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Muenster, 13.12.2017

Expert opinion by dermatological specialists concerning a

clinical-dermatological application study

in ten healthy volunteers with single application in the eye area

Test for dermal tolerability and

determination of individual wrinkle depth

Vitayes Instant Ageback Lifting Cream

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Table of contents

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	**Vitayes Instant Ageback Lifting Cream**
Product type	Lifting cream
Study design	Single-centre
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 - Individual wrinkle depth (PRIMOS handheld)
Number of subjects	Ten
Test period	Eight hours
Times of measurement	Individual wrinkle depth: T_0, T_{5min} und T_{8h}
Test area	Eye area
Frequency of application	Single application
Inclusion criteria	- 35 years and older - Female healthy volunteers - Skin type: any - With crow's feet (small wrinkles in the eye area) - 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	T_0	T_{5min}	T_{8h}
Information of the subjects	✔		
Informed Consent Form Sheet	✔		
Medical history	✔		
Dermatological examination	✔		✔
Compliance with the inclusion and exclusion criteria	✔	✔	✔
Measurement of individual wrinkle depth (PRIMOS handheld)	✔	✔	✔

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 is to precisely test the tolerability of the named product **Vitayes Instant Ageback Lifting Cream** with regard to its tolerability and efficacy with clinical-dermatological test criteria.

Before the subjects are included, the dermatological integument is examined for health and integrity. If there is a condition requiring medical attention, the subjects are excluded. Furthermore, an information talk takes place, in which the study conditions are 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 do not show any pathological changes of the skin in the application area, sign the consent statement of their own free will and accord or have it signed by their legal guardians, and fulfil all other inclusion and exclusion criteria, are they included in the study. During the study, the subjects

may 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 will take place.

3.1 Primary outcomes

Assessment of skin tolerability

- Application study

3.2 Secondary outcomes

Control of efficacy

- Individual wrinkle depth (PRIMOS handheld)

3.3 Study parameters

Monocentric non-interventional study with single application and examinations after five minutes and eight hours.

4 Selection of subjects

The test is carried out in ten female subjects aged 35 and over according to the inclusion and exclusion criteria. The subjects are 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 are informed by the attending study nurse or the attending dermatologist about the course of the study. Participation in the study is voluntary. All subjects can discontinue the study at any time and without giving any reason, without any negative consequences for the subjects.

4.2 Inclusion criteria

- 35 years and older
- Female healthy volunteers
- Skin type: any
- With crow's feet (small wrinkles in the eye area)
- Written informed consent is on hand

The subjects must 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	EiUt	f	50
2	HaHe	f	57
3	HeSt	f	37
4	HeAn	f	44
5	KaAr	f	55
6	KoSa	f	56
7	KrBe	f	39
8	PuDa	f	42
9	SoAn	f	50
10	WiCa	f	51

5 Test product

5.1 Application of the investigational product

The product is applied once to the eye area following the instructions for use. The subjects are 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 can be discontinued at any time by the subject or, if the clinical condition so requires, upon the investigator's decision. Each discontinuation is fully documented. It is 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

7.1 Measurement of the individual wrinkle depth (PRIMOS handheld)

In every human being, permanent wrinkles develop around the eyes over the course of his or her life. Due to the characteristic radiating structure, these wrinkles are colloquially also referred to as crow's feet. The older and more stressed the skin is, the more intense these wrinkles are. The depth of the wrinkles can be determined by means of the optical 3D in vivo skin measurement PRIMOS (***P**hase-shift **R**apid **I**n vivo **M**eas-urement **O**f **S**kin*), based on the digital strip projection technique (PRIMOS compact, GFMesstechnik GmbH). To measure wrinkle depth, parallel strip patterns are projected onto the skin and recorded by means of a CCD recording camera. Minute height differences deflect the parallel projection strips and thus form a quantitative and qualitative measure of the skin surface to be measured. Due to its overlay function, the corresponding software enables exact retrieval of the area, making direct comparison of the reference data set (data before) with a measurement data set (data after) possible. To determine wrinkle depth, the profile of a cutting line is selected, and the absolute depth of the wrinkle is measured.

