of this parameter is observed in the area treated with the product (IMMEDIATE SOOTHING EFFECT).

Erythema index ***hema index***

Descriptive analysis

			Treated			Untreated
Survey times	Mean	±	Standard deviation	Mean	±	Standard deviation
T0	148,4	±	28,0	154,1	±	30,8
T1	247,6	±	38,0	249,6	±	37,4
T30'	195,1	±	31,9	220,9	±	32,9
T60'	173,3	±	32,4	202,2	±	36,5

Description of the erythema variable at different observation times in the two areas.



Trend of the variable erythema index at follow-up time points stratified by type of treatment

*In the **untreated area**, compared to the baseline value (T0), it is observed a decrease of erythema index:*

- *of 11%* after 30 minutes;*
- *of 19%* after 60 minutes.*

** Comparing to the value obtained at [T0'] (soon after the irritation induction)*

*In the **treated area**, compared to the baseline value (T0), it is observed a decrease of erythema index:*

- *of 21%* after 30 minutes from product application;*
- *of 30%* after 60 minutes from product application.*

** Comparing to the value obtained at [T0'] (soon after the irritation induction)*

Two-Way Repeated Measures ANOVA

Variability	F	df	p-value	significance
time	133,32	3;57	<0,001	yes
product	49,790	1;19	0,00667	yes
time*product	**20**	3;57	**0,00269**	**yes**

2-way repeated measures ANOVA test to evaluate the effect of the treatment and time on erythema variable.

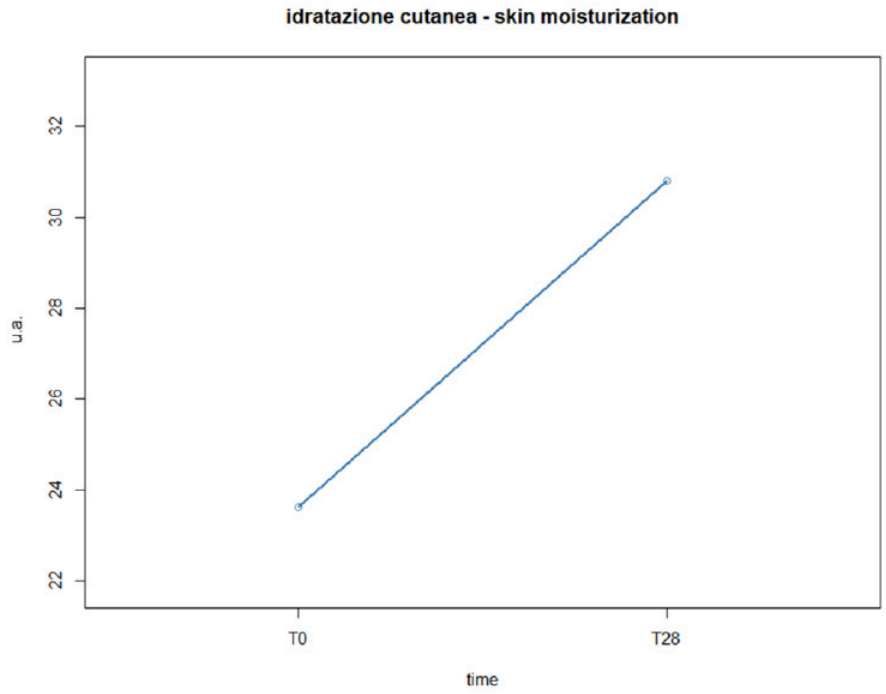
The table representing the result of the analysis of variance shows a statistically significant effect of the interaction between the product and time; therefore, it is possible to state that the evolution over time of erythema index is different between the area treated with the product compared to the untreated area. In particular, as we can see in the graph, a more marked reduction of this parameter is observed in the area treated with the product (IMMEDIATE SOOTHING EFFECT).

Skin moisturization ***ı moisturization***

Descriptive analysis

Survey times	Mean	±	Standard deviation	Median	IQR		
T0	23,6	±	3,8	23,5	21,6	-	26,7
T28	30,8	±	4,9	29,3	27,6	-	33,6

Description of the variable skin moisturization *at the two time points*



Trend of the variable skin moisturization *at the two time points*

Wilcoxon signed rank test

p-value and significance		
	T0	
T28	<0,001	**yes**

Wilcoxon signed rank test used to compare the variable skin moisturization at the two time points

The table shows a statistically significant difference between the means of the two comparison groups. The treatment had a significant effect on the parameter skin moisturization.

