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Muenster, August 14th 2020

Expert opinion by dermatological specialists concerning a

clinical-dermatological application study

in 20 volunteers with application twice a day on the face for a period of four weeks

Test for dermal tolerability with final questionnaire and determination of skin moisture, skin elasticity and skin roughness

RENU 28

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1 General information

Title

Clinical application study under dermatological control

Testing body

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1.1 Synopsis

Study title	Clinical application study under dermatological control
Test product	**RENU 28**
Product type	Face gel
Study design	Single-centre
Testing body	Dermatest GmbH Engelstr. 37 D-48143 Münster
Expert opinion version and date	V2 19.08.2020
Test period	May - July 2020
Primary study objectives	Assessment of skin tolerability From the time of the start of the study to the end of the study and 30 days beyond the latter, all skin reactions and any other adverse reactions are recorded in the reaction file.
Secondary study objectives	Assessment of efficacy - Query of the subjective impression by questionnaire - Skin moisture (corneometry) - Skin elasticity (cutometry) - Skin roughness (PRIMOS replicas)
Number of subjects	20
Application period	four weeks
Times of measurement	Questionnaire: T_{4Weeks} Skin moisture: T_0 and T_{4Weeks} Skin elasticity: T_0 and T_{4Weeks}
Test area	face
Frequency of application	two times a day
Inclusion criteria	- 31 years and older - Female healthy volunteers - All skin type - Written informed consent of the subjects or legal guardian is available
Exclusion criteria	- Severe or chronic skin inflammations - Severe internal or chronic diseases

	- Taking of drugs that may interfere with skin reactions (glucocorticoids, antiallergics, topical immune modulators, etc.) - Application of active substance-containing products and care products 7-10 days before the start of the test - Severe allergies or any serious side effects of cosmetic preparations ever occurred - Sun baths or solarium visits during the study - Known neoplastic disease - Pregnancy and breast-feeding

1.2 Schedule

Study day	Day 0	Day 28
Information of the subjects	✔	
Informed Consent Form Sheet	✔	
Medical history	✔	
Dermatological examination	✔	✔
Compliance with the inclusion and exclusion criteria	✔	✔
Query of the subjective impression		✔
Measurement of skin moisture (corneometry)	✔	✔
Measurement of skin elasticity (cutometry)	✔	✔
Measurement of skin roughness (PRIMOS replicas)	✔	✔

2 Introduction

The human skin is the largest and functionally most versatile human organ. It delimits the organism against the outside world and protects it against dehydration and environmental influences. The skin consists of three layers: Epidermis (upper skin layer), dermis (true skin) and subcutis (hypoderm). The epidermis, in turn, is composed of five layers and consists of 90% keratinocytes (horny cells). From the outside, the superimposed layers are the following: *Stratum corneum*, *stratum lucidum*, *stratum granulosum*, *stratum spinosum* and *stratum basale*.

These days, any products, in particular cosmetics, consumer goods and medical devices, are in contact with the skin daily and often over long periods. Good tolerability is therefore a prerequisite for the application of these products. Since alternative test methods such as animal testing are prohibited and cell culture experiments yield results that can be applied to human beings only to a limited extent, tests under medical supervision are currently required from an ethical and scientific point of view. For analysis of the skin tolerability of products, application studies, so-called home-in-use tests, can be carried out. Here, the product to be tested is applied over a prolonged period in the intended application area. The inclusion and exclusion criteria of the subjects are adapted to the target group as far as possible. Before each testing, a risk analysis of the contents of the test product is carried out. All available information is systematically analysed in order to identify potential hazards and to avert risks.

3 Study objective

The objective of this study was to precisely test the tolerability of the named product **RENU 28** with regard to its tolerability and efficacy with clinical-dermatological test criteria.

Before the subjects were included, the dermatological integument was examined for health and integrity. If there is a condition requiring medical attention, the subjects are excluded. Furthermore, an information talk took place, in which the study conditions were explained to the prospective study participants, and the rights and duties of the subjects in the context of the study by the attending study nurse or the attending dermatologist. Only if the subjects did not show any pathological changes of the skin in the application area, signed the consent statement of their own free will and accord or had it signed by their legal guardians, and complied with all other inclusion and exclusion criteria, were they included in the study. During the study, the subjects might consult the attending study nurse or the attending dermatologist in case of any objective and subjective skin changes. In accordance with the schedule, dermatological examinations took place.