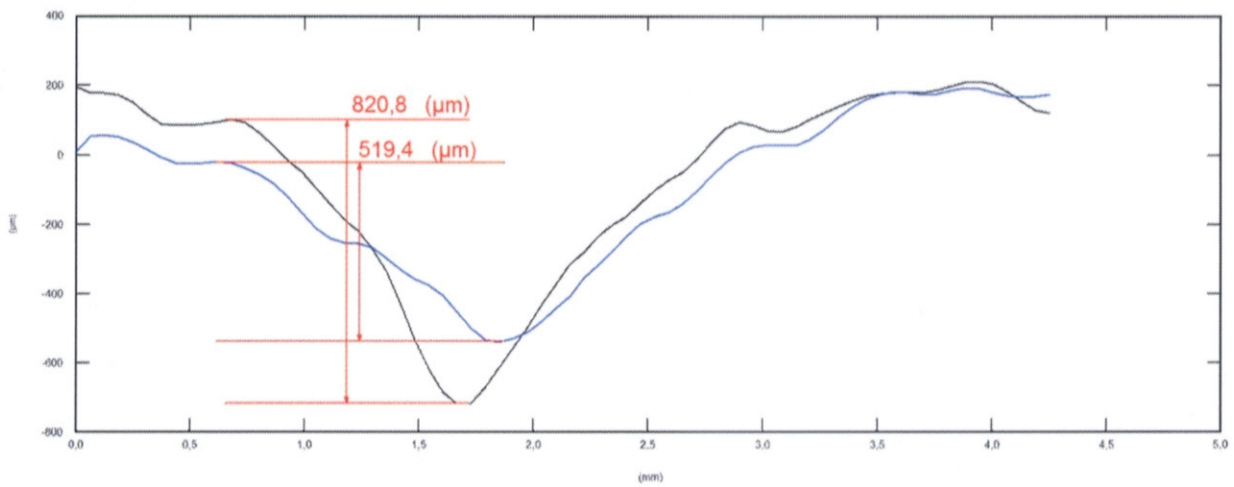

Figure: Graphical representation of individual wrinkle depth before (black line) and after (blue line) the application period. (Manual Optical 3D skin measuring device PRIMOS compact).

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

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- 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.

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	–	–	

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 PRIMOS handheld / individual wrinkle depth

The measurements of individual wrinkle depth were carried out at one point in the **test area** at the times indicated.

Subject №	T_0 [µm]	T_{5min} [µm]	Difference [µm]	Change [%]
1	263,0	136,9	-126,1	-47,95
2	363,8	216,0	-147,8	-40,63
3	256,0	104,3	-151,7	-59,26
4	518,1	100,6	-417,5	-80,58
5	147,0	48,5	-98,5	-67,01
6	298,0	99,6	-198,4	-66,58
7	322,5	57,2	-265,3	-82,26
8	142,4	48,5	-93,9	-65,94
9	371,5	183,2	-188,3	-50,69
10	266,1	116,5	-149,6	-56,22
Mean	**294,8**	**111,1**	**-183,7**	**-61,7**
Minimum	142,4	48,5	-417,5	-82,26
Maximum	518,1	216,0	-93,9	-40,63
Std.Dev.	110,4	55,7	96,4	13,50

Subject №	T_0 [µm]	T_{8h} [µm]	Difference [µm]	Change [%]
1	263,0	220,9	-42,1	-16,01
2	363,8	249,0	-114,8	-31,56
3	256,0	134,2	-121,8	-47,58
4	518,1	177,4	-340,7	-65,76
5	147,0	91,0	-56,0	-38,10
6	298,0	187,9	-110,1	-36,95
7	322,5	243,7	-78,8	-24,43
8	142,4	136,0	-6,4	-4,49
9	371,5	215,5	-156,0	-41,99
10	266,1	262,0	-4,1	-1,54
Mean	**294,8**	**191,8**	**-103,1**	**-30,8**
Minimum	142,4	91,0	-340,7	-65,76
Maximum	518,1	262,0	-4,1	-1,54
Std.Dev.	110,4	56,9	97,5	19,80

9 Assessment of the study results

9.1 Skin tolerability

The test product **Vitayes Instant Ageback Lifting Cream** was applied once by ten subjects onto the eye area. 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 for the tested product when this is used as intended

9.2 Efficacy

The efficacy of the test product **Vitayes Instant Ageback Lifting Cream** with respect to individual wrinkle depth was determined by means of optical 3D in vivo skin measurement (PRIMOS compact, GFMesstechnik GmbH). Improvement of individual wrinkle depth by 61,7 % after 5 minutes and by 30,8 % after 8 hour) in the test area could be shown.

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

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Muenster, 13.12.2017

Certificate

about the cosmetic product

Vitayes Instant Ageback Lifting Cream

Clinical application study under dermatological control

The test product was once by ten subjects onto the eye area. From the clinical-dermatological point of view, no relevant skin reactions occurred in the test area; the product was tolerated

very well.

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 for the tested product when this is used as intended.

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Muenster, 13.12.2017

Certificate

about the cosmetic product

Vitayes Instant Ageback Lifting Cream

Clinical application study under dermatological control and determination individual wrinkle depth

The test product was applied once by ten subjects onto the eye area. Determination of the individual wrinkle depth carried out under clinical-dermatological control showed an

improvement of individual wrinkle depth

by 61,7 % after five minutes and by 30,8 % after eight hours

in the test area.

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