Subjective evaluations

Questions	Median of responses	% Frequency of responses	
		positive	fully positive
Do you think that the product deeply moisturizes your skin?	8	100%	95%
Do you think that the product smoothes your skin?	8	100%	85%
Do you think the product is delicate and suitable for your skin?	8	100%	100%
Do you like the texture of your skin?	8	100%	95%
Do you find the fragrance / olfactory note of the product pleasant?	8	90%	80%
Do you think the product is easily absorbed by dry skin?	8	100%	100%
Do you think the product has a calming effect?	8	100%	90%
Overall opinion on the product	8	100%	95%
Would you buy it for its characteristics?	8	100%	95%

Summary table of the medians calculated from the responses to the self-evaluation survey and percentage frequencies of positive and fully positive answers.

The table above shows that 90%-100% of enrolled subjects gave a positive response to the questions and 80%-100% gave a fully positive response after 28 days of product use. Overall, the medians show that the subjects perceived good pleasantness and a good effect of the product.

CONCLUSIONS

The results obtained demonstrate the primary objective of the study: the soothing efficacy and moisturizing effect of the product BLEND OF MOISTURIZING AND SOOTHING ACTIVES REF 2501221L. Along with this phenomenon, good product pleasantness and effect were perceived.

Investigator

Dr. Fernando Marco BIANCHI, M.D.



Safety Assessor/Technical Scientific Committee Vice Chairman

Dr. Claudio ANGELINETTA



BIBLIOGRAPHY

[1] "Regulation (EC) no. 1223/2009 of the European Parliament and of the council of 30 November 2009 on cosmetic products".

[2] "Declaration of Helsinki - ethical principles for medical research involving human subjects adopted by the 18th wma general assembly, Helsinki, Finland, june 1964, and consecutive amendments (last amendment: 64th wma general assembly, Fortaleza, Brasil, Oc".

[3] "GUIDELINES FOR COSMETIC PRODUCT CLAIM SUBSTANTIATION Revising and expanding the Colipa Guidelines on Efficacy (2001/rev. 2008) 22 May 2019 Cosmetics Europe – The personal care association".

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Via A. Panizzi, 10 – MILAN ITALY

PRODUCT INFORMATION - INGREDIENT LIST

INCI

INGREDIENTS:

AQUA (WATER), POLYGLYCERYL-3 RICE BRANATE, DICAPRYLYL ETHER, CAPRYLIC/CAPRIC TRIGLYCERIDE, GLYCERYL STEARATE, GLYCERIN, ORYZA SATIVA BRAN OIL (ORYZA SATIVA (RICE) BRAN OIL), CANNABIDIOL, COCO-CAPRYLATE, CETEARYL ALCOHOL, BORAGO OFFICINALIS SEED OIL, LINUM USITATISSIMUM SEED OIL (LINUM USITATISSIMUM (LINSEED) SEED OIL), TOCOPHEROL, LECITHIN, XANTHAN GUM, ETHYLHEXYLGLYCERIN, TETRASODIUM GLUTAMATE DIACETATE, LACTIC ACID, ASCORBYL PALMITATE, SODIUM DEHYDROACETATE, PHENOXYETHANOL

DATA TABLES

TEWL (g/h m^2)								
Vol. n°	Untreated				Treated			
	T0	T1	T30'	T60'	T0	T1	T30'	T60'
1	9,5	14,6	10,1	9,6	9,3	15	13,3	12,8
2	8,6	13,5	11,7	10,8	8,4	12,6	12,5	11,3
3	10,9	15	13,3	12,1	10,8	13,5	13,8	11,8
4	12,3	16,2	13,2	14,0	12,6	15,5	15,9	14,9
5	13,3	15,6	9,8	11,5	12,3	14,5	11,6	11,3
6	13,6	16,5	16,3	14,3	14,4	17,5	16,4	15,4
7	11,4	14,6	12,5	11,6	11,3	14,7	13,6	13,3
8	11,6	14,6	12,1	11,7	11,5	14,4	12,4	13,7
9	8,9	11,2	9,5	10,1	8,8	12	12	11,2
10	8,9	16,2	9,2	9,2	8,3	15,3	10,1	10,6
11	11,9	15,7	13	13,9	13	16	16,5	15,2
12	8,7	14,2	12,5	10,2	8,2	14,6	13,8	13,0
13	11,8	14,6	13,5	11,7	10,9	14,2	13,3	11,8
14	10,9	14,3	11,1	9,3	11,2	16,6	10,4	10,2
15	12,2	15,5	15,9	12,7	12,3	15,2	13,9	13,6
16	10,2	11	9,9	10,3	9,8	12,5	12,3	11,2
17	10,3	13,5	9,7	10,5	10,2	14,2	13,5	12,8
18	11,5	14,7	11,5	11,0	12,1	14,8	12,8	12,2
19	8,8	11,4	9,4	10,7	9,4	10,9	11,3	11,4
20	10,3	11,8	9,8	9,8	9,4	10,7	11,1	10,9

