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CLEARGENTM

Anti-Acne Human Clinical Study



CLINICAL EVALUATION OF THE EFFICACY AND THE SAFETY OF ONE COSMETIC PRODUCT ON SUBJECTS WITH ACNE PRONE SKIN

Study carried out by DermScan Asia

Estimate:	#DA05008
Product(s):	Cleargen®
Form(s) and application(s):	Gel Applied on acne lesion on face
Sponsor:	Gencor Pacific Ltd. 21-e, elegance court Discovery bay, Hong Kong
Report date:	January 6, 2006

1. AIMS

1.1. Primary objective(s)

To evaluate the effect and safety of cosmetic product on subjects with acne prone skin after 28 days of twice daily use, by

- Clinical assessment by dermatologist responsible in this study

1.2. Secondary objective(s)

- To determine the product organoleptic characteristics, efficacy and safety by analyzing the answers given by the volunteers to a subjective questionnaire.

2. METHODS

2.1. Experimental plan

This was an open and intra-individual study; each subject is his/her own control.

2.2. Assessment criteria

2.2.1. Primary criteria

After 28 days of twice-daily use, evaluation of:

- the anti-acne effect by a clinical examination (numeration of retentional and inflammatory lesions) by a dermatologist,
- the cutaneous tolerance by clinical evaluation and by collecting volunteers sensations.

2.2.2. Secondary criteria

- Analysis of the subjects' answers to a subjective evaluation questionnaire.

2.2.3. Method (s) and instrument(s)

2.2.3.1. *Clinical examination*

2.2.3.1.1. Anti-acne effect

On D0 and D28, the dermatologist counted the retentional (open comedones= blackheads and closed comedones= microcysts) and inflammatory lesions (papules and pustules) on the entire face (except the nasal pyramid).

A variation in percentage is then calculated according to the following formula:

$$\frac{\text{Average nb on D28} - \text{Average nb on D0}}{\text{Average nb on D0}} \times 100$$

2.2.3.1.2. Cutaneous tolerance evaluation

On D28, the global tolerance of the product is assessed by clinical exam by the dermatologist.

This evaluation takes into account the elements reported by the volunteer (functional and physical signs) as well as those noted by the dermatologist (clinical signs). The confrontation of these signs is used to conclude the final safety of the tested product.

On D0 and D28, the dermatologist assesses the following criteria:

	no	slight	moderate	severe	very severe
Erythema	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Edema	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cutaneous dryness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Desquamation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Roughness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other :	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Define:.....					

2.2.3.2. Subjective evaluation questionnaire

The answers given by the volunteers to a subjective evaluation questionnaire are used to evaluate the organoleptic characteristics, efficacy and safety of the tested product. These subjective criteria give accurate indication of product(s) appreciation over time.

2.3. Operational aspect

2.3.1. Trial organization: schedule

On D0

- Subjects came to the laboratory without having applied any product to their face since the previous evening.
- An information sheet was provided to remind them of the study details.
- They read and signed the information and consent forms in duplicate.
- Clinical examination of the initial state of the skin by the dermatologist and counting of the retentional and inflammatory lesions on the entire face except the nasal pyramid.
- Distribution of the products to the volunteers who apply them twice-daily to the whole face for 28 days
- Distribution of a safety grid, completed by the subjects everyday.

On D28

- Subjects returned to the laboratory without any application of the product to the face; the last application of the product was done the evening before.
- New clinical examination by the dermatologist who counted retentional and inflammatory lesions and evaluated the safety of the product.
- Subjects answered the subjective questionnaire on D28.
- Subject bring their product and safety grid back to the laboratory in order to verify the compliance.

Ambient conditions during measurements were to have been:

- Ambient temperature: 25±1°C
- Relative humidity: between 40% and 60%.

2.3.2. Adverse Events/Serious Adverse Events

2.3.2.1. Definitions

An Adverse Event is defined as any expression or noxious and not wanted symptom suffered by subjects taking part in biomedical research, whether or not it relates to the tested product(s).

