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

RDV SRL

PASTA

Report no.

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ISO 9001 BUREAU VERITAS Certification

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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
Scegliere un elemento.

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.
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- 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: *CLAUDIA PERRONE, Bio Basic Europe Clinical Advisor, Degree in Medicinal Chemistry and Pharmaceutical Technology, University of Milan*

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ABSTRACT

The primary objective of this clinical trial is to assess whether the cosmetic product PASTA has a protective efficacy.
The protective action was assessed by analysis of the differences in erythema and TEWL increase in response to the irritation, compared with the untreated control area.
The trial also has the following secondary objectives: evaluating whether a positive pleasantness and effect of the product were perceived.

It was performed a clinical study and the product under investigation was assigned to 20 enrolled subjects. For the evaluation of the protective efficacy of the product, it was induced a slight skin irritation on specific forearm areas, which were pre-treated with the cosmetic product and untreated. Some definite endpoints variables were analysed at baseline time and post treatment and irritation.

The results obtained by the test demonstrated the primary objective of the study: the protective efficacy of the product.

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

OBJECTIVES

Primary objective

The aim of this study is to assess whether the cosmetic product PASTA has a protective efficacy.

The evaluation was performed by comparing treated locks with untreated area.

Primary endpoints:

Evaluation of the soothing efficacy of the product

- TEWL (quantitative endpoint)
- Erythema index (quantitative endpoint)

Secondary objectives

A series of sensory self-evaluations were collected by the enrolled subjects, with the aim of evaluating the effect and pleasantness of use of the product.

Secondary endpoints:

- subjective evaluations (quantitative discrete endpoint)

STUDY CHARACTERISTICS

Study design

The assessment of the protective efficacy of the product was carried out by comparing the results obtained after the application of the product and after skin irritation with the baseline data and with a control area.

The perceived pleasantness and effect were evaluated by analysing the results obtained after the application 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:

- both male and female sex;
- age between 18 and 60 years;
- with reddened skin / with atopic tendency;
- 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

Not applicable.

Trial scheme

Subject recruitment according to the eligibility criteria (n=20)	
↓	
Targeting of 2 enrolled subjects' forearm areas:	
Area 1 treated for the evaluation of the protective activity	Area 2 untreated-control area
↓	↓
Baseline evaluations (T0) of the primary endpoints	Baseline evaluations (T0) of the primary endpoints
↓	↓
Application of the investigated product	–
↓	↓
Application of a patch soaked into an irritating solution* for 20 minutes	Application of a patch soaked into an irritating solution* for 20 minutes
↓	↓
Evaluation of the primary and secondary endpoints immediately after patch removal (T01)	Evaluation of the primary endpoints immediately after patch removal (T01)

** 2x2 cm size patches soaked with 2 ml irritating gel composed of 40% glycolic acid and 10% salicylic acid. They were applied on the skin to induce a slight irritation, without causing any harm to the volunteer, in compliance with the ethical principles of the clinical research (Declaration of Helsinki.)*

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;
- non- compliance.

Endpoints

- Quantitative endpoints

  - TEWL trans epidermal water loss (instrumental analysis)
    Measured by TEWAMETER TM 300 (g/m² 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).

- Quantitative discrete endpoints

  - Subjective assessments

    The subjects enrolled in the trial are asked to fill in a survey, which consists of numerical rating scale questions.

    Specifically, it is used the 11-point Numerical Rating Scale (NRS), which ranges from 0 to 10 (0 is the minimum value and 10 the maximum one). The answerers are asked to indicate the numeric value which best describe their response.

The basal 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%).

Data analysis and statistical analysis

- Quantitative endpoints

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

A Shapiro-Wilk test was used to verify the normality of the endpoint variables, then a parametric two-way repeated measures analysis of variance model was applied to compare treatment-no treatment and the effect over time.

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.

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

A significance level of <0.05 was considered.

Analyses were performed using RStudio 2022.07.1 Build 554 © 2009-2022 RStudio, PBC.