Erythema index (u.a.)								
Vol. n°	Untreated				Treated			
	T0	T1	T30'	T60'	T0	T1	T30'	T60'
1	170	223	195	176	165	228	200	182
2	135	216	162	156	156	224	187	172
3	186	286	245	224	202	274	268	237
4	136	204	181	152	139	210	203	186
5	141	230	208	200	138	240	237	246
6	200	286	220	223	225	307	275	270
7	151	250	211	148	142	260	250	231
8	142	254	213	155	133	265	230	230
9	102	191	159	128	116	196	171	136
10	138	219	144	134	151	226	193	183
11	149	204	153	147	140	210	198	179
12	131	213	156	150	143	220	186	173
13	197	319	254	225	207	301	278	237
14	170	325	224	198	182	331	254	220
15	163	272	198	191	175	275	209	203
16	103	258	173	150	116	245	210	188
17	135	255	235	207	131	260	256	250
18	173	280	209	199	165	286	220	200
19	130	223	183	133	137	209	206	142
20	115	244	179	169	118	224	186	178

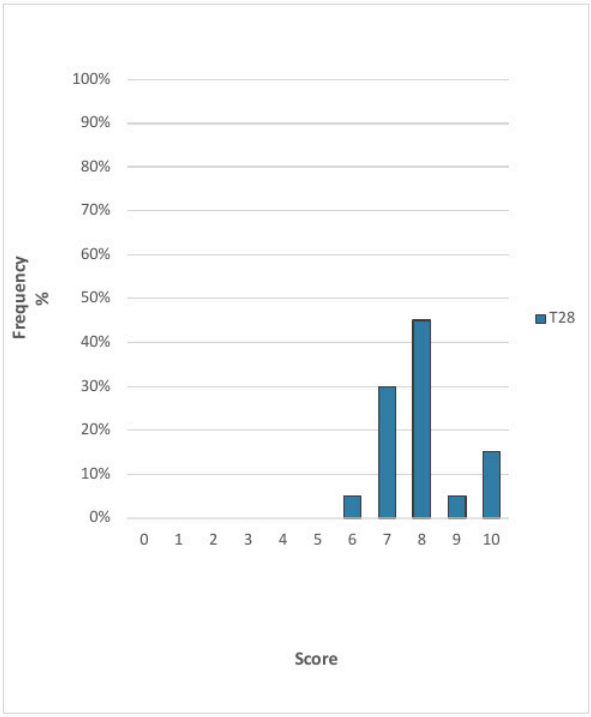
Skin moisturization (A.U.)

Slkin moisturization (u.a.)		
Vol. n°	T0	T28
1	22,9	24,4
2	26,8	40,6
3	23,1	27,5
4	19,9	25,7
5	23,2	40,2
6	24,3	28,9
7	18,8	26,7
8	28,3	31,0
9	21,1	27,8
10	29,4	33,3
11	22,9	29,2
12	19,6	23,5
13	24,8	37,4
14	23,8	28,9
15	26,3	34,2
16	27,0	29,3
17	27,8	34,9
18	26,6	31,5
19	14,1	27,6
20	21,8	33,4

Do you think that the product deeply moisturizes your skin?

Vol. n°	Judgement T28
01	7
02	8
03	9
04	10
05	8
06	8
07	8
08	8
09	7
10	7
11	10
12	7
13	10
14	7
15	7
16	6
17	8
18	8
19	8
20	8
Median	8,0

