CLINICAL TEST AIMED AT EVALUATING THE TOLERABILITY AND SAFETY OF A COSMETIC PRODUCT USED IN THE PERIOCULAR AREA

TORSTONE SA

Le Visage MASQUE RÉPARATEUR N°02 (01086.5)

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STUDY DESIGN

Title

Clinical test aimed at evaluating the tolerability and safety of a cosmetic product used in the periocular area.

Aim of the study

The test allows to assess whether the tested cosmetic product is tolerated and safe in the eye area. Product safety is tested through the analysis of adverse effects that may occur during the product use (lacrimation, redness, itching, burning).

Eye is a very delicate and vulnerable organ. Many anatomical elements naturally protect it: it is hollow in the eye socket, below frontal bones, and it has a great elasticity to lessen bumps and blunt traumas.
Eyelids represent a defence system too, because they protect the external eye area from foreign bodies and all irritating substances present in the environment. Furthermore, their continuous blinking allows to spread the fluids produced by lacrimal and conjunctival glands on the cornea, with lubricating, bactericidal and detergent functions able to maintain corneal transparency.
Conjunctiva is a mucous membrane covering the back surface of the eyelid and anterior portion of the eyeball: due to its lymphatic component, it is considered a lymph node covered by epithelium, able to react to different types of stimuli. Because of the extreme eye sensitivity to external elements and the stressful conditions which not infrequently is exposed (contact lenses, make-up, sun exposure,...), it is important to pay close attention to this organ reactions, as they may be a symptom of serious damage.
During the study period, the experimenter asks the volunteers about the onset of symptoms such as lacrimation, burning, itching, redness, irritating sensations that occurred after product application. Any adverse reactions towards the product lead to treatment interruption and specific controls, aimed to verify that no eye damages occurred (keratitis, blepharitis, conjunctivitis, chemosis). Here below the main changes that may occur to the eye mucosa:

- **Blepharitis** is an eyelid margin inflammation characterized by redness, swelling, crusts, scales and ulcers. There are two types of blepharitis: ulcerative if it is caused by bacterial infection (stapphylococcum, almost always) and non-ulcerative (squamous or seborrheic) with unknown causes, usually associated to skin and scalp seborrhoea (dandruff) or of allergic nature. The first manifestation is foreign body sensation, together with lacrimation and light sensitivity. Moreover, it is associated to itching, redness and swelling of eyelid margins.
- **Conjunctivitis** is the most common form of ocular inflammation. The most frequent symptoms are redness, strong lacrimation, mucous or mucopurulent secretion, eyelid swelling, photosensitivity and foreign body sensation. Sometimes conjunctivitis is caused by allergy to substances such as pollen, dust, cosmetics, food, pets such as cat, etc. In addition to the common symptoms, allergic conjunctivitis can be recognized by strong itching and conjunctiva swelling (chemosis), which sometimes is so evident and strong to frighten the patient or his/her family especially due to its sudden onset.
- **Cheratitis** is a cornea inflammation, it causes a lesion of the superficial layer of the cornea with pain, lacrimation, photosensitivity and foreign body sensation.

Tested Product

Information provided by the Customer

- Product name:

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- The tested cosmetic product complies with REGULATION (EC) No 1223/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 30th November 2009 on cosmetic products (recast) (Text with EEA relevance) and its annexes.
- Qualitative INCI formula
  Filed

Evaluated parameters

- Product tolerability
- Mucosa and skin alterations

Ethical requirements

The study was carried out in compliance with the following ethical requirements:

- All subjects participating in the study are healthy volunteers at least 18 years old.
- All subjects participating in the study are selected under dermatologist's supervision, according to inclusion/non-inclusion criteria (see respective paragraph "Inclusion criteria" and "Non- inclusion Criteria").
- Volunteer participation in the study is totally free.
- All subjects participating in the study are informed of the aim and nature of the study.
- All subjects participating in the study are informed of the potential risks involved.
- All subjects participating in the study signed their informed consent form at the beginning of the study.
- Before volunteers were exposed to the product to be tested, all relevant safety information about the product itself and each ingredient were collected and evaluated.
- All the study procedures are carried out in accordance with the ethical principles for medical research (Ethical Principles for Medical Research Involving Human Subjects, adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964 and successive amendments)
- All necessary precautions were taken in order to avoid any adverse skin reactions.
- If any unexpected/adverse skin reactions occur, the dermatologist evaluates the severity of the reaction (reporting it on the data collecting sheet) and, if necessary, proceeds with the appropriate therapy.