A Serious Adverse Event (SAE) is defined by one of the following criteria:

- death,
- life threatening,
- hospitalization,
- persistent or significant disability or incapacity,
- congenital anomaly,
- overdose,
- cancer,
- other event considered clinically significant by the investigator.

2.3.2.2. Documentation

Any or all Adverse Events related to the tested product (adverse reaction or effect) will be reported in the Case Report Form (CRF) and the study report.

Any or all concomitant treatment will be reported in the CRF and the study report.

Any or all Serious Adverse Events will be reported in the CRF and the study report.

2.3.2.3. Notification

All Serious Adverse Events will be transmitted by fax to the sponsor within 24 hours after knowledge of its occurrence, and then confirmed by mail within 48 hours.

2.3.2.4. Early termination of the study

X Test exit conditions

* In compliance with the Helsinki/Tokyo/Venice declaration and French law dated December 20, 1988 concerning the protection of subjects used in biomedical research, subjects had the right to exit from the study at any time and for any motive.

* The investigator also could have interrupted the treatment prematurely in the case of an intercurrent disease or undesirable effect.

* The sponsor could have demanded that any subject be excluded from the test for major infringements of the protocol, for administrative reasons or any other motive.

Nevertheless, premature removal of a high percentage of subjects from the test could have made the test difficult or impossible to interpret. Consequently, any premature exit without valid motives should have been avoided as much as possible.

Every premature exit must have been classified under one of the following headings:

- Adverse Event occurrence,
- Serious Adverse Event occurrence,
- withdrawal of consent,
- untraceable panelist,
- appearance of exclusion criteria,
- non-adherence to the protocol,
- other reason.

× Replacement conditions

If the premature exit was not related to the test treatment(s), the subject was replaced. Any replacement must have been previously discussed with the trial manager.

2.3.3. Collection and validation of data

The technician responsible for the test added data to subject case report form and to a computerized data base.

Data were then validated by the trial manager.

2.3.4. Trial monitoring visit

A trial monitoring visit may be carried out at sponsor request. It allows the sponsor to verify the study according to the determined protocol.

2.3.5. Quality assurance

The test report is written by the technician responsible for the study and controlled by the trial manager and by a person entitled to exercise the quality control of the study before being sent to the sponsor.

2.4. Subject selection

2.4.1. Inclusion criteria

2.4.1.1. General criteria

- Healthy subjects.
- Subjects having given their informed, written consent.
- Cooperative subjects, aware of the necessity and duration of controls so that perfect adherence to the protocol established by the clinical trial center could have been expected.

2.4.1.2. Specific criteria

- Age: 18-35 years old.
- Subjects with greasy facial skin and acneic lesions.
- Type: Asian female.
- Phototype: III, IV or V.

2.4.2. Non-inclusion criteria

- Pregnant or nursing women.
- Cutaneous pathology on face, other than acne (eczema, etc).
- Serious or progressive diseases that the investigator judges may interfere with the study.
- Volunteers undergoing a topical or systemic treatment:
 - anti-inflammatories and/or anti-histamines during the previous week,
 - cough suppressants and/or corticoids during the four previous weeks,
 - retinoids and/or immuno-suppressors during the six previous months.
- Any acne treatment within the previous month by oral or local route.
- Unstable weight.
- Excessive exposure to sunlight or UV rays during study within previous month.
- Excessive use of alcohol or tobacco.

2.4.3. Compliance assessment

If the protocol was not respected and if the deviation was minor, the technician responsible for the study warned the subject of the importance of respecting the prescribed protocol. If the subject persisted or if the deviation was major, the subject was declared non-compliant. In this case, the subject was removed from the test for non-compliance.

2.4.4. Associated treatment during the study

No systemic treatment likely to modify the skin condition was authorized during the test.

No use of dermopharmaceutical or cosmetic products other than cleansing products was authorized on the test zones the previous evening or during the study.

2.5. Number of subjects

The study is carried out on 22 subjects at sponsor request (complete study at least 20 subjects).