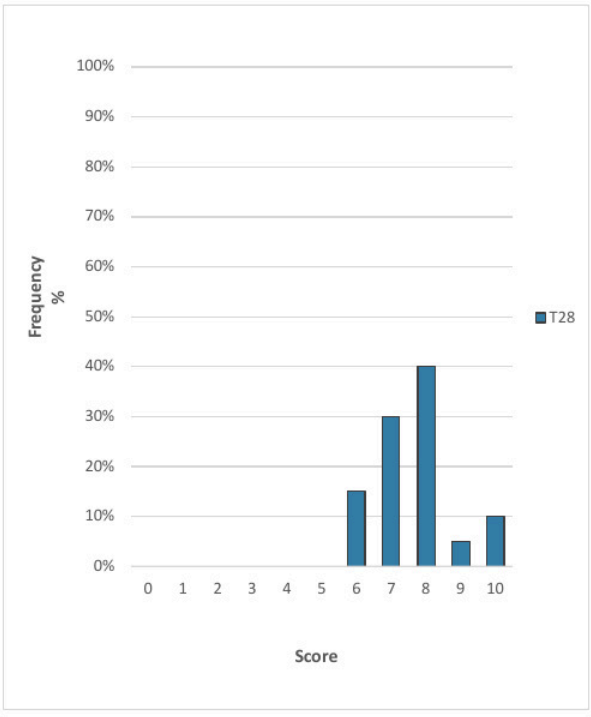
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1	0%
2	0%
3	0%
4	0%
5	0%
6	5%
7	30%
8	45%
9	5%
10	15%



Do you think that the product smoothes your skin?

Vol. n°	Judgement T28
01	6
02	8
03	8
04	10
05	7
06	9
07	8
08	8
09	7
10	6
11	7
12	8
13	10
14	7
15	7
16	6
17	8
18	8
19	7
20	8
Median	8,0

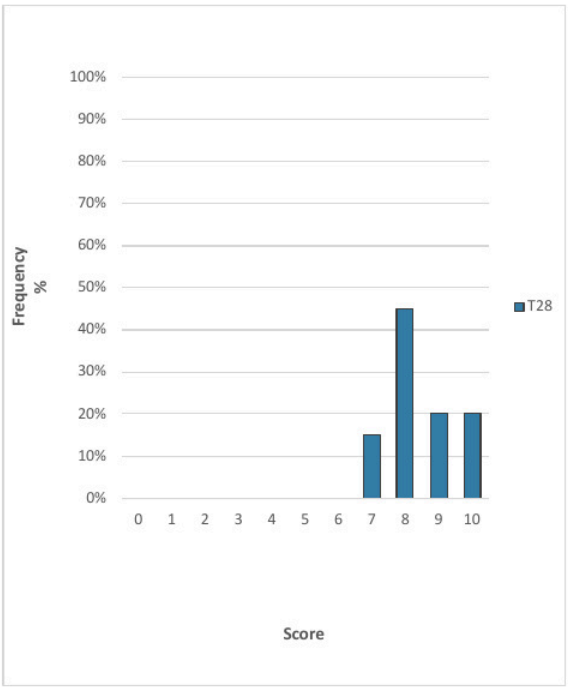
Score	Frequency %
0	0%
1	0%
2	0%
3	0%
4	0%
5	0%
6	15%
7	30%
8	40%
9	5%
10	10%



Do you think the product is delicate and suitable for your skin?

Vol. n°	Judgement T28
01	8
02	8
03	10
04	10
05	8
06	9
07	8
08	8
09	8
10	7
11	10
12	9
13	10
14	8
15	7
16	7
17	9
18	8
19	9
20	8
Median	8,0

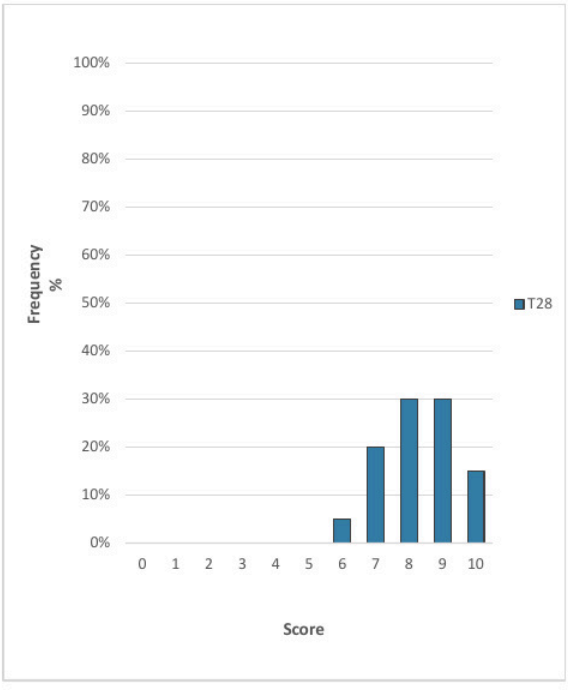
Score	Frequency %
0	0%
1	0%
2	0%
3	0%
4	0%
5	0%
6	0%
7	15%
8	45%
9	20%
10	20%



Do you like the texture of your skin?