All the study procedures are carried out in accordance with the ethical principles for medical research (Ethical Principles for Medical Research Involving Human Subjects, adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964 and successive amendments)
- All necessary precautions were taken in order to avoid any adverse skin reactions.
- If any unexpected/adverse skin reactions occur, the dermatologist evaluates the severity of the reaction (reporting it on the data collecting sheet) and, if necessary, proceeds with the appropriate therapy.

Subjects selection

Volunteers recruitment

20 volunteers were recruited in order to take part in the test, in accordance with the following inclusion and non-inclusion criteria:

Inclusion criteria

- ☑ Caucasian female subjects
- ☑ Age over 18 years
- ☑ Healthy subjects
- ☑ No eye problems (red eyes, lacrimation, foreign body sensation) that could affect ophthalmologist evaluation
- ☑ Commitment not to use other similar products during the study period
- ☑ Subjects informed about test purposes

Non-inclusion criteria

- ✘ Subjects who do not fit the inclusion criteria
- ✘ Pregnant or breastfeeding women
- ✘ Subjects with dermatological problems in the test area
- ✘ Subjects under pharmacological treatment local/systemic that could interfere with the execution of the test
- ✘ Positive anamnesis for atopy (if this condition interferes with the execution of the test)

Withdrawal criteria

The volunteers are withdrawn from the study if

- ✘ They do not follow the conditions required on the Study Information Sheet they receive after recruitment
- ✘ They suffer any illness, accidents or develop any conditions during the study which could affect the outcome of the study
- ✘ They no longer wish to participate in the study.

Product application method

The product (a masque) has been applied for a month, according to the customer's specifications: “apply on face and eye contour, with movements from the inside to the outside. Leave for 10 minutes and then remove excess with a cotton disk. Use 2 times a week.”

Test execution

Subjects’ suitability to take part in the study is evaluated during the first visit, when they receive the product and all the directions about the way of use (daily). Each enrolled subject is instructed to immediately stop the treatment if any unwanted side effects occur and to immediately inform (also by telephone) the specialist about any discomforts that may be attributed to the use of the product itself. Then, the volunteer comes back to our centre after 14 and 28 days of product use, and the specialist evaluates, with volunteer’s collaboration, if the product is tolerated and safe for skin and eye mucosa.

Ophthalmologic study evaluations

At each monitored time the experimenter evaluate clinically or with the collaboration of the subject the following parameters:

- Lacrimation
- Vasodilatation (redness, hyperemia)
- Foreign body sensation
- Photophobia
- Itching and/or burning
- Periocular swelling
- Other

The occurrence of these disorders could mean that the product in question is cause of serious alterations of the ocular mucosa such as: conjunctivitis, keratitis, blepharitis, chemosis, oedema and redness on the external eye area. The intensity of each recorded reaction is classified according to a 5 points score:

- absent
  very mild
- mild
- moderate
- severe

and described for its duration, frequency and extension.
The onset of alterations to palpebral skin or ocular mucosa is assessed according to the scores shown in Tables 1-2.

Global evaluation of the product
The product is ultimately classified as:

o **Ophthalmologically tested and safe** for its use if none or at most 15% of subjects show a discomfort, related to the application of the product which causes their drop out from the clinical study, in the absence of alteration to conjunctival mucosa and / or eyelid skin.

o **not tolerated** during its use, if more than 15% of the subjects show a discomfort related to the application of the product which causes their drop out from the clinical study.

o **not safe** for its use if one or more subjects show an alteration to conjunctival mucosa and / or eyelid skin.