2.6. Tested product(s)

2.6.1. Confidentiality procedure

The products supplied by the sponsor were encoded.

2.6.2. Storage

Before the beginning of the study, each product was kept at room temperature in a dedicated air-conditioned room. This room is locked and access controlled.

2.6.3. Reference(s)

Cleargen®

2.6.4. Aspect(s)

Brown gel.

2.6.5. Labeling

Example of labeling of each product by the clinical trial center:

DERMSCAN Study # Volunteer #..... Zone: Ref.: Emergency telephone number: xx xxx xxxx Dermscan ref.: Batch #: Conservation: Ambient Temperature For clinical trials: to be used only under strict medical surveillance

2.6.6. Dosage

Twice-daily (morning and evening), during 28 days.

2.6.7. Application site(s) and method(s)

Application site: acne lesion on face.

Application method: under normal condition of use.

2.7. Treatment allocation method

2.7.1. Randomization method

The subject number was given according to the order of inclusion in the study.

2.8. Statistical method(s)

2.8.1. Data analysis

2.8.1.1. Clinical evaluation

Data from this test were analyzed with a paired signed ranks test. This method is based on the calculation of the differences observed between values obtained before and after use of the product, on a same volunteer, the ranks of these differences not taking into account their signs and the calculation of the sum of the ranks of the positive differences (Y+) and the sum of the ranks of the negative differences (Y-). If the treatment is not effective, Y+ and Y- should be equal.

Example:

Volunteer	Clinical score before treatment	Clinical score after treatment	Differences	Ranks
1	4	2	-2	2
2	3	2	-1	1
3	2	5	3	3
4	4	0	-4	4
5	4	4	0	-

$Y^+ = 3$

$Y^- = 7$

For all non-parametric tests, if a difference is of 0, the corresponding paired comparisons are discarded from the analysis and the n value is consequently reduced. The null hypothesis (H0) is that the treatment has no efficacy. Under (H0), the probability of obtaining a difference between before and after treatment at least as big as the one observed is calculated.

If this probability is less than or equal to 5%, the null hypothesis (H0) is rejected. The alternative hypothesis (H1) that there is a significant difference between before and after treatment is accepted. Probability p characterizes the signification level of this conclusion.

On the other hand, if p is greater than 5%, there is no reason for rejecting the null hypothesis (H0). From these data, no differences between before and after treatment could be evidenced.

Before carrying out a test, a type I error of 5% is chosen (which corresponds to the risk of rejecting a true null hypothesis).

2.8.2. Statistical software

The software used was SPSS 11.0.

2.9. Archives

Data will be securely archived digitally and on paper for fifteen years from the date of dispatch of the final report. At the end of this period, the study archives will be destroyed unless otherwise stipulated in writing by the sponsor.

A sample of each tested product will be kept by the laboratory for one year.

3. TEST FOLLOW-UP

- The test was done on 22 female
- 100% of subjects finished the study
- Trial monitoring visit: no visit took place
- The experimental conditions were conformed to the protocol:

4. SUBJECT CHARACTERISTICS

Tables, below, present the observations concerning all the volunteers included.

No. of Subject	Name (the 3 first letters)	First name (the 2 first letters)	Age	Sex	Phototype	Previous medical or surgical events or medical treatment	Current medical events or treatment
1	TAN	AR	20	F	III	NO	NO
2	WON	CH	20	F	III	NO	NO
3	LEO	NU	24	F	IV	NO	NO
4	TEA	AU	21	F	III	NO	NO
5	JUN	NU	23	F	IV	NO	NO
6	WOR	OB	25	F	III	NO	NO
7	TUP	NU	29	F	IV	NO	NO
8	BOO	PI	20	F	IV	NO	NO
9	NIR	AN	20	F	III	NO	NO
10	JUN	KA	26	F	III	NO	NO
11	SEA	SU	22	F	IV	NO	NO
12	TAN	KA	20	F	IV	NO	NO
13	KOS	SU	21	F	IV	NO	NO
14	BUA	TI	27	F	IV	NO	NO
15	TAM	MO	27	F	IV	NO	NO
16	BUA	WA	27	F	IV	NO	NO
17	BUA	WA	24	F	IV	NO	NO
18	PAK	WE	20	F	IV	NO	NO
19	PUM	PU	28	F	III	NO	NO
20	JIN	CH	20	F	IV	NO	NO
21	JUN	JU	27	F	IV	NO	NO
22	CHI	SU	22	F	IV	NO	NO
Mean			23	22	F	0	I
Median			23	0	M	0	II
<i>Minimum</i>			20			7	III
<i>Maximum</i>			29			15	IV
SEM			1			0	V
						0	VI