3.1 Primary outcomes

Assessment of skin tolerability and possibly sensitisation potential

- Application study

3.2 Secondary outcomes

Control of efficacy

- Query of the subjective impression by questionnaire
- Skin moisture (corneometry)
- Skin elasticity (cutometry)
- Skin roughness (PRIMOS replicas)

3.3 Study parameters

Monocentric clinical trial over a period of a total of four weeks.

4 Selection of subjects

The test was carried out in 20 female subjects aged 31 and over according to the inclusion and exclusion criteria. The subjects were selected from the subject database, but volunteers are also sought by means of flyers, social networks and newspaper entries.

4.1 Information of the subjects

Before the study, the participants were informed by the attending study nurse or the attending dermatologist about the course of the study. Participation in the study was voluntary. All subjects could discontinue the study at any time and without giving any reason, without any negative consequences for the subjects.

4.2 Inclusion criteria

- 31 years and older
- Female healthy volunteers
- All skin type
- Written informed consent is on hand

The subjects had to be able to communicate with the attending study nurse or the attending dermatologist and to understand and follow the requirements of this clinic-dermatological application study.

4.3 Exclusion criteria

- Severe or chronic skin inflammations
- Severe internal or chronic diseases
- Taking of drugs that may interfere with skin reactions (glucocorticoids, antiallergics, topical immune modulators, etc.)
- Application of active substance-containing products and care products 7-10 days before the start of the test
- Severe allergies or any serious side effects of cosmetic preparations ever occurred
- Sun baths or solarium visits during the study
- Known neoplastic disease
- Pregnancy and breast-feeding

4.4 Exclusion of subjects from the clinical-dermatological application study

The investigator can exclude a subject from the clinical-dermatological application study if any of the following conditions occurs:

- Revocation of the consent
- Occurrence of an undesirable event
- Deterioration of the clinical condition

The premature withdrawal of a subject is fully documented. The subjects continue to be taken care of for a reasonable time in order to control the clinical condition and occurrence of adverse events.

4.5 List of subjects

Subject №	Initials	Sex [f/m]	Age
1	BeKi	f	44
2	BlBi	f	51
3	CiMa	f	59
4	CzEv	f	39
5	DaCl	f	47
6	DeRo	f	38
7	FrBr	f	62
8	KöSi	f	59
9	KoJu	f	31
10	KrEl	f	57
11	LiEl	f	50
12	PlGi	f	55
13	RaCh	f	57
14	RoTa	f	43
15	ScAl	f	41
16	SeSt	f	46
17	StJu	f	36
18	UßUt	f	53
19	WiBr	f	64
20	ZsMa	f	53

5 Test product

5.1 Application of the investigational product

Over the entire application period, the product was applied on the face twice a day. The subjects were instructed not to use any equivalent product in the test area during the test period.

5.2 Interruptions / Discontinuation of the application

Application of the product to be tested could be discontinued at any time by the subject or, if the clinical condition so requires, upon the investigator's decision. Each discontinuation was fully documented. It was the investigator's responsibility to assess when conditions for discontinuation are given.

6 Benefit-risk weighing and precautions

There is no known risk in the use of the product. If a residual risk is detected, or if a change in the acceptance of the product is evident, the sponsor is notified immediately.

If during the study 10% or more of the test subjects experience a product-related reaction that is not acceptable for the corresponding product category, the study is terminated immediately, and the sponsor is notified accordingly.

7 Methods

In order to minimise fluctuations caused by external influences such as room temperature and relative humidity, the measurements are always carried out at the same physical ambient conditions in rested condition (≈20 °C, humidity 40–60 %).

7.1 Query of the subjective impression

By means of a final questionnaire, very disparate and non-measurable parameters (subjectively experienced effect, smell, taste, consistency, influence on the appearance of the skin, etc.) can be determined. To this end, each subject independently fills in the respective questionnaire at the query times. In case of uncertainty, the attending study nurse or the attending dermatologist can be consulted and questioned at any time.