Vol. n°	Judgement T28
01	8
02	8
03	9
04	10
05	9
06	9
07	8
08	7
09	8
10	8
11	10
12	9
13	10
14	7
15	7
16	7
17	9
18	9
19	6
20	8
Median	8,0

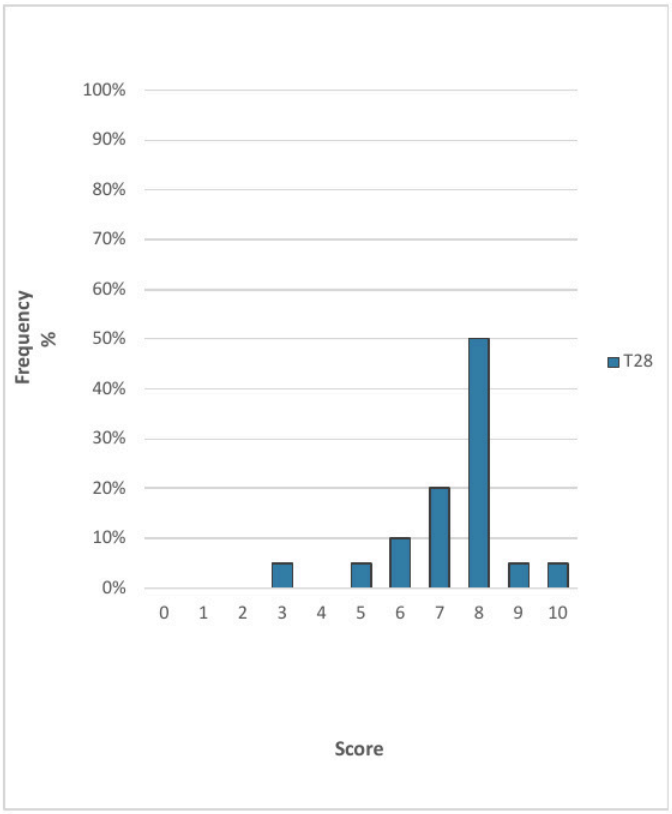
Score	Frequency %
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1	0%
2	0%
3	0%
4	0%
5	0%
6	5%
7	20%
8	30%
9	30%
10	15%



Do you find the fragrance / olfactory note of the product pleasant?

Vol. n°	Judgement T28
01	8
02	8
03	7
04	5
05	8
06	8
07	8
08	7
09	8
10	8
11	3
12	8
13	10
14	7
15	7
16	6
17	9
18	8
19	6
20	8
Median	8,0

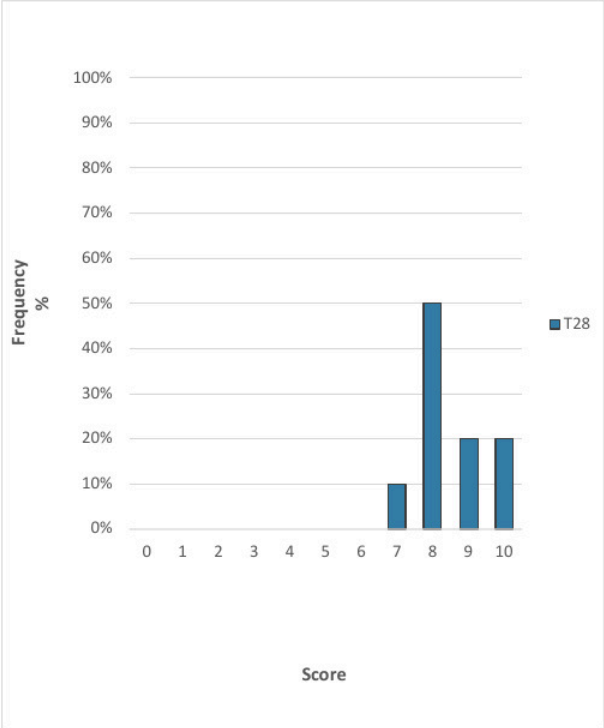
Score	Frequency %
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1	0%
2	0%
3	5%
4	0%
5	5%
6	10%
7	20%
8	50%
9	5%
10	5%



Do you think the product is easily absorbed by dry skin?

