ABICH S.r.l.
Biological and Chemical Analysis
Toxicology, Research and Services

Final Report

EVALUATION OF THE EFFECTIVENESS OF A COSMETIC PRODUCT COADJUVANT IN THE TREATMENT OF ACNE

(*IN VIVO* LONG TERM TEST)

STUDIO N° / *STUDY N°*	**KH585/14-01**
COMMITTENTE / *SPONSOR*	**LABORATOIRE DR PAUL ET KARIN HERZOG SA Route de Taillepied, 1 1095 Lutry - SWITZERLAND**
CAMPIONE / *SAMPLE*	**Oxygen Face Normalizing Cream – Oily and Combination Skin Batch: 051 0816**
DATA RAPPORTO / *REPORT DATE*	**02/04/2015**
RELAZIONE N° / *REPORT N°*	**REL/0635/2015/CLI/SAB**

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Dr.ssa Giulia Caccia – Biologa / Biologist
Dr.ssa Erika Giudice – CTF

AUTENTICITA' DEI RISULTATI
AUTHENTICITY OF RESULTS

Dichiaro che lo studio oggetto del presente rapporto è stato condotto sotto la mia responsabilità, in accordo al protocollo sperimentale e al piano della qualità di Abich s.r.l.. Dichiaro inoltre che, dove applicabile, le procedure utilizzate sono in accordo con i principi delle GCP (Good Clinical Practice).
Tutte le osservazioni e i dati registrati durante questo studio sono stati inclusi nel presente dossier.
Certifico la rilettura di questo rapporto e confermo il mio consenso circa il suo contenuto.

I hereby declare that the study concerned by this report was carried out under my responsibility, according to the experimental protocol and the quality plan of Abich S.r.l. I also state that, where applicable, all procedures were compliant with the principles of Good Clinical Practice.
All relevant observations and data recorded during the test are reported in this study report.
I certify the re-reading of this report and I do agree with its content.

Il Direttore dello studio / The Study Director

Dott. Samuele Burastero _____

INDEX

1. SUMMARY 5
2. DISCLAIMER 5
3. REGULATORY ASPECTS 5
4. TEST SUBSTANCE 5
5. PANEL RECRUITMENT 6
6. ARCHIVING 7
7. INSTRUMENTATION AND MATERIALS 8
8. EXPERIMENTAL DESIGN 8
9. ASSAY METHODOLOGY 8
10. TOLERABILITY 8
11. REPRESENTATIVE IMAGES OF THE TREATED AREAS 9
12. QUESTIONNAIRE CONCERNING A SENSORIAL / PSICHORHEOLOGICAL ASSESSMENT RELATIVE TO THE TESTED PRODUCT 10
13. DISCUSSION AND CONCLUSIONS 12
14. BIBLIOGRAPHY 13

1. SUMMARY

On behalf of **Laboratoire dr Paul et Karin Herzog SA**, on the test substance **OXYGEN FACE NORMALIZING CREAM – OILY AND COMBINATION SKIN BATCH: 051 0816** an *in vivo* test on 20 healthy volunteers was performed in order to evaluate its efficacy as coadjuvant in the treatment of acne. For this purpose, were performed pictures of the volunteers' cheeks taken with a digital reflex camera equipped with macro objective. The pictures were taken before and 60 days after the bi-daily application of the product (T0 and T60).
Moreover at the end of this period the participants to the study, filled in a questionnaire relative to a subjective evaluation of the cosmetic pleasantness, of the organoleptic characteristics, of the perception of efficacy and to a general satisfaction of the product and its performances (see annex).

The study was performed at the Abich Cosmetic Lab. in Via Bruno Buozzi, 4 – 20090 – Vimodrone (Milan), Italy.
The experimentation started the 14th October, 2014 and ended the 14th January, 2015.

2. DISCLAIMER

According to COLIPA guidelines, the test was performed with the assumption that the Sponsor under its responsibility provided to the personnel of Abich Cosmetic Lab. truthful information on any ingredient of the test product endowed with potential toxicological relevance.
On the basis of such information, a general assessment of the toxicological information concerning the product was preliminarily carried out and ethical implications as to its use during the present study have been considered.