7.2 Measurement of skin moisture (corneometry)

In corneometry, the skin moisture of the “upper layer” of the skin, the stratum corneum, is determined by a capacity measurement. The measurement is carried out with the Corneometer® CM 825 (Courage + Khazaka electronic GmbH), whose measurement principle is based on a capacitive measurement. The capacitor of the measuring head consists of two parallel plates insulated from each other, and it measures the permittivity (ε, dielectric conductivity) of a dielectric (weakly conductive or non-conductive, non-metallic substance). Water has a high relative permittivity ($\varepsilon_r = 80$). The higher the water content of the skin, the higher the permittivity of the skin.

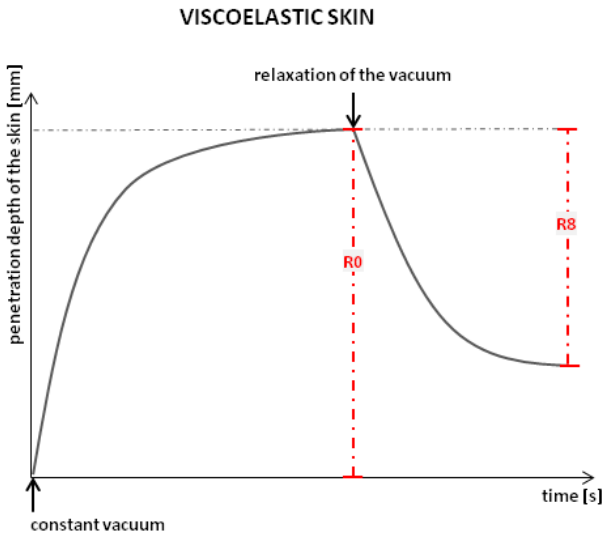
Due to the low penetration depth of the Corneometer® CM 825 in measurements (10–20 µm of the stratum corneum) and the speed of the measurement (1 second per measurement), unwanted influences of lower structures such as blood vessels and possible occlusions are avoided.

The measurement results of the Corneometer® CM 825 are indicated in relative units (arbitrary units = AU, min. = 0, max. = 130, accuracy ± 3%).

At least three measurements are carried out at distinct points in the test area per time of measurement. An untreated skin area is used as control area.

7.3 Measurement of skin elasticity / skin strength (cutometry)

The skin is viscoelastic (both firm and elastic) due to structural proteins such as collagen and elastin. The Cutometer® dual MPA 580 (Courage + Khazaka electronic GmbH) is able to determine skin elasticity and strength using the so-called suction method. Here a specific vacuum is generated in the measuring head for a defined period, and the penetration depth of the skin is detected without contact by an optical method. This optical measuring system consists of a light source, a receiver diode and two juxtaposed mirror prisms. The light intensity is influenced by the penetration depth of the skin and automatically converted into mm (accuracy ± 3%). This measuring principle allows measurement of various parameters. The paramount ones are the parameters R0 (strength of the skin, ability of the skin not to be sucked in), R2 (elasticity of the skin, ability to return to the original condition) and R8 (total restitution after relaxation of the pressure).



$$R2 = \frac{R8}{R0}$$

Figure: Illustration of viscoelasticity: R0: maximum penetration depth and thus the strength of the skin (ability of the skin not to be sucked in); R2 (elasticity of the skin, ability to return to the original condition); R8 (total restitution after relaxation of the pressure); (Information and instructions for use of the Cutometer® MPA 580, Courage + Khazaka electronic GmbH)

The lower R0, the stronger the skin. The closer R8 is to R0 (R2Max = 1), i.e. the higher R2 is, the more elastic the skin is.

At least three measurements are carried out at distinct points in the test area per time of measurement. An untreated skin area is used as control area.

7.4 Measurement of skin roughness (PRIMOS replicas)

The skin surface of every human being is characterised by an individual micro-relief consisting of fine creases and deep wrinkles. The older and more stressed the skin is, the more intense is the manifestation of the micro-relief. This structure of the skin surface can be determined by means of the optical 3D in vivo skin measurement PRIMOS (***P**hase-shift **R**apid **I**n vivo **M**easurement **O**f **S**kin*), based on the digital strip projection technique (PRIMOS compact, GFMesstechnik GmbH). When measuring skin roughness using PRIMOS replicas, silicone imprints (replicas) are created in the application area. To measure roughness, parallel strip patterns are projected onto this impression and recorded by means of a CCD recording camera. Minute height differences deflect the parallel projection strips and form a quantitative and qualitative measure of the surface to be measured. The corresponding software enables exact matching of the reference data record (data before) with a measurement data set (data after). Analysis of the measured data includes derivation of a roughness profile from the surface relief by alignment and filtering, as well as the calculation of standard roughness characteristics (DIN 4762-4768 and DIN EN ISO 4287).

