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Study report #22E2145

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EVALUATION OF THE CUTANEOUS ACCEPTABILITY AND EFFICACY OF A DERMOCOSMETIC PRODUCT -USE TEST UNDER DERMATOLOGICAL CONTROL -

VIHREÄ TEE & KAMOMILLA SHAMPOO

CLINICAL INVESTIGATION CENTER	
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Document 1/1 including 43 pages

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KEY ELEMENTS OF THE STUDY #22E2145

EVALUATION OF THE CUTANEOUS ACCEPTABILITY AND EFFICACY OF A DERMOCOSMETIC PRODUCT
- USE TEST UNDER DERMATOLOGICAL CONTROL -

Claim

- Tolerance tested under dermatological control.

Objectives

To evaluate for the studied product:

- its ability to maintain human body in good condition (cutaneous acceptability) proven by clinical examination by the dermatologist;
- its global efficacy by clinical score by the dermatologist;
- its efficacy on itching and dandruff by auto-score by subjects;
- its efficacy on rash by clinical scoring by the dermatologist;
- subjectively its cosmetic acceptability, efficacy and future use by analysis of the subjects' answers to a subjective evaluation questionnaire;
- potential adverse events collection.

Methodology

- Open, intra-individual study; each subject is his/her own control;
- Before / After.

Kinetics

	Evaluation zone	D0	D0-D27	D28 (±1)
Information of the subject about study conditions and collection of his/her informed consent.	Scalp	●		
Verification of inclusion and non-inclusion criteria.		●		
Clinical examination by the dermatologist to assess the cutaneous state of the scalp.		●		●
Global efficacy clinical score by the dermatologist.		●		●
Evaluation of itching and dandruff by the subjects.		●		●
Efficacy of rash by the dermatologist.		●		●
Distribution (d) / collection (c) of the daily log and study product.		● (d)		● (c)
Product application by the subjects at home.			●	
Subjective evaluation questionnaire.				●
Potential adverse event collection.				●

Dates

Product reception	Study start	Study end	1st results by e-mail
July 26th, 2022	August 29th, 2022	October 19th, 2022	November 23rd, 2022

Product

Reference	Form	Application zone
VIHREÄ TEE & KAMOMILLA SHAMPOO	Dark green bar of shampoo	Scalp

Study Population

Specific inclusion criteria

- **Sex:** female and/or male;
- **Age:** 18 years old and above;
- **Phototype:** I to IV;
- Subjects with mild to moderate scalp psoriasis without treatment:

Mild	Moderate
• affects <50% of the scalp, • presence of one or more of: - mild erythema, - mild scaling - minimal thickness (barely detectable or no infiltration) - mild pruritus	• affects <50% of the scalp, • presence of one or more of: - moderate erythema, - moderate scaling, - moderate thickness (some infiltration), - mild to moderate pruritus

	Number of subjects analyzed	Average age
	22 for tolerance and questionnaire 20 for efficacy	45(±3) years (between 19 and 66)

Conclusion

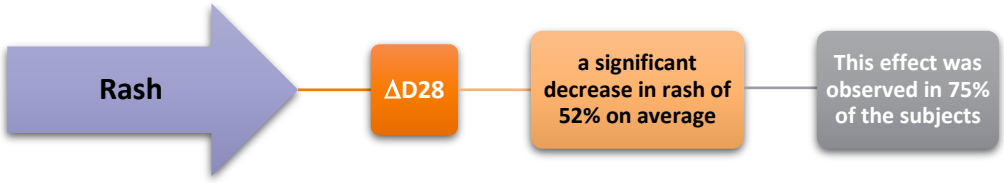
Under these study conditions, after 28 days of three to seven times a week use, the product "VIHREÄ TEE & KAMOMILLA SHAMPOO":

- **was assessed by the dermatologist as having a good tolerance on the cutaneous level;**
- **presented a global improvement of the scalp skin state, characterized by Investigator's Global Improvement Score (IGIS) assessed by the dermatologist:**

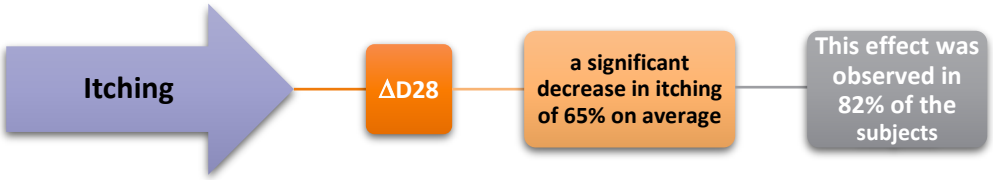
Investigator's Global improvement Score (IGIS):

- completely clear of 5%,
- almost clear of 20%,
- marked improvement of 55%,
- moderate improvement of 15%,
- no change of 5%;