Vol. n°	Judgement T28
01	7
02	8
03	9
04	10
05	8
06	9
07	8
08	8
09	8
10	8
11	10
12	10
13	10
14	8
15	8
16	7
17	8
18	9
19	9
20	8
Median	8,0

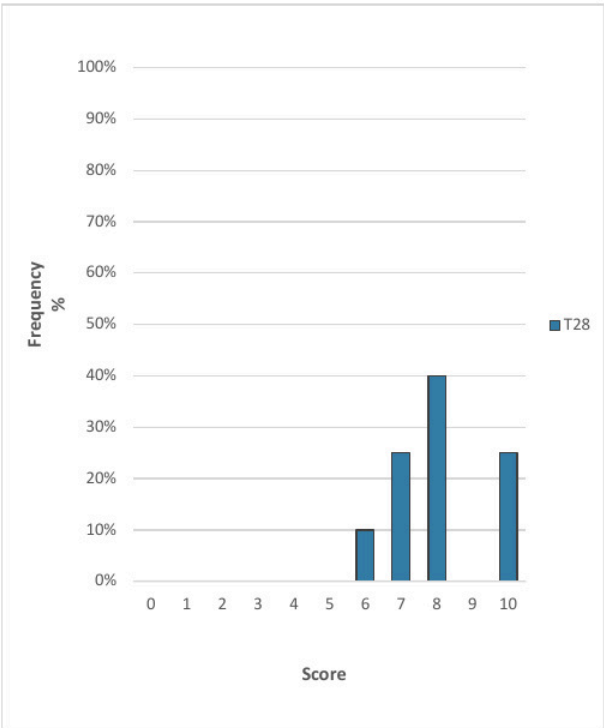
Score	Frequency %
0	0%
1	0%
2	0%
3	0%
4	0%
5	0%
6	0%
7	10%
8	50%
9	20%
10	20%



Do you think the product has a calming effect?

Vol. n°	Judgement T28
01	7
02	8
03	8
04	10
05	7
06	10
07	8
08	8
09	8
10	6
11	7
12	8
13	10
14	7
15	10
16	6
17	10
18	8
19	7
20	8
Median	8,0

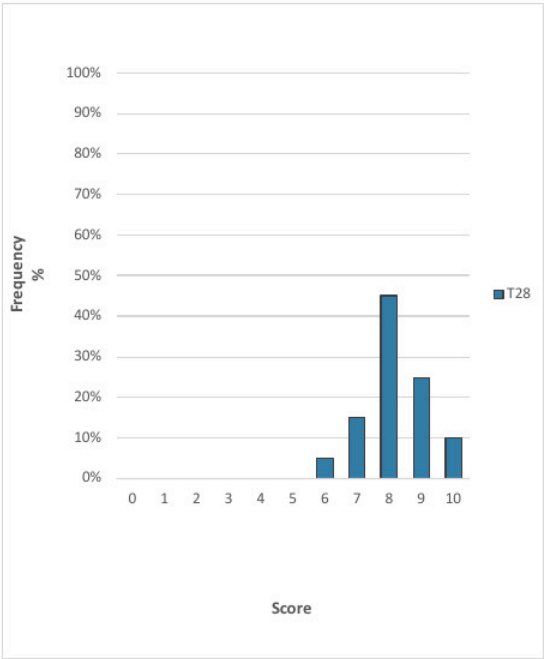
Score	Frequency %
0	0%
1	0%
2	0%
3	0%
4	0%
5	0%
6	10%
7	25%
8	40%
9	0%
10	25%



Overall opinion on the product

Vol. n°	Judgement T28
01	7
02	8
03	9
04	10
05	8
06	9
07	8
08	8
09	8
10	8
11	8
12	9
13	10
14	7
15	9
16	6
17	9
18	8
19	7
20	8
Median	8,0

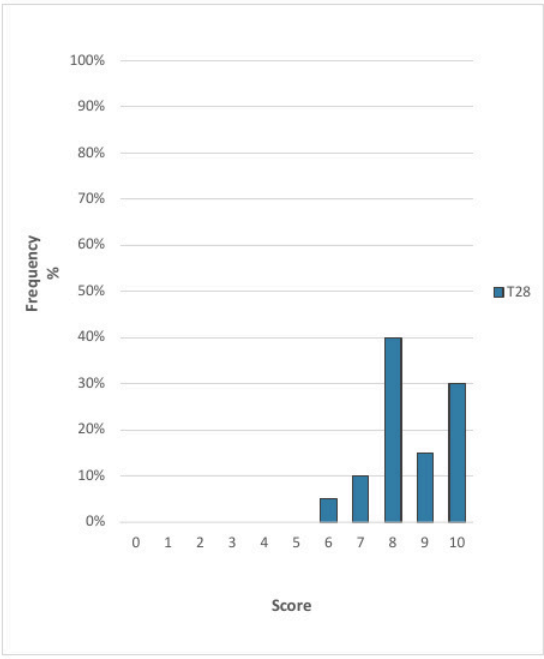
Score	Frequency %
0	0%
1	0%
2	0%
3	0%
4	0%
5	0%
6	5%
7	15%
8	45%
9	25%
10	10%



Would you buy it for its characteristics?