5. RESULTS

5.1. Clinical assessment

5.1.1. *Efficacy on acne lesions*

The efficacy on acne lesions were carried out by dermatologist responsible in this study under the same conditions, counted the retentional and inflammatory lesions on the entire face (except the nasal pyramid), at D0 and D28 after used product.

The variations (Δ) of the number of acne were calculated according to the following formula:

$$\Delta = T_i - T_0$$

with:

T_i: the number of acne at each time of kinetics.

T₀: the number of acne at starting time after used blotter

A variation in percentage is then calculated according to the following formula:

$$\frac{\text{Average nb on D28} - \text{Average nb on D0}}{\text{Average nb on D0}} \times 100$$

Table 1 and Graph 1 below express the average numbers obtained for each type of acne lesion at the beginning and end of the study as well as the total number of these lesions.

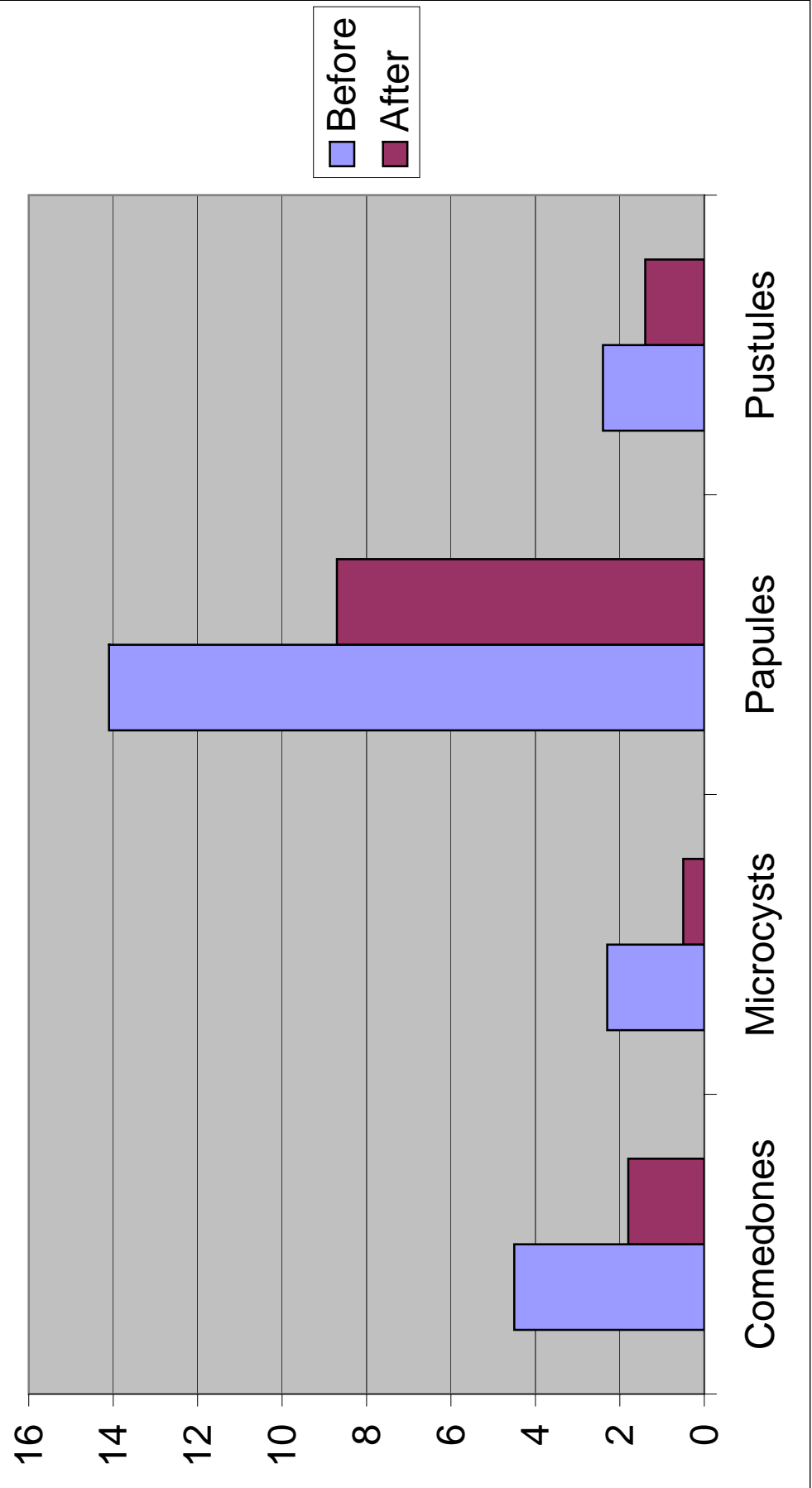
Vol	Comedones			Microcysts			Papules			Pustules			Total nb of lesions		
	D0	D28	ΔD28	D0	D28	ΔD28	D0	D28	ΔD28	D0	D28	ΔD28	D0	D28	ΔD28
1	0	0	0	1	0	-1	8	4	-4	2	0	-2	11	4	-7
2	3	3	0	0	0	0	5	2	-3	0	0	0	8	5	-3
3	3	4	1	3	3	0	50	18	-32	4	3	-1	60	28	-32