- 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
$x < 6$	Insufficient pleasantness and perceived effect
$6 \leq x < 7$	Sufficient pleasantness and perceived effect
$7 \leq x < 8$	Moderate pleasantness and perceived effect
$8 \leq x < 9$	Good pleasantness and perceived effect
$x \geq 9$	Excellent pleasantness and perceived effect

RESULTS

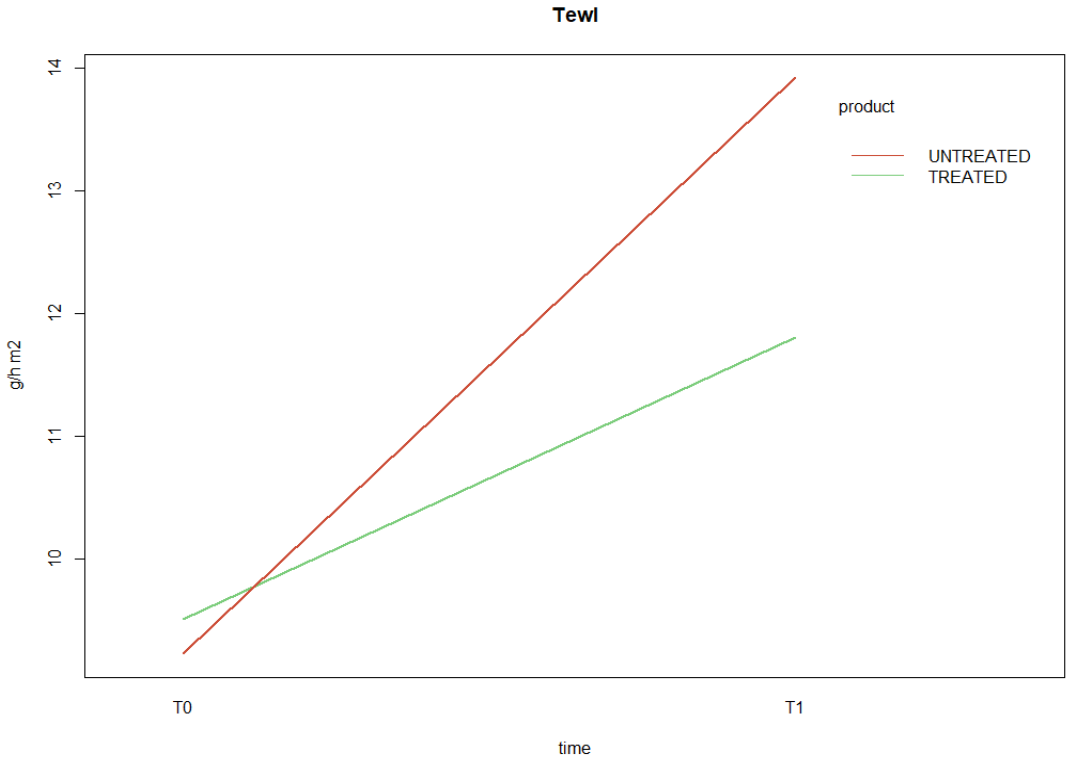
During the trial, no subject developed undesirable effects or breached the established inclusion/exclusion criteria. Furthermore, there were no cases of drop-out. Therefore, the analysis refers to a sample of 20 subjects.

TEWL

Descriptive analysis

	Treated			Untreated		
Survey times	Mean	±	Standard deviation	Mean	±	Standard deviation
T0	9,5	±	2,0	9,2	±	1,9
T01	11,8	±	3,0	13,9	±	2,8

Description of the variable TEWL in the two areas at the time points



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

In the area treated with the product under study it can be observed an increase of the variable TEWL compared to the baseline value (T0) of 24% after the removal of the patch soaked in the irritating solution.

In the untreated area it can be observed an increase of the variable TEWL compared to the baseline value (T0) of 52% after the removal of the patch soaked in the irritating solution.