Table 1

Eyelid skin alterations	
No alteration	**0**
Slight alteration	**1**
Moderate alteration	**2**
Evident alteration	**3**

Table 2

Conjunctival mucosa alterations	
No alteration	**0**
Slight alteration	**1**
Moderate alteration	**2**
Evident alteration	**3**

Monitored checks

Volunteers use the product to be tested for 28 days and the evaluations are performed by the experimenter during the first visit (T0) and after 14 (T14) and 28 (T28) days of treatment.

Report change record

The table below reports all the changes made to the document since its initial approval.

Rev. no	Date	Description
0	17/09/19	First release

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DEMOGRAPHY

n°	Vol id	Age	Sex	Contact lens wearers	Eyeglass wearers	Sensitive eyes	Sensitive skin	Eyes Colour
1	P1492V	57	F	NO	YES	YES	YES	brown
2	P2591C	55	F	NO	YES	NO	YES	blue
3	S3831A	64	F	NO	YES	YES	YES	brown
4	G0138O	66	F	NO	NO	YES	YES	brown
5	T3581R	48	F	NO	YES	YES	YES	brown
6	D2925G	55	F	NO	NO	NO	YES	brown
7	V1341A	51	F	NO	NO	YES	YES	brown
8	A3893A	58	F	NO	YES	NO	NO	blue
9	A2458S	52	F	NO	NO	YES	YES	blue
10	D0097E	56	F	NO	YES	NO	NO	brown
11	M0196D	63	F	NO	NO	NO	NO	brown
12	Z3554A	57	F	NO	YES	YES	YES	brown
13	A4087L	54	F	NO	YES	NO	YES	brown
14	B0039C	57	F	NO	YES	YES	YES	brown
15	G0656C	52	F	NO	NO	YES	YES	brown
16	A1462R	72	F	NO	YES	NO	NO	brown
17	B0015R	64	F	NO	YES	YES	YES	blue
18	V2130R	53	F	NO	NO	NO	NO	brown
19	G0165F	61	F	NO	NO	YES	YES	brown
20	R1784M	59	F	NO	NO	NO	NO	brown

RESULTS

TABLE 1

	Volunteer no	Lacrimation	Vasodilatation	Foreign body sensation	Photophobia	Itching	Stinging eyes	Periocular swelling	Other
	T0								
1	P1492V	0	0	0	0	0	0	0	0
2	P2591C	0	0	0	0	0	0	0	0
3	S3831A	0	0	0	0	0	0	0	0
4	G0138O	0	0	0	0	0	0	0	0
5	T3581R	0	0	0	0	0	0	0	0
6	D2925G	0	0	0	0	0	0	0	0
7	V1341A	0	0	0	0	0	0	0	0
8	A3893A	0	0	0	0	0	0	0	0
9	A2458S	0	0	0	0	0	0	0	0
10	D0097E	0	0	0	0	0	0	0	0
11	M0196D	0	0	0	0	0	0	0	0
12	Z3554A	0	0	0	0	0	0	0	0
13	A4087L	0	0	0	0	0	0	0	0
14	B0039C	0	0	0	0	0	0	0	0
15	G0656C	0	0	0	0	0	0	0	0
16	A1462R	0	0	0	0	0	0	0	0
17	B0015R	0	0	0	0	0	0	0	0
18	V2130R	0	0	0	0	0	0	0	0
19	G0165F	0	0	0	0	0	0	0	0
20	R1784M	0	0	0	0	0	0	0	0

Table 1 summarizes the ophthalmological evaluation at T0 time

TABLE 2

Table 2 summarizes the ophthalmological evaluation at T14 time (after 14 days of product use)