3. REGULATORY ASPECTS

This study has been carried out in compliance with the most recent recommendations of the World Medical Association Declaration of Helsinki- ethical principles for medical research involving human subjects (Helsinki Declaration 64th WMA General Assembly, Fortaleza, Brazil, October 2013) and according to the Colipa Guidelines for the evaluation of the efficacy of cosmetic products.

4. TEST SUBSTANCE

The test substance consists of a white emulsion.

Name:	**OXYGEN FACE NORMALIZING CREAM – OILY AND COMBINATION SKIN**
Batch/ Formule code:	051 0816
Sample Code Abich:	6656/14-01
INCI composition:	see annex
Pao / Expiration date:	Pao 5M
Storage conditions:	room temperature

The characterization of the test substance is under responsibility of the Sponsor.

5. PANEL RECRUITMENT

a) Ethical aspects

In order to comply with the ethical requirements of studies in humans, the following criteria were applied:
- Volunteers were selected according to defined inclusion and exclusion criteria;
- All volunteers were informed regarding the aim of the study and freely signed an informed consent prior to study start;
- Before any volunteer was exposed to the product, the Sponsor was asked to provide its safety profile according to available toxicological information (see disclaimer, above);
- All necessary precautions were taken to avoid excessive skin reactions or any other negative effects on the subject's health;
- Each volunteer was invited to communicate the possible decision to interrupt his/her participation in the study with at least 48 hours notice.

Table 1: Volunteers participant to the study.

N°VOLUNTEER	CODE	AGE	SEX
1	STTR104	25	F
2	GIAM543	18	F
3	SIBI496	20	F
4	ANVI256	28	F
5	FIAI416	19	M
6	VABA502	21	F
7	ALCA511	22	F
8	ALFO132	22	F
9	LOSE516	23	F
10	GITO475	22	F
11	ANGA401	18	M
12	MADI532	39	M
13	CLBE483	40	F
14	FRMI537	19	M
15	LUCR113	28	F
16	GICA358	27	F
17	SOVA404	21	F
18	MAMU403	41	F
19	LUMO31	29	M
20	SIMA160	23	M

b) Characteristics of the panel

The study was performed on 20 male and female volunteers, aged from 18 to 50 , who were identified from the database of volunteers of the Abich Test Centre, and who were evaluated as appropriate for participation in the study and not suffering from diseases to the skin areas to treat.
Before the beginning of the study each volunteer has read and signed an informative form (informed consent form, C.I.). Each volunteers has had the opportunity to ask any kind of questions regarding the study to which was given an exhaustive answer. The volunteer was explained the aim of the test, the procedure and the possible risks related.
Only after signature of the informed consent the participation in the study was permitted.
Only volunteers in good general health conditions were included in the study.

c) Inclusion criteria

The following criteria of inclusion were applied:

- Female and male subjects age between18 and 50 years;
- Good conditions of general health;
- Capacity to understand the characteristics of the study, the requested observation times, the tasks implied and the possible risks, and all other information included in the informed consent (in particular, the ability to supply in full awareness the informed consent form).

d) Exclusion criteria

The following criteria of exclusion were applied:

- Pregnancy or nursing condition.
- Medication (local and/or systemic) which might interfere with the test evaluation.
- Subjects with signs of irritation at the application site.
- Subjects with dermatological problems which that might interfere with the study.
- Simultaneous participation to other studies, which that might interfere with the test evaluation.
- Subjects otherwise evaluated as not suitable by the Doctor.

e) Criteria for study withdrawal

After study start, the following withdrawal criteria were applied:

- volunteers who did not longer wish to participate in the study;
- volunteers who during the study suffered any illness or accident or developed any condition which could affect the outcome of the study;
- volunteers who did not follow the conditions as described in the Study Protocol.