Two-Way Repeated Measures ANOVA

Variability	F	df	p-value	significance
time	91,92	1;19	<0,001	yes
product	14,43	1;19	<0,001	yes
time*product	**67,33**	1;19	<0,001	**yes**

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

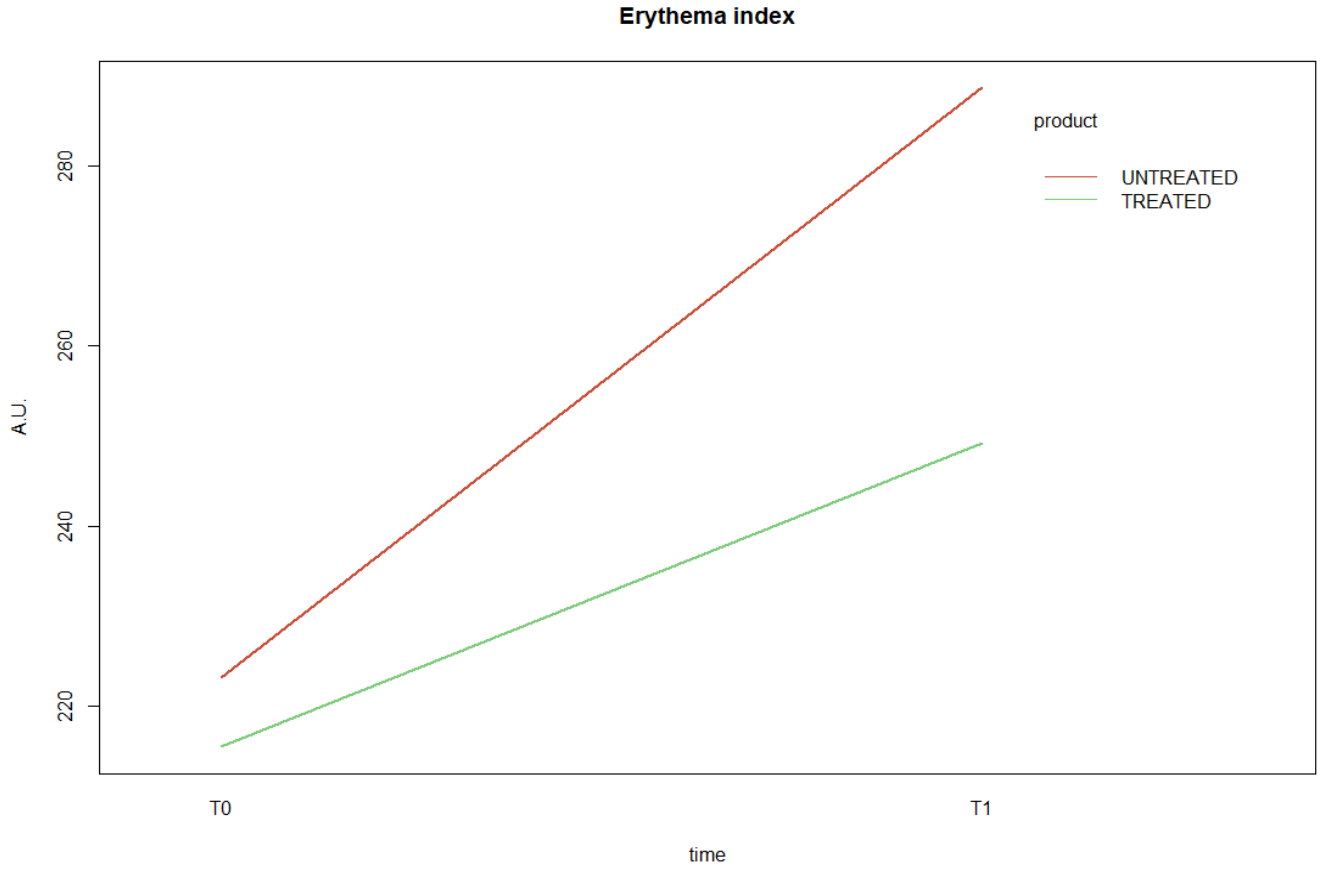
The table, displaying the result of the analysis of variance, shows a statistically significant interaction treatment-time; hence, it can be stated that the trend of the variable TEWL over time is different in the area treated with the product under study and in the untreated area.
Specifically, in the area treated with the product under study it can be observed a lower increase of the parameter (increased in response to the irritation that was induced), compared to the untreated area.