Vol. n°	Judgement T28
01	7
02	8
03	9
04	10
05	8
06	9
07	8
08	8
09	10
10	8
11	8
12	8
13	10
14	10
15	10
16	6
17	9
18	10
19	7
20	8
Median	8,0

Score	Frequency %
0	0%
1	0%
2	0%
3	0%
4	0%
5	0%
6	5%
7	10%
8	40%
9	15%
10	30%



The results reported in this document are to be referred exclusively to the tested sample, whose safety was previously assessed.

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Annex C

ART. 1 INTRODUCTION

The Technical Scientific Committee of Bio Basic Europe S.r.l. is an independent and impartial work group, constituted in accordance with interdisciplinarity criteria and with autonomous decision-making powers. Its task and responsibility are to ascertain compliance of the methodologies and validate scientific and clinical research protocols. The TSC formulates operating proposals and opinions on Bio Basic Europe S.r.l. research projects carried out at the CDC Dermo Clinical Research Institute of Milan, at the microbiological, chemical/physical and in vitro analysis laboratories of the Technical Scientific Park of the University of Pavia, or at laboratories, medical clinics and hospital institutes that collaborate with the company. The TSC acts in compliance with the ethical principles of the Helsinki Declaration, Clinical and Laboratory Best Practice Standards, all applicable national and European regulatory frameworks, and the recommendations and guidelines of the main competent international organizations and institutions.

ART. 2 INDEPENDENCE OF THE TECHNICAL SCIENTIFIC COMMITTEE

The independence of the TSC is guaranteed:

- by the lack of hierarchical subordination of the TSC to the principal;
- by the presence of experts who are not employed by the principal;
- by the absence of conflicts of interest of TSC members with regard to the trials proposed.

ART. 3 FUNCTIONS OF THE TECHNICAL SCIENTIFIC COMMITTEE

In brief, the TSC performs the following functions:

- It assesses clinical trial protocols and scientific protocols, ascertaining conformity of the procedures and compliance with all mandatory regulatory frameworks, expressing its opinion and validating in particular:
  - clinical trials and laboratory analyses that assess cosmetic products, nutraceutical products, medical and diagnostic devices, medical/surgical aids, detergents, hazardous substances, biocides, and chemical substances in general;
  - protocols that assess the adoption of new clinical and scientific operating procedures;
  - observational studies and monitoring.
- It may propose information/training/refresher initiatives for the operators involved in the trials, as well as workshops on pertinent scientific topics.

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ART. 4 COMPOSITION OF THE TECHNICAL SCIENTIFIC COMMITTEE

The TSC is composed of members who are internal and external to Bio Basic Europe S.r.l., with multidisciplinary skills, so that it can guarantee the qualifications and experience required to assess the scientific, methodological and ethical aspects of the protocols presented. The members of the TSC have proven skills and qualifying experience in the sector covered by the study.

For this purpose, at least the following persons participate in all TSC meetings:

a. The Chairman and/or the Vice Chairman of the TSC
b. The University of Pavia Director of Research
c. The Investigator/Medical Director of the CDC Dermo Clinical Research Institute*
d. The expert of Bio Basic Europe S.r.l. depending on the issue on which the opinion is formulated

**In the specific case of in vitro, microbiological and chemical/physical tests, member c. will be replaced by member d., or by one of the members who specialise in topics pertinent to Bio Basic Europe.*

In general, the TSC work group comprises at least:

e. one chemist/cosmetic chemist
f. one toxicologist
g. one pharmacist/pharmacologist
h. one physician
i. one biologist
j. one biostatistician
k. one microbiologist/virologist/expert in genetics
l. one clinician

MANAGING MEMBERS OF THE TECHNICAL SCIENTIFIC COMMITTEE

- **Prof. ORNELLA PASTORIS**
  TSC Chair and Scientific Director, Lazzaro Spallanzani Faculty of Biology and Biotechnologies, University of Pavia
- **Dr. CLAUDIO ANGELINETTA**
  TSC Vice Chair, Chemist/Cosmetic chemist
- **Dr. FERNANDO MARCO BIANCHI, M.D.**
  Medical Director of the CDC Dermo Clinical Research Institute, specialising in dermatology and venereology

MEMBERS AFFILIATED WITH THE UNIVERSITY INSTITUTES AND RESEARCH CENTRES

- **Prof. GIULIANO MAZZINI**
  National Research Council, Pavia Institute of Molecular Genetics, expert in genetics
- **Prof. FIORENZO PEVERALI**
  National Research Council, Pavia Institute of Molecular Genetics, expert in genetics

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MEMBERS AFFILIATED WITH BIO BASIC EUROPE S.R.L.