6. ARCHIVING

The clinical study protocol, the corresponding raw data and the final report are kept in the archives of Abich Testing Centre, in Via Buozzi, 4, 20090-Vimodrone (MI), both in electronic format and in reduced paper format for a period of 10 years from the issue of the final report. The control samples of the test substance and eventual specific reference material will be kept at last for 3 month, or more, if requested by the Sponsor.

7. INSTRUMENTATION AND MATERIALS

The following instrumentations and materials were used:

- **Canon EOS350D MACRO®:** digital reflex camera equipped with macro objective (Canon Italia,Milano).

8. EXPERIMENTAL DESIGN

Structure of the study
The study has been executed with an open observational modality.

Aim of the study
This study was aimed to evaluate the efficacy of the product under examination as coadjuvant in the treatment of acne.

Environmental conditions
The study was carried out under standard environmental conditions for each reading time, monitoring and maintaining constant temperature and humidity.

Method of application
Each subject applied the test product **OXYGEN FACE NORMALIZING CREAM – OILY AND COMBINATION SKIN BATCH: 051 0816** twice a day for a period of 60 days on the entire face.
The volunteers was asked to come in laboratory with clean face skin, without any other cosmetic product or any make-up which could interfere with the measurements.

Evaluated skin areas
The pictures were taken at the level of left and right cheek before (T0) and after 60 days of bi-daily application.

9. ASSAY METHODOLOGY

Study duration
The treatment has been carried out for 60 consecutive days.

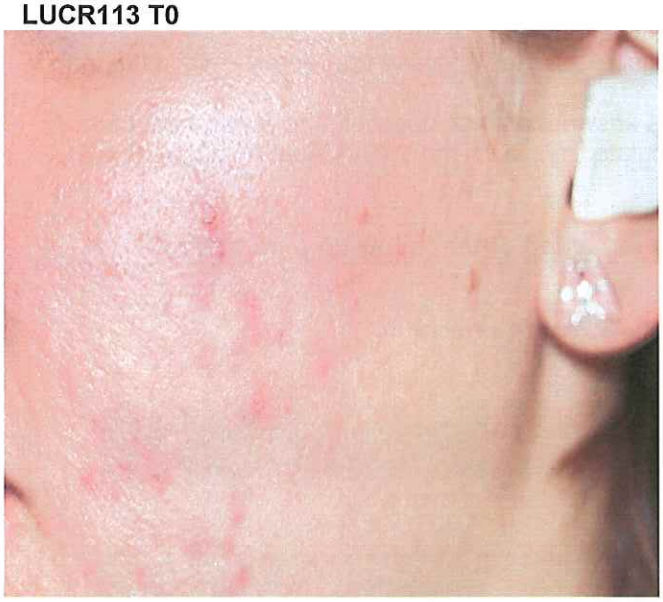
Preparation of the volunteer
Before taking pictures at T0 and T60 days, each volunteer was allow to relax in an air conditioned room to avoid anomalous sampling due to excessive sweating or stress.

10. TOLERABILITY

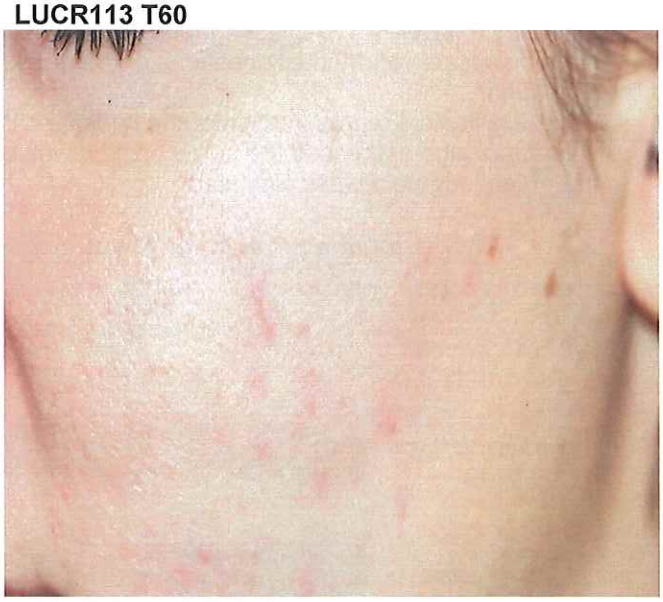
None of the 20 volunteers enrolled in this study, during the product use, showed signs of intolerance or allergic reactions to the product.