The surface parameters most commonly used to evaluate skin structures are the following:

R_z	(DIN) Arithmetic mean of the individual depths of five contiguous individual measuring sections of the (digitally) filtered profile of equal length
R_{max}	Greatest individual depth Z_i of the (digitally) filtered profile occurring within the total measuring distance (l_m) during the determination of R_z (DIN)

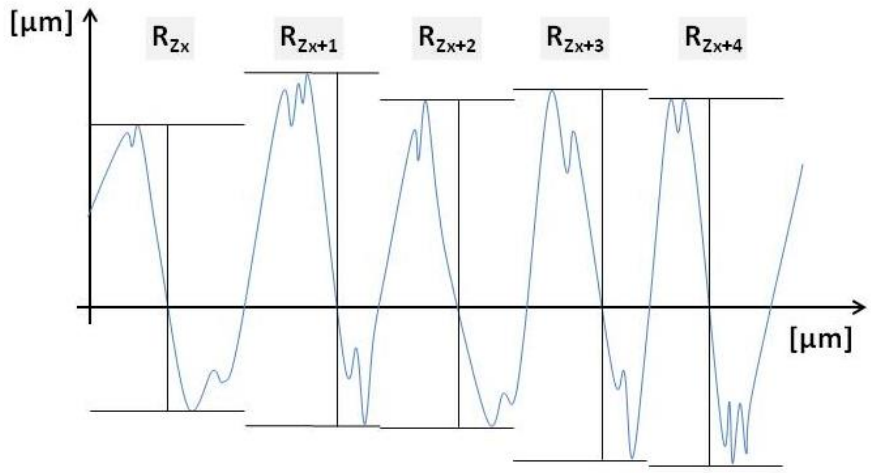


Figure: The mean roughness depth (R_{Zx}, aka. ten-point height) according to DIN 4762-4768 and DIN EN ISO 4287 is determined and compared. R_{Zx} is the sum of the height of the maximum and the minimum within a single measurement section. R_Z results from the averaging of the results of 5 individual measurement distances per replica (R_{Zx}, R_{Zx+1}, R_{Zx+2}, etc.) ("Oberflächenbeurteilung", Dipl.-Ing. Pat.-Ing. S. Jung, Institute for Machine Elements, University of Stuttgart).

For the silicone impressions (replicas), kneading silicone precision impression material (silicone plasticine, Orbis Dental) is used. The impression material is prepared immediately before use. In this case, for 12 ml of kneading silicone 2.5 cm of paste hardener (universal paste hardener for silicone impression material, Orbis Dental) are used. After a mixing time of 45 seconds, the mass is uniformly applied to the skin area without pressure, and it is cured after approx. 2 to 3 minutes. This now elastic impression is carefully detached from the skin surface and then completely cured.

One replica of the test area is created per time of measurement.

REFERENCES:

- S. Jung “Oberflächenbeurteilung”, Institute for Machine Elements, University of Stuttgart
- S. Jaspers, H. Hopermann, G. Sauermann, U. Hoppe, R. Lunderstädt, J. Ennen: “Rapid in vivo measurement of the topography of human skin by active image triangulation using a digital mircromirror device”, Skin Research & Technology, Vol. 5, Issue 3, August 1999, pp. 195-207.
- R. Lunderstädt, U. Müller: “Laserprofilometrie zur quantitativen Analyse der menschlichen Haut”, Technisches Messen tm 59 (1992), S. 448-453.

7.5 Statistics

The values of the individual measurements are averaged, and the differences of the before and after values and the relative change of the mean values are calculated.