4	0	0	0	0	0	0	15	9	-6	4	1	-3	19	10	-9
5	8	0	-8	1	0	-1	2	2	0	4	0	-4	15	2	-13
6	25	7	-18	0	0	0	15	5	-10	0	0	0	40	12	-28
7	1	0	-1	5	2	-3	14	10	-4	2	0	-2	22	12	-10
8	0	2	2	0	0	0	12	9	-3	3	3	0	15	14	-1
9	3	1	-2	3	0	-3	0	0	0	0	0	0	6	1	-5
10	1	1	0	6	2	-4	0	8	8	4	0	-4	11	10	-1
11	0	2	2	5	0	-5	10	6	-4	2	8	6	17	16	-1
12	4	3	-1	0	0	0	30	25	-5	3	3	0	37	31	-6
13	5	0	-5	5	0	-5	7	8	1	0	0	0	17	8	-9
14	3	2	-1	3	0	-3	25	9	-16	5	2	-3	36	13	-23
15	3	0	-3	2	1	-1	25	8	-17	6	1	-5	36	10	-26
16	3	1	-2	2	0	-2	11	3	-8	2	0	-2	18	4	-14
17	25	9	-16	0	1	1	6	9	3	0	0	0	31	19	-12
18	3	3	0	3	0	-3	50	33	-17	7	5	-2	63	41	-22
19	0	0	0	3	0	-3	7	7	0	3	1	-2	13	8	-5
20	7	0	-7	3	1	-2	15	9	-6	0	2	2	25	12	-13
21	0	0	0	3	0	-3	0	5	5	2	1	-1	5	6	1
22	3	2	-1	3	0	-3	4	3	-1	0	0	0	10	5	-5
Mean	4.5	1.8	-2.7	2.3	0.5	-1.9	14.1	8.7	-5.4	2.4	1.4	-1.0	23.4	12.3	-11.1
<i>Median</i>	3.0	1.0	-1.0	3.0	0.0	-2.0	10.5	8.0	-4.0	2.0	0.5	-1.0	17.5	10.0	-9.0
<i>Minimum</i>	0.0	0.0	-18.0	0.0	0.0	-5.0	0.0	0.0	-32.0	0.0	0.0	-5.0	5.0	1.0	-32.0
<i>Maximum</i>	25.0	9.0	2.0	6.0	3.0	1.0	50.0	33.0	8.0	7.0	8.0	6.0	63.0	41.0	1.0
SEM	1.5	0.5	1.1	0.4	0.2	0.4	3.0	1.6	1.9	0.4	0.4	0.5	3.4	2.1	2.0
P*	0.016			0.001			0.007			0.037			0.000		