11. REPRESENTATIVE IMAGES OF THE TREATED AREAS

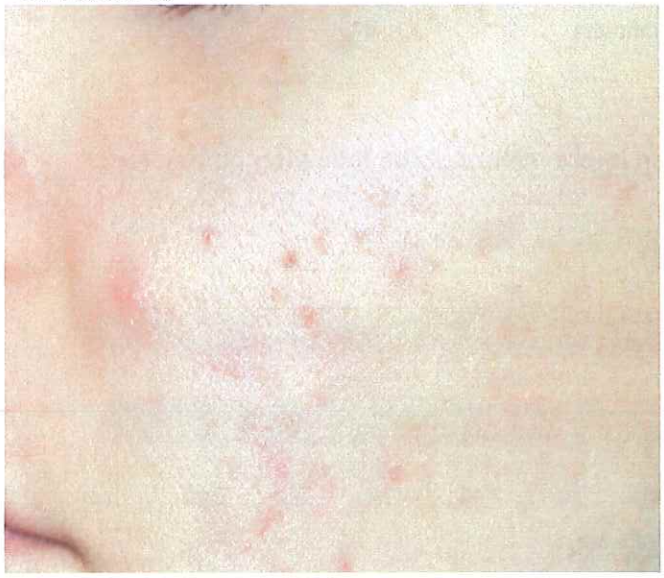
LUCR113 T0



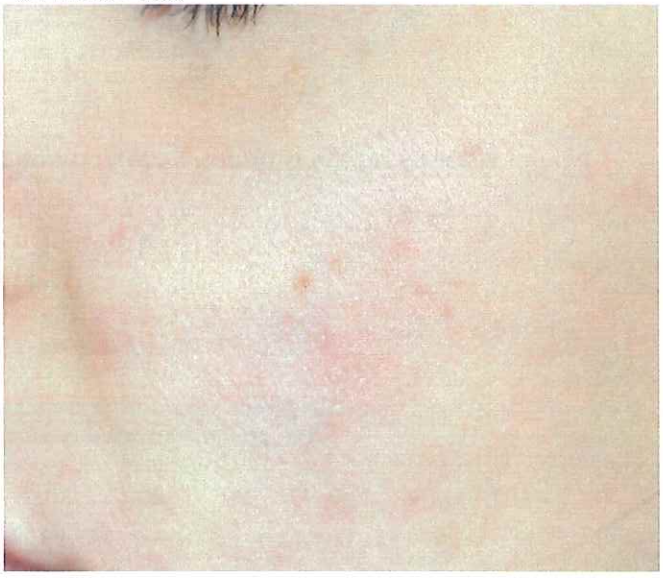
LUCR113 T60



STTR104 T0



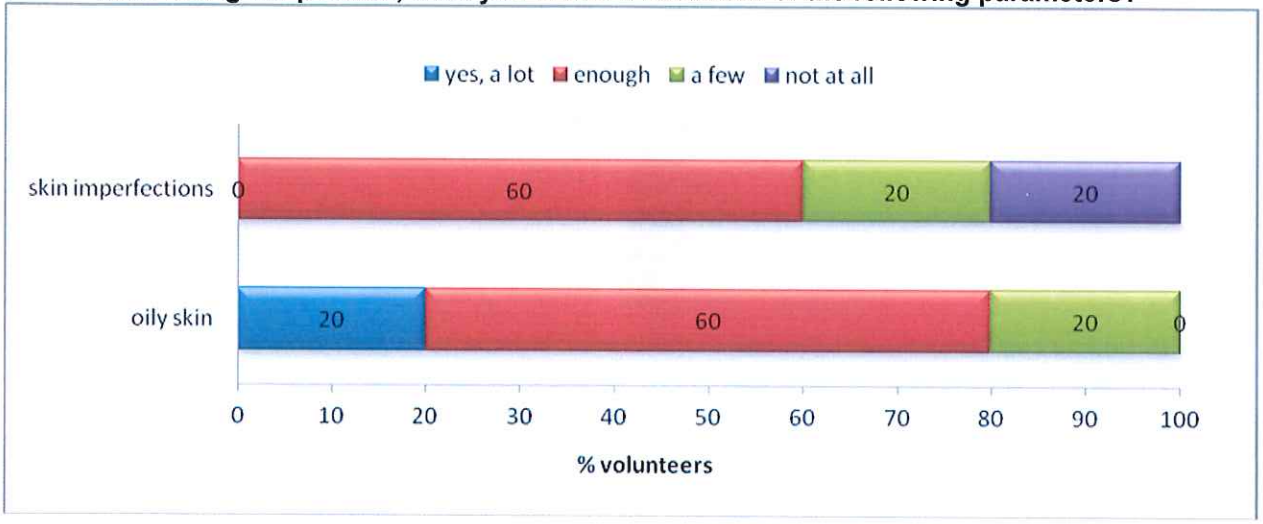
STTR104 T60



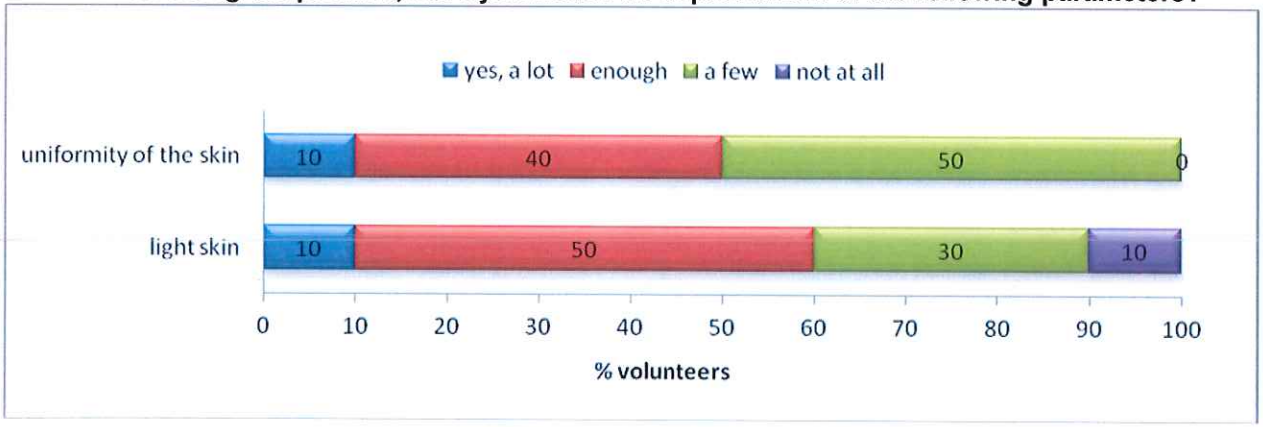
12. QUESTIONNAIRE CONCERNING A SENSORIAL / PSICHORHEOLOGICAL ASSESSMENT RELATIVE TO THE TESTED PRODUCT

To obtain a judgment from potential customers on product performances, the 20 subjects who took part to the study answered to a questionnaire on a subjective evaluation of the tested product.
Here below are reported all questions of the questionnaire and their answers are represented in the form of graphs.
For the graphical representation of the multiple choice answers of each question, the percentage of volunteers who expressed the same opinion was calculated, while for the VAS (Visual Analogue Scale), the mean judgment was calculated.