Clinical research experts:

- **Dr. DANIELA GANDINI**
  Bio Basic Europe Safety Clinical Test Reporting Contact Person, expert in in vivo safety tests
- **Dr. ANTONELLA PRATICO'**
  Bio Basic Europe Clinical Test Reporting Coordinator, expert in clinical research
- **Dr. GAETANA RIZZI**
  Bio Basic Europe Medical Device and Food Supplement Clinical Tests Reporting Contact Person, expert in clinical research
- **Dr. ROBERTA VILLA**
  Bio Basic Europe Statistical Analysis Coordinator and Efficacy Clinical Test Reporting Contact Person, expert in clinical statistics

Other experts:

- **Dr. MARA FOPPIANI**
  Head of Bio Basic Europe Microbiology Laboratory, expert in microbiology and virology
- **Dr. ELIANA REGOLA, PhD**
  Bio Basic Europe Laboratory Test Coordinator, expert in microbiology and virology
- **Dr. FRANCESCA VALLOTTO**
  Coordinator of the Regulatory Department of Bio Basic Europe, expert in cosmetic chemistry and toxicology
- **Dr. RICCARDO VICINI, PhD**
  Head of Bio Basic Europe Vitro Laboratory, expert in pharmacology and toxicology

CLINICAL INVESTIGATORS

- Dr. MAURIZIO BARBIERI CARONES, M.D., specialising in gynaecology
- Dr. ANTONELLA COLOMBO, M.D., specialising in dermatology and venereology
- Dr. ALESSANDRA DI BENEDETTO, M.D., specialising in dermatology and venereology
- Dr. TIZIANA DIVINO, M.D., specialising in aesthetic medicine and dermosurgery
- Dr. EVELYN FALCONI KLEIN, M.D., specialising in dermatology and venereology
- Dr. GIORGIO GRASSI, M.D., specialising in ophthalmology
- Dr. ANDREA RAMONI, M.D., specialising in ophthalmology
- Dr. LUCA VETTORUZZO, M.D., specialising in dentistry and dental prosthesis

In the case of evaluations pertaining to areas not covered by its members, the Chairman of the TSC may convene experts who are not members of the TSC for specific consultations. In the case of resignation or departure for any reason of one of the mandatory members of the TSC, the Chairman ensures that they are promptly replaced.

ART. 5 FUNCTIONS OF THE CHAIRMAN

- he/she is the official representative and spokesperson of the TSC;
- he/she is the contact person for any critical issues of a clinical/scientific nature that arise during the activity of the TSC;
- he/she decides on possible supplementation of the TSC composition and on replacement of members who have been deprived of office and/or resigned;
- he/she convenes, moderates and conducts the meetings of the TSC;
- he/she supervises the decisions adopted by the TSC.

The Vice Chairman replaces the Chairman in all functions in case of absence or temporary impediment and assists the Chairman, who may confer specific assignments. The Chairman uses the services of a Scientific Secretary for administrative/scientific activities. The Secretary participates in meetings with advisory and supporting functions and takes the minutes.

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ART. 6 DUTIES OF THE MEMBERS

The Members of the TSC:

- are personally responsible for the activities under their remit carried out in the TSC;
- are bound to secrecy with regard to the actions related to their activity in the TSC;
- must communicate any bias or lack of impartiality that may have an impact on their participation in the TSC.

ART. 7 VALIDATION OF THE PROJECTS

The TSC is called upon to express opinions on and ascertain the completeness of scientific and clinical protocols prepared by Bio Basic Europe S.r.l. The TSC certifies the adequacy of the documentation and the conformity of the procedures and methodologies followed in designing and developing the research project, in compliance with the applicable rules and regulations. Each protocol, once confirmed by the mandatory members of the TSC as indicated in Art. 4, is signed by the Investigator/Medical Director of the CDC Dermo Clinical Research Institute, or by the Head of the Laboratory in the case of test reports, and thereafter by the Safety Assessor/Vice Chairman of the TSC, who attests the validity of the document with a digital signature. Each protocol approved by the TSC is archived and made available to all members of the TSC.

TSC Chairman and Scientific Director, University of Pavia	*TSC Vice Chairman*	*The Investigator and Medical Director of the CDC Dermo Clinical Research Institute*
		