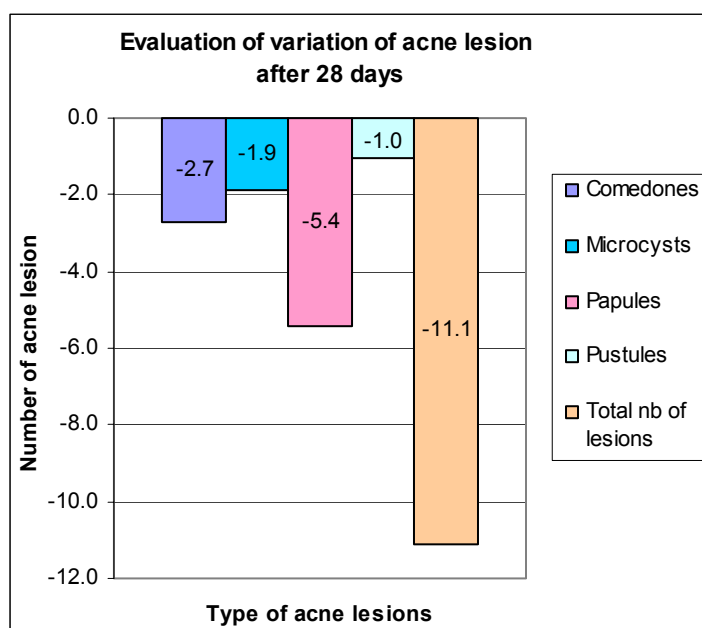
* Test of Wilcoxon: P>0.05 non significant

P<0.05 significant

The counting of acne lesions at the beginning of the study before any application and at the end of the study after 28 days of twice-daily use showed a statistically significant decrease of these lesions, particularly with the number of papules.

ClearGen™ 28 days Clinical study for ACNE





5.1.2. Cutaneous tolerance

Table 2 below expresses the clinical examination of the cutaneous state of the face done by the dermatologist as well as the sensations reported by the volunteers.

Vol	Signs reported by the volunteers		Clinical signs observed by the dermatologist on D28
	Functional signs	Physical signs	
1	NO	NO	NO
2	NO	NO	NO
3	NO	NO	NO
4	NO	NO	NO
5	NO	NO	NO
6	NO	NO	NO
7	NO	NO	NO
8	NO	NO	NO
9	NO	NO	NO
10	slightly burning sensation and itching for 3 days after start apply product	slightly redness and skin slightly dryness for 2-3 days after start to apply product.	NO
11	NO	NO	NO
12	NO	NO	NO
13	NO	NO	NO
14	NO	NO	NO
15	NO	NO	NO
16	NO	NO	NO
17	NO	NO	NO
18	NO	NO	NO
19	NO	NO	NO
20	NO	NO	NO
21	NO	NO	NO
22	NO	NO	NO

Synthesis

	Number of volunteers	Percentage
Total reported signs	1	4.5%
Pertinent reported signs	0	0%
Total observed clinical signs	0	0%
Pertinent observed clinical signs	0	0%

Under these study conditions, the product could be considered very well tolerated on the cutaneous level: the reported signs did not last more than five minutes after application and are normal with this kind of product.

5.2 Subjective evaluation questionnaire

Globally, the volunteers appreciate the tested product. A Majority of volunteers noticed an improvement effect on their acne in particular for the variation in the number of blackhead and a variation in the number, size and inflammation of pimples after this treatment.

The synthesis of the answers that were given by the volunteers to the subjective evaluation questionnaire is presented below.