8 Results

8.1 Dermatological examination results

The examinations were carried out according to clinical-dermatological evaluation criteria. All test persons showed healthy skin in the test area before, during and after the application study. No pathological skin lesions were found in any form. No test interruption, even less treatment by a specialist in dermatology was performed in any case. The product named was very well tolerated, and it did not lead to dermatologically relevant skin changes in any subject.

Subject №	Findings before	Findings after	Type of reaction
1	–	–	
2	–	–	
3	–	–	
4	–	–	
5	–	–	
6	–	–	
7	–	–	
8	–	–	
9	–	–	
10	–	–	
11	–	–	
12	–	–	
13	–	–	
14	–	–	
15	–	–	
16	–	–	
17	–	–	
18	–	–	
19	–	–	
20	–	–	

If skin reactions occur, the type of the reaction is assessed clinically-dermatologically, and the findings are documented using the following scale:

–	no pathological findings
1	mild reaction
2	moderate reaction
3	severe reaction

8.2 Query of the subjective impression

The question of the subjective impression was made with the help of a final questionnaire.

1. What did you particularly like about the product?

[2 x] it is quickly absorbed
[1 x] that it is effective
[1 x] the scent, the easy application
[1 x] it is quickly absorbed into the skin and there was a feeling of freshness
[1 x] after the application my skin is fresher and firmer
[1 x] that it is not sticky like some other gels
[1 x] the neutral scent, it is absorbed well and evenly
[1 x] the easy application, the quick absorption
[1 x] after the application my skin feels firmer and smooth
[1 x] it is easy to spread, very economical
[1 x] the cream is absorbed well
[1 x] the easy application
[1 x] the feeling on the skin
[1 x] the fresh, the firm skin sensation
[1 x] there was nothing I liked about this product
[4x] no statement

2. What did you not like about the product?

[1 x] the smell
[1 x] consumed too fast because very thin
[1 x] the "chlorous" smell, the sticky consistency
[1 x] if the room temperature is too high, it liquefies slightly
[1 x] the feel of tension on the skin after it has been absorbed
[1 x] the feel of tension on the skin after after application
[1 x] slips off the skin quickly making handling somewhat difficult
[1 x] the scent and the consistency: even after intensive shaking, solids and liquids components not mixed well
[1 x] does not smell good
[11 x] no statement

3. How do you assess the effectiveness of the test product on wrinkles or wrinkle reduction?

eye area	**forehead**	**around the mouth**	**at the décolleté / at the neck**
[4 x] clearly visible	[2 x] clearly visible	[2 x] clearly visible	[2 x] clearly visible
[6 x] visible	[7 x] visible	[6 x] visible	[6 x] visible
[10 x] unchanged	[11 x] unchanged	[12 x] unchanged	[12 x] unchanged

4. How do you rate the product overall?

[4 x] very good
[7 x] good
[9 x] neither nor
[0 x] bad
[0 x] very bad

5. How do you rate the skin sensation after application?

[5 x] very good
[10 x] good
[3 x] neither nor
[2 x] bad
[0 x] very bad

6. How do you rate the fragrance of the product?

[5 x] very pleasant
[3 x] pleasant
[8 x] neutral
[2 x] unpleasant
[2 x] very unpleasant

7. How do you rate the skin compatibility of the product?

[6 x] very good
[14 x] good
[0 x] neither nor
[0 x] bad
[0 x] very bad

8. How do you rate the spreadability of the product?

[5 x] very good
[14 x] good
[1 x] neither nor
[0 x] bad
[0 x] very bad

9. Please rate the following statement: „By using the test product my skin acts /is wrinkle-free.“

[5 x] I totally agree
[6 x] I agree
[7 x] neither nor
[2 x] I do not agree
[0 x] I do not agree at all

10. Please rate the following statement: „By using the test product my skin acts /is firmer.“

[4 x] I totally agree
[7 x] I agree
[8 x] neither nor
[1 x] I do not agree
[0 x] I do not agree at all

11. Please rate the following statement: „Using the test product creates a feeling of smoother skin.“

[5 x] I totally agree
[7 x] I agree
[7 x] neither nor
[1 x] I do not agree
[0 x] I do not agree at all

12. Please rate the following statement: „Using the test product gives me a fresher and younger appearance.“

[3 x] I totally agree
[4 x] I agree
[12 x] neither nor
[1 x] I do not agree
[0 x] I do not agree at all