Erythema index

Descriptive analysis

	Treated			Untreated		
Survey times	Mean	±	Standard deviation	Mean	±	Standard deviation
T0	216	±	26	223	±	33
T01	249	±	31	289	±	43

Description of the variable erythema index in the two areas at the time points



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

In the area treated with the product under study it can be observed an increase of the variable erythema index compared to the baseline value (T0) of 16% after the removal of the patch soaked in the irritating solution.

In the untreated area it can be observed an increase of the variable erythema index compared to the baseline value (T0) of 29% after the removal of the patch soaked in the irritating solution.

Two-Way Repeated Measures ANOVA

Variability	F	df	p-value	significance
time	196,25	1;19	<0,001	yes
product	18,02	1;19	<0,001	yes
time*product	**74,79**	**1;19**	**0,045**	**yes**

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

The table, displaying the result of the analysis of variance, shows a statistically significant interaction treatment-time; hence, it can be stated that the trend of the variable erythema index over time is different in the area treated with the product under study and in the untreated area.
Specifically, in the area treated with the product under study it can be observed a lower increase of the parameter (increased in response to the irritation that was induced), compared to the untreated area.

Subjective evaluations

Questions	Median of responses	% Frequency of responses	
		positive ≥6	fully positive ≥7
Do you think the product is delicate on the skin?	7,5	100%	100%
Do you think the product protects against ittitations, reddenings, itching?	7	90%	80%
Do you think that the product creates a barrier effect that protects and preserves the most delicate areas from irritation and cracking?	7	95%	80%
Do you think that the product maintains proper hydration of the skin in the treated areas?	8	90%	90%
Global opinion aboit the product	7	95%	90%

Summary table of the median calculated on the response to the self evaluation survey and percentage frequencies of positive and fully positive answers

The table above shows that the 90%-100% of enrolled subjects gave a positive reply to the question and the 80%-100% a fully positive one, soon after product application.

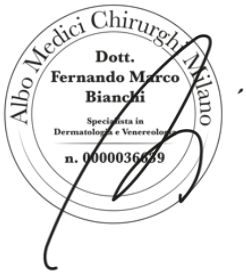
Furthermore, the medians show overall that the subjects perceived a moderate pleasantness and effect of the product soon after product application.

CONCLUSIONS

The results obtained by the test demonstrated the primary objective of the study: the protective efficacy of the product **PASTA**.

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

Investigator	*Safety Assessor/Technical Scientific Committee Vice Chairman*
Dr. Fernando Marco BIANCHI, M.D.	Dr. Claudio ANGELINETTA



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[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".

Annex A

PRODUCT INFORMATION - INGREDIENT LIST

INCI

Annex B

DATA TABLES

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

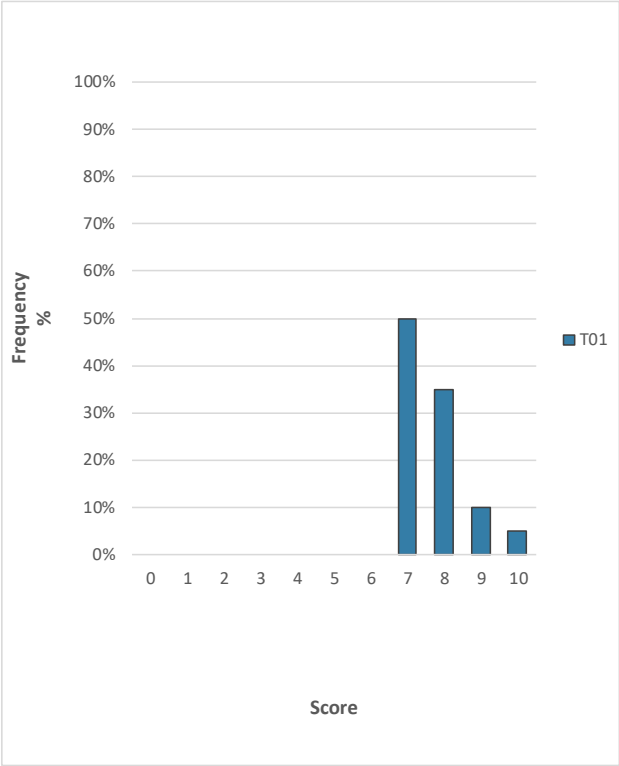
TEWL (g/h m^2)				
Vol. n°	Treated		Untreated	
	T0	T01	T0	T01
1	6,7	7,8	6,5	9,2
2	8,6	9,7	8,9	13,2
3	7,1	8,5	7,5	10,1
4	6,4	7,1	6,9	8,1
5	8,4	10,5	8,0	14,3
6	11,4	15,3	10,8	16,0
7	10,4	11,5	10,9	13,8
8	9,4	9,2	10,3	12,3
9	11,1	17,0	8,1	17,5
10	11,2	14,2	10,5	13,8
11	9,9	10,9	8,3	13,5
12	14,8	19,0	15,1	20,3
13	8,9	11,6	9,6	16,4
14	8,6	13,4	9,1	15,4
15	10,5	13,8	10,3	16,3
16	9,3	12,1	9,2	14,0
17	11,0	12,0	7,6	13,5
18	8,7	9,6	8,1	11,8
19	10,3	12,6	9,7	14,4
20	7,5	10,3	9,2	14,5