GLOBAL APPRECIATION OF THE PRODUCTS AND THEIR PROPERTIES

Q1 – *Do you usually use a product to treat acne?*

Yes	87%
No	13%

Q2 – *What is your global opinion about the products?*

Very pleasant	9%
Pleasant	61%
Neither unpleasant nor pleasant	30%
Unpleasant	0%
Very unpleasant	0%

Q3 to Q5 – *What do you think of their aspect, texture and fragrance?*

	Very pleasant	Pleasant	Neither pleasant nor unpleasant	Unpleasant	Very unpleasant
Q3 - Aspect	0%	52%	39%	9%	0%
Q4 - Texture	0%	52%	30%	17%	0%
Q5 – Fragrance	0%	48%	22%	26%	4%

Q6 to Q8 – *Immediately after application, did these products leave your skin:*

	Yes	No
Q6 - Sticky	43%	57%
Q7 - Oily	43%	57%
Q8 - Shiny	39%	61%

Q9- *Did the product spread easily?*

Very easily	18%
Fairly easily	73%
Fairly difficultly	9%
Very difficultly	0%

Q10 – Did the product penetrate quickly ?

Very quickly	10%
Fairly quickly	62%
Fairly slowly	29%
Very slowly	0%

PRODUCT EFFICACY

Q11 – Did you notice an improvement on your skin state or aspect after 28 days of treatment?

Important improvement	22%
Moderate improvement	26%
Slight improvement	35%
No change	17%

Q12 – Regarding blackheads, did you notice a variation in their number after 28 days of treatment?

number of *blackheads*:

much less	17%
less	70%
no change	13%
more	0%
much more	0%

Q13 to Q15 – Did you notice a variation in the number, size and inflammation of pimples after this treatment ?

Q13 – number of pimples:

much less	0%
less	91%
no change	9%
more	0%
much more	0%

Q14 – average size of these pimples:

much smaller	17%
smaller	74%
no change	9%
bigger	0%
much bigger	0%

Q15 – pimples redness:

much less red	17%
less red	61%
no change	22%
more red	0%
much more red	0%

TOLERANCE

Q16 – Did you feel any intolerance sensations when using this product?

Yes	9%
No	91%

Q17 – *Did you stop using the product?*

Yes	0%
No	100%

Q18 – if yes, time of interruption :

If it was interrupted, was it :

Q26 • because of an intolerance reaction?

Yes	0%
No	0%

Q27- • for other reasons?

Yes	0%
No	0%

if yes, specify:

FUTURE USE OF THE PRODUCT

Q19 *At the end of this test, would you like to continue using the product?*

Yes	87%
No	13%

Q20- *Would you like to buy this product?*

Certainly	13%
Probably	70%
Maybe	13%
Probably not	4%
Certainly not	0%

6. CONCLUSION AND SIGNATURE(S)

The aim of the study was to determine, on volunteers, the efficacy and safety of product on acne lesions on face at 28 days after used twice-daily.

Study conditions:

Product reference(s)	Cleargen®
Measurement zone(s)	Acne lesions / Face
Number of volunteers included in the data analysis	22 (all of females)
Age	23±1 (between 20 and 29)
Specific inclusion criteria	Subjects having acne prone skin
Application for each product	Under normal condition of use : twice-daily
Protocol	Before /After treatment
Measurement kinetics	D0 and D28 after used product

1. Clinical evaluations; efficacy and safety of product

After used the product “ Cleargen” on acne lesions for 28 days, the number of acne lesions include of comedones, microcysts, papules and pustules showed a significant decreased from the beginning.

And for the cutaneous tolerance, the product “ Cleargen” could be considered very well tolerated on the cutaneous level.

2. Subjective evaluation questionnaires

Globally, the volunteers appreciate the tested product. A Majority of volunteers noticed an improvement effect on their acne in particular for the variation in the number of blackhead and a variation in the number, size and inflammation of pimples after this treatment.

Scientific Director
Aeumporn Srigritsanapol, Ph.D.

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