13. Please rate the following statement: „Using the test product creates a feeling of firmer, smoother skin.“

[5 x] I totally agree
[6 x] I agree
[8 x] neither nor
[1 x] I do not agree
[0 x] I do not agree at all

14. Please rate the following statement: „Using the test product smoothes my skin.“

[5 x] I totally agree
[4 x] I agree
[10 x] neither nor
[1 x] I do not agree
[0 x] I do not agree at all

15. Please rate the following statement: „Using the test product refines my skin.“

[5 x] I totally agree
[9 x] I agree
[5 x] neither nor
[1 x] I do not agree
[0 x] I do not agree at all

16. Please rate the following statement: „My skin feels beautiful after using the test product.“

[4 x] I totally agree
[8 x] I agree
[7 x] neither nor
[1 x] I do not agree
[0 x] I do not agree at all

17. Please rate the following statement: „Using the test product gives a fresh appearance.“

[5 x] I totally agree
[6 x] I agree
[8 x] neither nor
[1 x] I do not agree
[0 x] I do not agree at all

18. Please rate the following statement: „Using the test product makes my skin radiant.“

[3 x] I totally agree
[7 x] I agree
[9 x] neither nor
[1 x] I do not agree
[0 x] I do not agree at all

19. Would you buy this product after this application test?

[11 x] yes
[9 x] no, because

[1 x] the smell is not good
[1 x] the product has not convinced me
[1 x] I couldn't see any change
[1 x] too little success
[1 x] the desired effect is not present
[1 x] I see no reduction in my wrinkles
[1 x] little benefit for me personally
[1 x] there are no changes from the time before the application, it shows no effect on my skin, the skin in the facial area even looks slightly drier than before the application
[1 x] I do not like the smell + the consistency

8.3 Corneometry / skin moisture

Per subject, three skin moisture measurements were carried out at distinct points in the **test area** at the times indicated, and the values were averaged.

Subject №	T_0 [AU]	T_{4Weeks} [AU]	Difference [AU]	Change [%]
1	28,9	33,0	4,1	14,19
2	34,9	44,3	9,4	26,93
3	39,8	57,8	18,0	45,23
4	37,3	40,5	3,2	8,58
5	38,5	44,1	5,6	14,55
6	35,1	46,3	11,2	31,91
7	31,6	33,8	2,2	6,96
8	34,7	43,2	8,5	24,50
9	36,3	38,6	2,3	6,34
10	25,0	32,2	7,2	28,80
11	41,7	50,7	9,0	21,58
12	40,8	42,5	1,7	4,17
13	26,4	35,2	8,8	33,33
14	34,5	39,3	4,8	13,91
15	33,7	38,2	4,5	13,35
16	34,7	45,8	11,1	31,99
17	31,1	57,0	25,9	83,28
18	34,1	52,8	18,7	54,84
19	42,9	45,8	2,9	6,76
20	39,3	57,0	17,7	45,04
Mean	**35,1**	**43,9**	**8,8**	**25,80**
Minimum	25,0	32,2	1,7	4,17
Maximum	42,9	57,8	25,9	83,28
Std.Dev.	4,8	8,0	6,6	19,84

Per subject, three skin moisture measurements were carried out at distinct points in the **control area** at the times indicated, and the values were averaged.

Subject №	T_0 [AU]	T_{4Weeks} [AU]	Difference [AU]	Change [%]
1	27,4	25,9	-1,5	-5,47
2	36,6	36,5	-0,1	-0,27
3	42,3	42,2	-0,1	-0,24
4	38,4	37,0	-1,4	-3,65
5	38,7	41,5	2,8	7,24
6	33,0	31,4	-1,6	-4,85
7	32,6	32,4	-0,2	-0,61
8	34,9	34,6	-0,3	-0,86
9	30,6	29,4	-1,2	-3,92
10	29,6	29,1	-0,5	-1,69
11	44,3	44,4	0,1	0,23
12	34,8	34,0	-0,8	-2,30
13	33,0	32,9	-0,1	-0,30
14	39,9	40,2	0,3	0,75
15	37,0	35,9	-1,1	-2,97
16	26,9	28,4	1,5	5,58
17	25,7	33,2	7,5	29,18
18	27,0	28,7	1,7	6,30
19	39,9	38,3	-1,6	-4,01
20	42,6	42,5	-0,1	-0,23
Mean	**34,8**	**34,9**	**0,2**	**0,90**
Minimum	25,7	25,9	-1,6	-5,47
Maximum	44,3	44,4	7,5	29,18
Std.Dev.	5,7	5,4	2,1	7,52

Measurements of the untreated control area revealed no relevant changes in the physiology of the skin due to external influences.