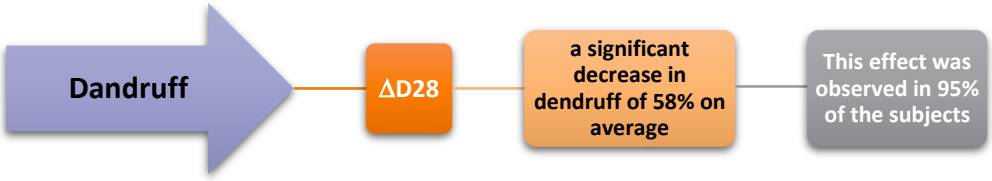
- **presented an improvement of the scalp rash state (psoriasis area), characterized by clinical score assessed by the dermatologist:**



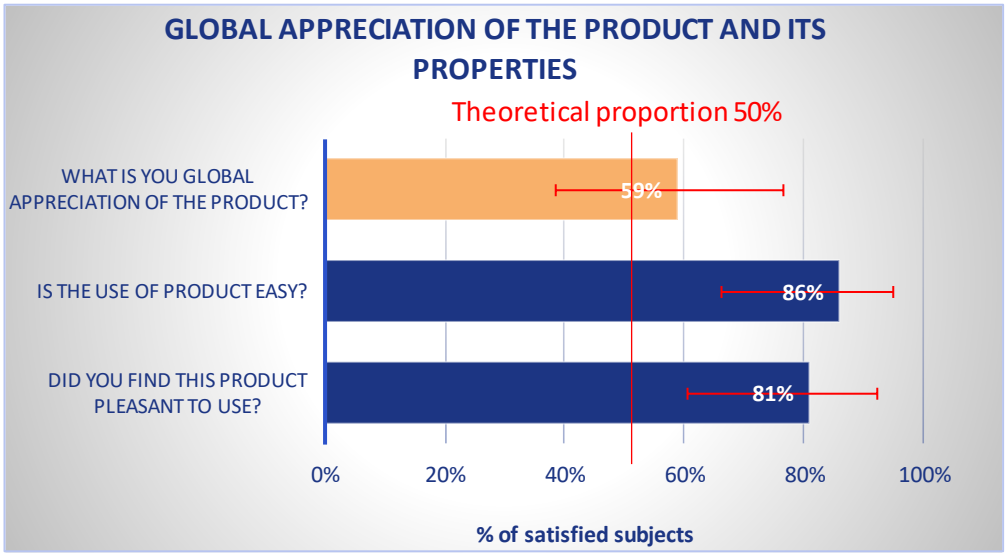
- **presented an improvement of the itching, characterized by auto-score assessed by the subjects:**



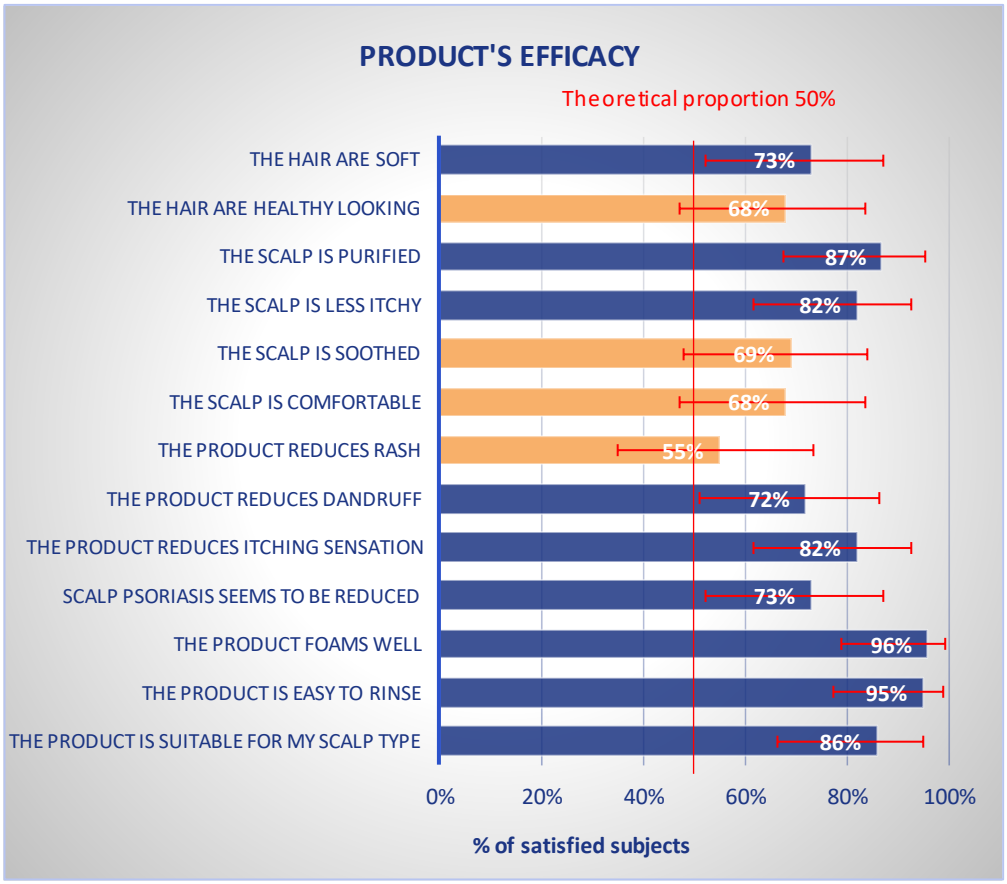
- **presented an improvement of the dandruff state, characterized by auto-score assessed by the subjects:**