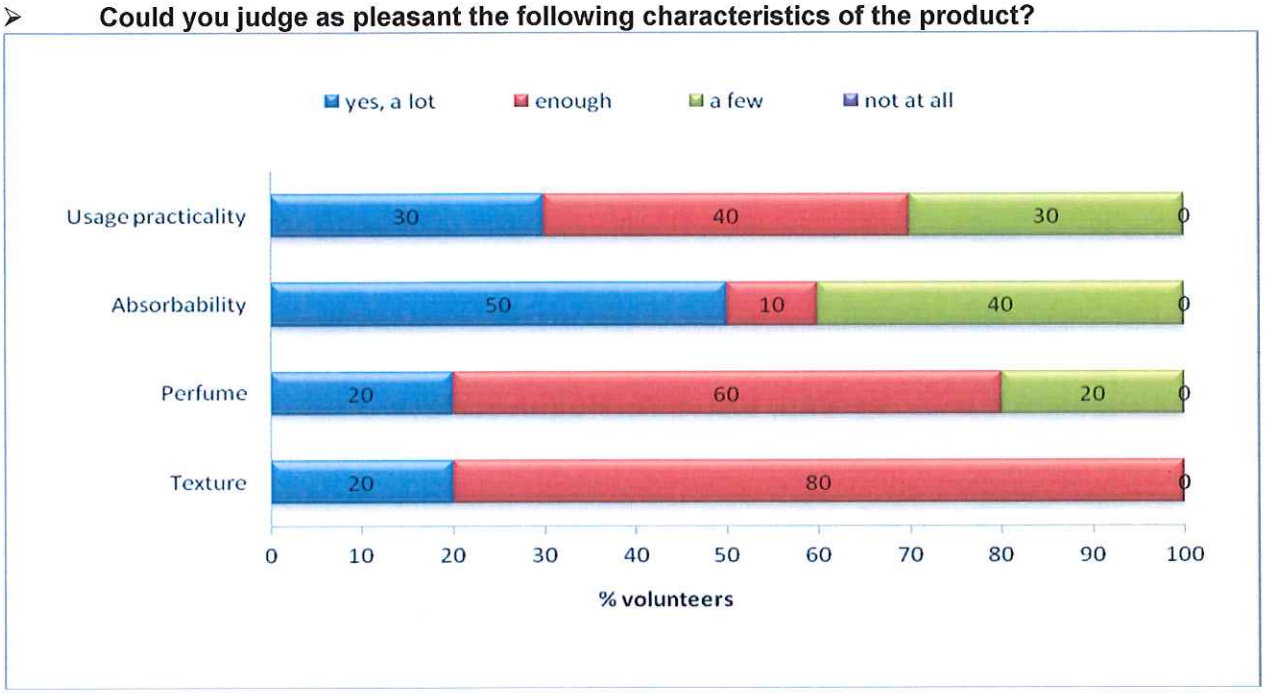
➢ **After using the product, have you notice a reduction of the following parameters?**



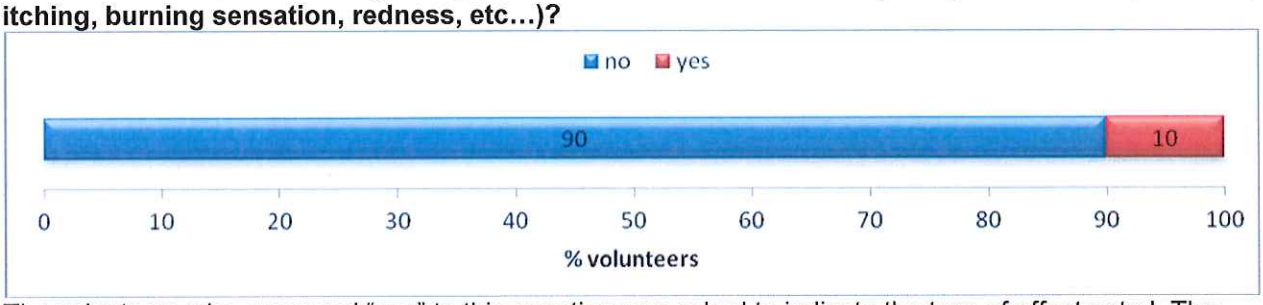
➢ **After using the product, have you notice an improvement of the following parameters?**