Erythema index (u.a.)				
Vol. n°	Treated		Untreated	
	T0	T01	T0	T01
1	209	229	224	249
2	240	270	239	290
3	211	255	222	294
4	231	264	244	327
5	188	211	174	245
6	206	240	195	284
7	197	205	181	221
8	204	227	213	259
9	199	254	263	356
10	240	273	255	316
11	231	256	205	274
12	246	259	233	277
13	160	185	138	197
14	263	303	234	303
15	248	305	257	355
16	231	289	264	361
17	194	231	249	314
18	199	235	216	281
19	224	255	217	296
20	189	240	240	274

Do you think the product is delicate on the skin?

Vol. n°	Judgement T01
01	7
02	7
03	8
04	8
05	8
06	7
07	7
08	7
09	7
10	9
11	8
12	7
13	8
14	7
15	7
16	8
17	7
18	8
19	10
20	9
Median	7,5

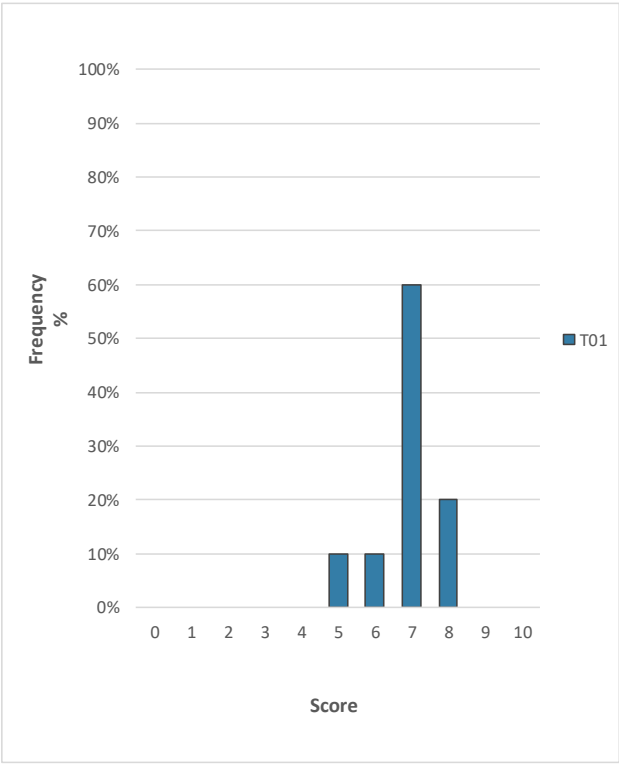
Score	Frequency %
0	0%
1	0%
2	0%
3	0%
4	0%
5	0%
6	0%
7	50%
8	35%
9	10%
10	5%



Do you think the product protects against ittitations, reddenings, itching?

