Sponsor

Study number 1911266653

Petra GmbH
Schumannstraße 27
60325 Frankfurt am Main
GERMANY

Muenster, 18.02.2020

Expert opinion by dermatological specialists concerning a

clinical-dermatological application study

in 20 volunteers with application at least three times a week to the eye area for a period of four weeks

Test for dermal tolerability

Vitayes Instant Ageback

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1 General information

Title

Clinical application study under dermatological control

Testing body

Dermatest GmbH
Engelstr. 37
D-48143 Münster

Specialists in dermatology

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Specialist in Dermatology
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Study coordinator

PhD Tanja Emmler
Biologist

1.1 Synopsis

Study title	Clinical application study under control
Test product	**Vitayes Instant Ageback**
Product type	Eyecream
Study design	Single-centre
Testing body	Dermatest GmbH Engelstr. 37 D-48143 Münster
Expert opinion version and date	V1 18.02.2020
Test period	December 2019/ January 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.
Number of subjects	20
Application period	Four weeks
Test area	Eye area
Frequency of application	At least three times a week
Inclusion criteria	- 18 years and older - Female healthy volunteers - Skin type: any - 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	✔	✔

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 **Vitayes Instant Ageback** with regard to its tolerability with clinical-dermatological test criteria and.

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 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 35 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

- 35 years and older
- Female healthy volunteers
- Skin type: any
- 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	AbMa	f	44
2	ArDo	f	38
3	BaRo	f	54
4	BeAn	f	44
5	BöAn	f	59
6	DeMe	f	36
7	EhJa	f	42
8	EiUt	f	52
9	FeCh	f	50
10	FrHe	f	40
11	GeAn	f	53
12	HeDo	f	58
13	HöGe	f	39
14	HuBe	f	41
15	KaCl	f	44
16	KnDo	f	44
17	NeEl	f	60
18	NeNe	f	69
19	NiMa	f	51
20	PoEr	f	79

5 Test product

5.1 Application of the investigational product

Over the entire application period, the product was applied to the eye area at least three times a week. 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 Results

7.1 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 Assessment of the study results

8.1 Skin tolerability

The test product **Vitayes Instant Ageback** was applied during a period of four weeks by 20 subjects at least three times a week to 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 and sensitisation for the tested product when this is used as intended.

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Venereology, Allergology,
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Signature

Dr. med. Gerrit Schlippe
Specialist in Dermatology and Venerology

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Signature

PhD Tanja Emmler
Biologist

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Signature

9 Addendum

9.1 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.

9.2 Certificates

- Skin tolerability

Company name

Petra GmbH
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60325 Frankfurt am Main
GERMANY

Muenster, 18.02.2020

Certificate

about the cosmetic product

Vitayes Instant Ageback

Clinical application study under dermatological control

The test product was applied during a period of four weeks by 20 subjects at least three times a week to the eye area. 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.

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