➢ **Could you judge as pleasant the following characteristics of the product?**



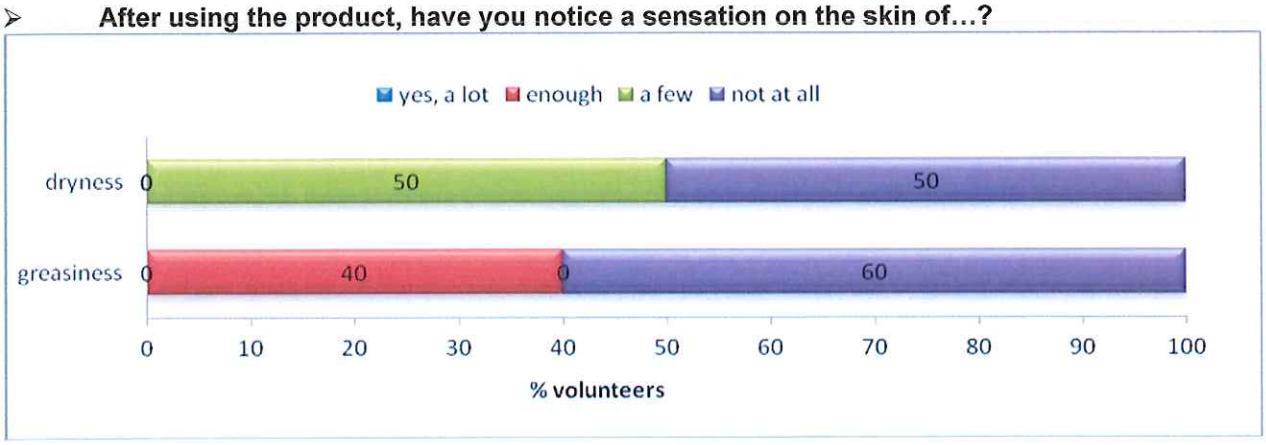
➢ **After the product usage did you note adverse effect caused by the product itself (irritation, itching, burning sensation, redness, etc…)?**



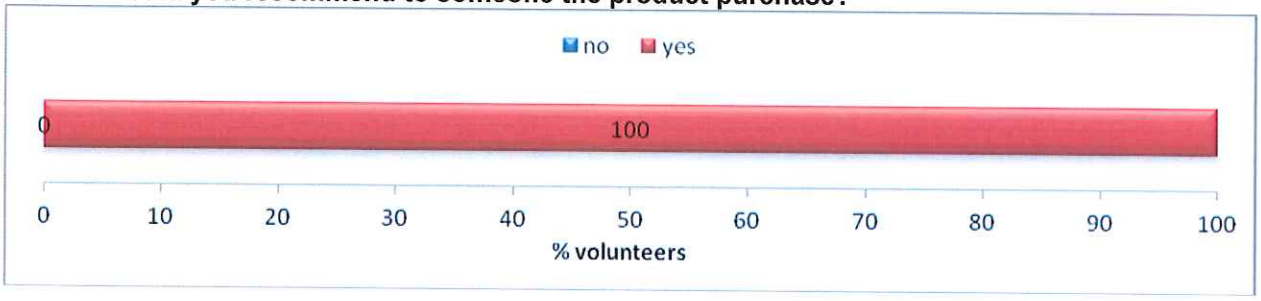
The volunteers who answered "yes" to this question was asked to indicate the type of effect noted. The anwers were:

- I notice a light redness, but it disappeared quickly.