8.4 Cutometry / skin elasticity (R2)

Per subject, three skin elasticity measurements were carried out at distinct points in the **test area** at the times indicated, and the values were averaged.

Subject №	R2 value T_0	R2 value T_{4Weeks}	Difference	Change [%]
1	0,6412	0,8587	0,2175	33,92
2	0,7160	0,7038	-0,0122	-1,70
3	0,5984	0,6771	0,0787	13,15
4	0,5889	0,7491	0,1602	27,20
5	0,7615	0,7723	0,0108	1,42
6	0,7162	0,8995	0,1833	25,59
7	0,5432	0,7665	0,2233	41,11
8	0,7141	0,8664	0,1523	21,33
9	0,6907	0,6847	-0,0060	-0,87
10	0,8238	0,7962	-0,0276	-3,35
11	0,7521	0,7548	0,0027	0,36
12	0,7040	0,8504	0,1464	20,80
13	0,6838	0,7999	0,1161	16,98
14	0,6504	0,9047	0,2543	39,10
15	0,6800	0,9232	0,2432	35,76
16	0,6553	0,7691	0,1138	17,37
17	0,7336	0,6954	-0,0382	-5,21
18	0,6125	0,6230	0,0105	1,71
19	0,6124	0,7514	0,1390	22,70
20	0,7876	0,7669	-0,0207	-2,63
Mean	**0,6833**	**0,7807**	**0,0974**	**15,24**
Minimum	0,5432	0,6230	-0,0382	-5,21
Maximum	0,8238	0,9232	0,2543	41,11
Std.Dev.	0,0715	0,0827	0,1001	15,59

Per subject, three skin elasticity measurements were carried out at distinct points in the **control area** at the times indicated, and the values were averaged.

Subject №	R2 value T_0	R2 value T_{4Weeks}	Difference	Change [%]
1	0,6171	0,6170	-0,0001	-0,02
2	0,6607	0,7516	0,0909	13,76
3	0,5225	0,5564	0,0339	6,49
4	0,7044	0,5081	-0,1963	-27,87
5	0,8312	0,8560	0,0248	2,98
6	0,6481	0,6412	-0,0069	-1,06
7	0,6257	0,5083	-0,1174	-18,76
8	0,6782	0,7466	0,0684	10,09
9	0,7662	0,6539	-0,1123	-14,66
10	0,7013	0,7434	0,0421	6,00
11	0,7334	0,8437	0,1103	15,04
12	0,6967	0,6790	-0,0177	-2,54
13	0,6666	0,6294	-0,0372	-5,58
14	0,6666	0,6989	0,0323	4,85
15	0,7423	0,6523	-0,0900	-12,12
16	0,6346	0,6000	-0,0346	-5,45
17	0,6740	0,7037	0,0297	4,41
18	0,7122	0,7340	0,0218	3,06
19	0,5776	0,6977	0,1201	20,79
20	0,7198	0,7285	0,0087	1,21
Mean	**0,6790**	**0,6775**	**-0,0015**	**0,03**
Minimum	0,5225	0,5081	-0,1963	-27,87
Maximum	0,8312	0,8560	0,1201	20,79
Std.Dev.	0,0677	0,0940	0,0800	11,81

Measurements of the untreated control area revealed no relevant changes in the physiology of the skin due to external influences.

8.5 PRIMOS replicas / skin roughness

The skin roughness measurements were carried out using a replica at one point in the **test area** at the times indicated.