	Volunteer no	Lacrimation	Vasodilatation	Foreign body sensation	Photophobia	Itching	Stinging eyes	Periocular swelling	Other
	T14								
1	P1492V	0	0	0	0	0	0	0	0
2	P2591C	0	0	0	0	0	0	0	0
3	S3831A	0	0	0	0	0	0	0	0
4	G0138O	0	0	0	0	0	0	0	0
5	T3581R	0	0	0	0	0	0	0	0
6	D2925G	0	0	0	0	0	0	0	0
7	V1341A	0	0	0	0	0	0	0	0
8	A3893A	0	0	0	0	0	0	0	0
9	A2458S	0	0	0	0	0	0	0	0
10	D0097E	0	0	0	0	0	0	0	0
11	M0196D	0	0	0	0	0	0	0	0
12	Z3554A	0	0	0	0	0	0	0	0
13	A4087L	0	0	0	0	0	0	0	0
14	B0039C	0	0	0	0	0	0	0	0
15	G0656C	0	0	0	0	0	0	0	0
16	A1462R	0	0	0	0	0	0	0	0
17	B0015R	0	0	0	0	0	0	0	0
18	V2130R	0	0	0	0	0	0	0	0
19	G0165F	0	0	0	0	0	0	0	0
20	R1784M	0	0	0	0	0	0	0	0

TABELLA 3 / TABLE 3

	Volunteer no T28	Lacrimation	Vasodilatation	Foreign body sensation	Photophobia	Itching	Stinging eyes	Periocular swelling	Other
1	P1492V	0	0	0	0	0	0	0	0
2	P2591C	0	0	0	0	0	0	0	0
3	S3831A	0	0	0	0	0	0	0	0
4	G0138O	0	0	0	0	0	0	0	0
5	T3581R	0	0	0	0	0	0	0	0
6	D2925G	0	0	0	0	0	0	0	0
7	V1341A	0	0	0	0	0	0	0	0
8	A3893A	0	0	0	0	0	0	0	0
9	A2458S	0	0	0	0	0	0	0	0
10	D0097E	0	0	0	0	0	0	0	0
11	M0196D	0	0	0	0	0	0	0	0
12	Z3554A	0	0	0	0	0	0	0	0
13	A4087L	0	0	0	0	0	0	0	0
14	B0039C	0	0	0	0	0	0	0	0
15	G0656C	0	0	0	0	0	0	0	0
16	A1462R	0	0	0	0	0	0	0	0
17	B0015R	0	0	0	0	0	0	0	0
18	V2130R	0	0	0	0	0	0	0	0
19	G0165F	0	0	0	0	0	0	0	0
20	R1784M	0	0	0	0	0	0	0	0

Table 3 summarizes the ophthalmological evaluation at T28 time (after 28 days of product use)

Table 4 and 5 summarize respectively the alterations of eyelid skin and conjunctival mucosa.

TABLE 4

ALTERATIONS OF EYELID

Volunteer no	T0	T14	T28
P1492V	0	0	0
P2591C	0	0	0
S3831A	0	0	0
G0138O	0	0	0
T3581R	0	0	0
D2925G	0	0	0
V1341A	0	0	0
A3893A	0	0	0
A2458S	0	0	0
D0097E	0	0	0
M0196D	0	0	0
Z3554A	0	0	0
A4087L	0	0	0
B0039C	0	0	0
G0656C	0	0	0
A1462R	0	0	0
B0015R	0	0	0
V2130R	0	0	0
G0165F	0	0	0
R1784M	0	0	0

TABLE 5

ALTERATIONS OF CONJUNCTIVAL MUCOSA

Volunteer no	T0	T14	T28
P1492V	0	0	0
P2591C	0	0	0
S3831A	0	0	0
G0138O	0	0	0
T3581R	0	0	0
D2925G	0	0	0
V1341A	0	0	0
A3893A	0	0	0
A2458S	0	0	0
D0097E	0	0	0
M0196D	0	0	0
Z3554A	0	0	0
A4087L	0	0	0
B0039C	0	0	0
G0656C	0	0	0
A1462R	0	0	0
B0015R	0	0	0
V2130R	0	0	0
G0165F	0	0	0
R1784M	0	0	0

CONCLUSIONS

According to the previous results, we can conclude that:

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HAS BEEN OPHTALMOLOGICALLY TESTED. IT IS SAFE TO BE USED IN THE PERIOCULAR AREA

Indeed, no enrolled volunteers showed any significant alterations on their eyelid skin or eye mucosa during the study period.

Experimenter

Dr. Francesco Sandolo

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Data analysis and Report

Dr. Carmen Palumbo

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