Vol. n°	Judgement T01
01	7
02	7
03	7
04	7
05	7
06	6
07	7
08	5
09	7
10	7
11	7
12	7
13	8
14	6
15	7
16	5
17	7
18	8
19	8
20	8
Median	7,0

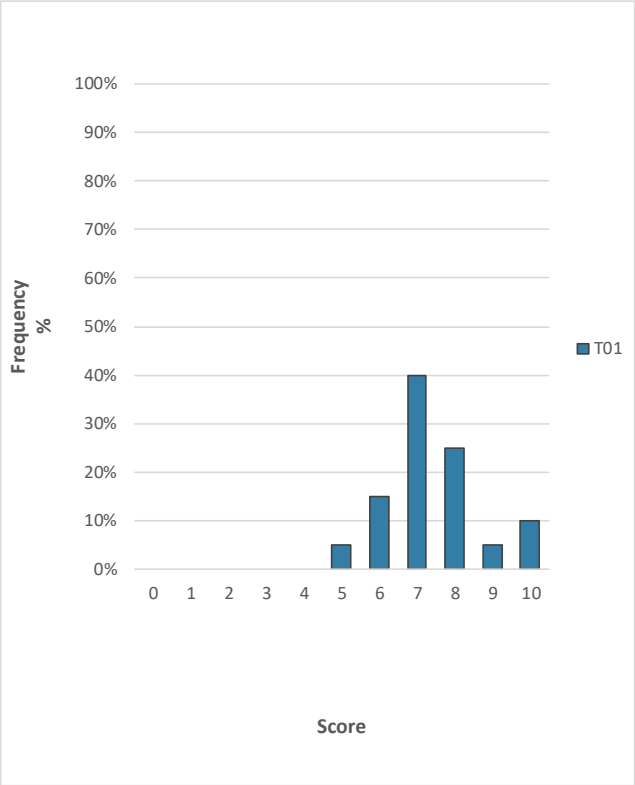
Score	Frequency %
0	0%
1	0%
2	0%
3	0%
4	0%
5	10%
6	10%
7	60%
8	20%
9	0%
10	0%



Do you think that the product creates a barrier effect that protects and preserves the most delicate areas from irritation and cracking?

Vol. n°	Judgement T01
01	7
02	7
03	10
04	6
05	8
06	7
07	7
08	6
09	7
10	8
11	8
12	7
13	8
14	6
15	7
16	5
17	7
18	8
19	10
20	9
Median	7,0

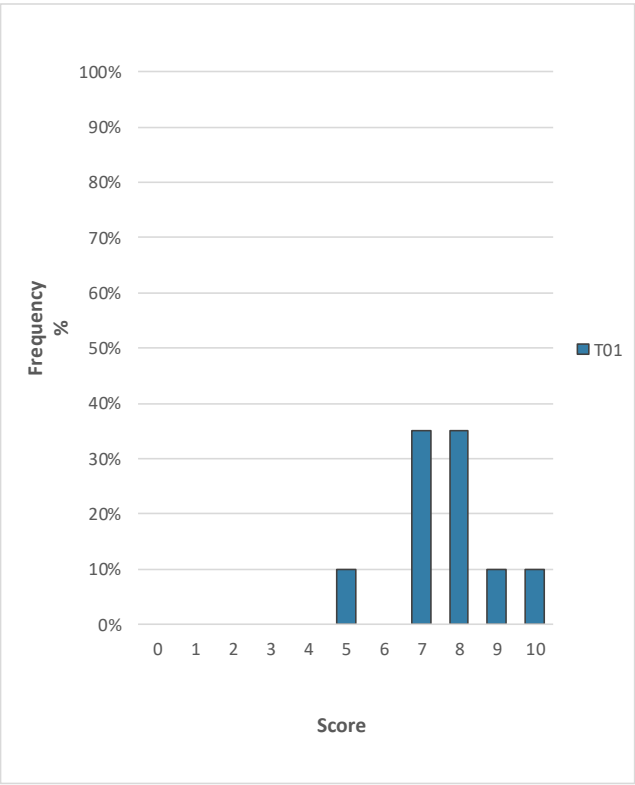
Score	Frequency %
0	0%
1	0%
2	0%
3	0%
4	0%
5	5%
6	15%
7	40%
8	25%
9	5%
10	10%



Do you think that the product maintains proper hydration of the skin in the treated areas?