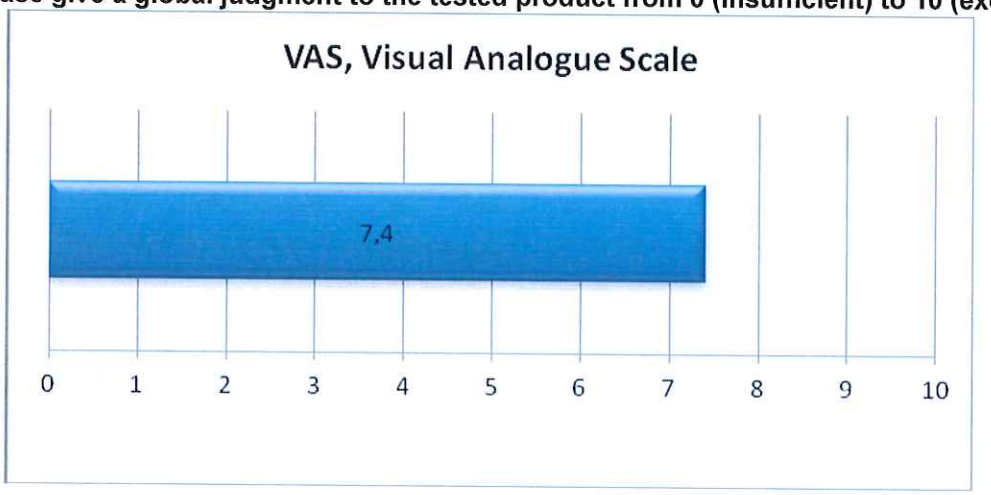
➢ **After using the product, have you notice a sensation on the skin of…?**



➢ **Would you recommend to someone the product purchase?**



➢ **Please give a global judgment to the tested product from 0 (insufficient) to 10 (excellent).**



13. DISCUSSION AND CONCLUSIONS

On the basis of the results obtained with the photographical analysis and the subjective evaluation, it can be concluded that the substance under examination

OXYGEN FACE NORMALIZING CREAM – OILY AND COMBINATION SKIN BATCH: 051 0816

on the subjects that had undergone the test, determines a general improvement of skin complexion and a reduction of skin imperfection. Hence the treatment has been proved to have an efficacy as coadjuvant in the treatment of acne.

14. BIBLIOGRAPHY

Joachim W. Fluhr Practical aspects of cosmetic testing Springer, 2011.

Haralick RM, Shanmugam K and Dinstein I. Textural features for image classification. IEEE Transactions on systems, man and cybernetics 1973; 3(6): 610-621

Tupin F, Tigelle M and Maitre H. Definition of a spatial entropy and its use for texture discrimination. Proceedings of international conference on image processing; 2000; Vancouver p725-728

Mendez A, Garcia B, Ruiz I, Iturricha I Vocal folds evaluation measuring vascularization level and texture Proceedings of the 7th WSEAS International Conference on signal processing, robotics and automation (ISPRA '08)

COLIPA guidelines for the evaluation of the efficacy of cosmetic products, May 2008.

Declaration WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI
Ethical Principles for Medical Research Involving Human Subjects
Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington 2002 (Note of Clarification on paragraph 29 added)
55th WMA General Assembly, Tokyo 2004 (Note of Clarification on Paragraph 30 added)
59th WMA General Assembly, Seoul, October 2008
64th WMA General Assembly, Fortaleza, Brazil, October 2013

http://www.springerimages.com/Images/RSS/1-10.1208_s12249-008-9061-9-0

Consensus documents Number 4.
OECD SERIES ON PRINCIPALES OF GLP AND COMPLIANCE MONITORING
"Quality assurance and GLP" 26 Oct. 1999.

Consensus documents Number 5.
OECD SERIES ON PRINCIPALES OF GLP AND COMPLIANCE MONITORING
"Compliance of laboratory suppliers with GLP principles" 28 Sept. 2000.

Consensus documents Number 7.
OECD SERIES ON PRINCIPALES OF GLP AND COMPLIANCE MONITORING
"The application of to GLP principles to short term studies" 15 Sept. 1999.

Consensus documents Number 8.
OECD SERIES ON PRINCIPALES OF GLP AND COMPLIANCE MONITORING
"The role and responsibility of the Study Director in the GLP studies" 15 Sept. 1999.