Subject №	T_0 [µm]	T_{4Weeks} [µm]	Difference [µm]	Change [%]
1	150,4	136,5	-13,9	-9,24
2	146,8	131,1	-15,7	-10,69
3	171,4	148,2	-23,2	-13,54
4	114,0	101,3	-12,7	-11,14
5	127,8	104,9	-22,9	-17,92
6	157,2	150,1	-7,1	-4,52
7	132,6	119,5	-13,1	-9,88
8	120,8	102,2	-18,6	-15,40
9	110,4	102,8	-7,6	-6,88
10	172,5	108,2	-64,3	-37,28
11	123,7	120,6	-3,1	-2,51
12	156,8	128,4	-28,4	-18,11
13	120,5	116,6	-3,9	-3,24
14	124,5	116,3	-8,2	-6,59
15	113,4	98,9	-14,5	-12,79
16	138,4	132,4	-6,0	-4,34
17	115,1	107,9	-7,2	-6,26
18	117,1	114,5	-2,6	-2,22
19	122,9	117,1	-5,8	-4,72
20	127,1	120,3	-6,8	-5,35
Mean	**133,2**	**118,9**	**-14,3**	**-10,13**
Minimum	110,4	98,9	-64,3	-37,3
Maximum	172,5	150,1	-2,6	-2,2
Std.Dev.	19,4	15,0	13,8	8,1

9 Assessment of the study results

9.1 Skin tolerability

The test product **RENU 28** was applied during a period of four weeks by 20 subjects twice a day on the face. There were no relevant skin reactions in the test area from the clinical-dermatological perspective; the product was very well tolerated. No intolerance reactions suggestive of irritation or allergic reactions (contact dermatitis) were detected.

Accordingly, from the dermatological viewpoint, there is no high potential for irritation and sensitisation for the tested product when this is used as intended.

9.2 Efficacy

The efficacy of the test product **RENU 28** with respect to skin moisture was determined by means of a Corneometer® CM 825 (Courage + Khazaka electronic GmbH). Improvement of the skin moisture by 25,80 % in the test area could be shown. The change in the skin moisture in the control area amounted to 0,90 %.

The efficacy of the test product **RENU 28** with respect to skin elasticity was determined by means of a Cutometer® MPA 580 (Courage + Khazaka electronic GmbH). Improvement of the skin elasticity in the test area by 15,24 % could be shown. The change in the skin elasticity in the control area amounted to 0,03 %.

The efficacy of the test product **RENU 28** with respect to skin roughness was determined by means of PRIMOS replicas (PRIMOS compact, GFMesstechnik GmbH). Improvement of the skin roughness by 10,13 % in the test area could be shown.

Dr. med. Werner Voss _____
Specialist in Dermatology *Signature*
Venereology, Allergology,
Phlebology and Environmental Medicine

Dr. med. Gerrit Schlippe _____
Specialist in Dermatology and Venerology *Signature*

Pia Beer _____
Biologist *Signature*

10 Addendum

10.1 Quality control, quality assurance and data protection

The quality of the study implementation and of the data recording is ensured by ISO 9001 and checked at regular intervals internally and externally by monitoring by TÜV Rheinland.

The provisions of the applicable data privacy legislature are observed. All data of the subjects are handled confidentially and are disclosed to the sponsor only in a pseudonymised version. All data are stored for ten years.

10.2 Certificates

- Skin tolerability
- Efficacy

ASEA GLOBAL LLC

1488 Pleasant View Drive
Pleasant Grove
84062 Utah
USA

Muenster, August 14th 2020

Certificate

about the cosmetic product

RENU 28

Clinical application study under dermatological control

The test product was applied during a period of four weeks by 20 subjects twice a day on the face. From the clinical-dermatological point of view, no relevant skin reactions occurred in the test area; the product was tolerated

excellently.

Neither intolerance reactions suggestive of irritation nor allergic reactions (contact dermatitis) were detected. Accordingly, from the dermatological viewpoint, there is no high potential for irritation and sensitisation for the tested product when this is used as intended.

Dr. med. Gerrit Schlippe
Specialist in Dermatology and Venereology

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Muenster, August 14th 2020

Certificate

about the cosmetic product

RENU 28

Clinical application study under dermatological and control and determination of skin moisture

The test product was applied during a period of four weeks by 20 subjects twice a day on the face. Determination of the skin moisture carried out under clinical-dermatological control showed

improvement of the skin moisture by 25,80 %

in the test area.

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