Vol. n°	Judgement T01
01	7
02	8
03	10
04	8
05	8
06	7
07	7
08	5
09	8
10	8
11	8
12	9
13	8
14	7
15	7
16	5
17	7
18	7
19	10
20	9
Median	8,0

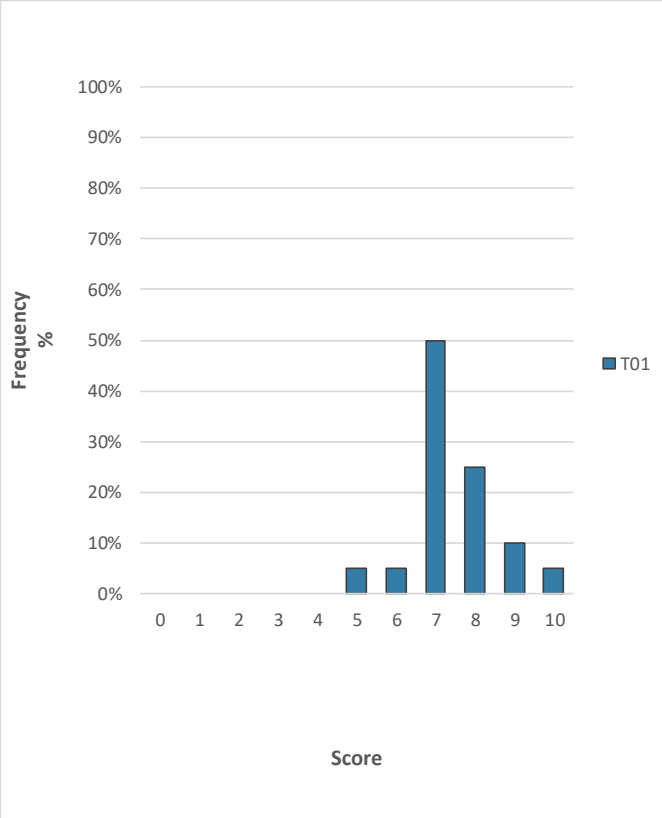
Score	Frequency %
0	0%
1	0%
2	0%
3	0%
4	0%
5	10%
6	0%
7	35%
8	35%
9	10%
10	10%



Global opinion aboit the product

Vol. n°	Judgement T01
01	7
02	8
03	7
04	7
05	8
06	7
07	7
08	6
09	7
10	8
11	8
12	7
13	8
14	7
15	7
16	5
17	7
18	9
19	10
20	9
Median	7,0

Score	Frequency %
0	0%
1	0%
2	0%
3	0%
4	0%
5	5%
6	5%
7	50%
8	25%
9	10%
10	5%



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Annex C

TECHNICAL SCIENTIFIC COMMITTEE STATUTE – REGULATION

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, whose task and responsibility is to ascertain the compliance of the methodologies and validate scientific and clinical research protocols. The TSC is called upon to formulate operating proposals and opinions on Bio Basic Europe S.r.l. research projects 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 contained in the Helsinki declaration, with the Clinical and Laboratory Best Practice Standards and with all applicable national and European related regulatory frameworks, as well as with 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 the clinical trial protocols and the scientific protocols, ascertaining the conformity of the procedures and the 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.

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 may 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 to 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

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 convoke, for specific consultations, experts who are not members of the TSC. In the case of resignation or of the exit on any grounds of one of the mandatory members of the TSC, the Chairman of the TSC ensures that they are promptly replaced.

ART. 5 FUNCTIONS OF THE CHAIRMAN

The Chairman exercises the following functions:

- 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 the possible supplementation of the TSC's composition and on the replacement of members who have been deprived of their office and/or have resigned
- he/she convokes, 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 his/her functions in case of absence or temporary impediment. He/she assists the Chairman who may confer specific assignments thereto. The Chairman uses the services of a Scientific Secretary for the performance of activities of an administrative/scientific nature. The Secretary participates in the meetings with advisory, supporting functions and takes the minutes.

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 and lack of impartiality that may have an impact on their participation in the TSC

ART. 7 VALIDATION OF THE PROJECTS

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The TSC is called upon to express opinions on and ascertain the completeness of scientific and clinical protocols by Bio Basic Europe S.r.l. 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 case of test reports, and thereafter by the Safety Assessor/Vice Chairman to the TSC, who attests the validity of the document with digital signature. Each protocol approved by the TSC will be archived and be 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