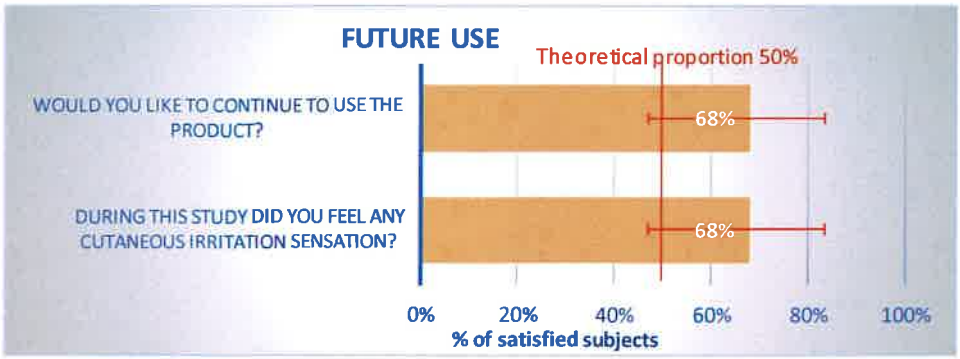
➢ **was appreciated by majority of subjects for its properties and efficacy:**



Not significant
Significant



Not significant
Significant



Not Significant

The product "VIHREÄ TEE & KAMOMILLA SHAMPOO" can claim "TOLERANCE TESTED UNDER DERMATOLOGICAL CONTROL"

	Name and job title	Date	Signature
Project Manager Assistant	Karina KUPPER	01/12/2022	Kupper
Investigator	Ewa KARAMON (dermatologist)	01/12/2022	

1 QUALITY CONTROL STATEMENT

The person responsible for the final quality control certifies that the study above was conducted as closely as possible to Good Clinical Practice (GCP-ICH), in compliance with the study protocol and EUROFINS Dermscan/Pharmascan standard operating procedures and that the study report reflects raw data.

QUALITY CONTROL ASSESSOR	
Last name	CZERMAŃSKA
First name	Anna
Date	11/12/2022
Signature	

2 STUDY PROCESS

EUROFINS Dermscan/Pharmascan is certified ISO: 9001-2015.

EUROFINS Dermscan/Pharmascan benefits from a governmental Research Tax Credit from the French Ministry of Research.

The study is carried out on a cosmetic product whose safety has been assured by the Sponsor.
Its aim is to further confirm, under normal and reasonably foreseeable use conditions, the capacity of a product to maintain human body in good condition.

The European Directive 2001/20/EC and regulations issued by the Minister of Health (Order of the Minister of Health of May 2, 2012 regarding Good Clinical Practice, Dz.U. 2012, item 491) is not applicable. Therefore, this study is considered as non-interventional and does not require the Ethics Committee Approval and the Competent Authority Authorization.

+ See ethical requirements and regulatory standards in **Appendix 8.**

This study was conducted under the following conditions:

2.1 POPULATION

2.1.1 Selection

INCLUSION CRITERIA	
Specific	
• **Sex:** female and/or male; • **Age:** 18 years old and above; • **Phototype:** I to IV; • Subjects with mild to moderate scalp psoriasis without treatment	
Mild • affects <50% of the scalp, • presence of one or more of: - mild erythema, - mild scaling - minimal thickness (barely detectable or no infiltration) - mild pruritus	**Moderate** • affects <50% of the scalp, • presence of one or more of: - moderate erythema, - moderate scaling, - moderate thickness (some infiltration), - mild to moderate pruritus
General	
• Healthy subject; • Subject having given his/her free informed, written consent; • Subject willing to adhere to the protocol and study procedures.	

NON-INCLUSION CRITERIA
• For women: pregnant or nursing woman or woman planning to get pregnant during the study; • Cutaneous pathology on the study zone – except psoriasis (eczema, etc.); • Using a biotherapy treatment for psoriasis within the 6 previous months; • Use of other systemic oral treatment for psoriasis during the previous one month before the beginning of the study (acitretin, cyclosporine, methotrexate,…); • Use of topical treatment for psoriasis during the previous 2 weeks (corticosteroid, vitamin D analogs,…); • Use of phototherapy for psoriasis within the previous month; • Use of a kerato-reducing, moisturizing cosmetic products (e.g. shampoo) for psoriasis within the previous week; • Use of topical or systemic treatment during the previous weeks liable to interfere with the assessment of the cutaneous acceptability and efficacy of the study product;

- Subject having undergone a surgery under general anesthesia within the previous month;
- Excessive exposure to sunlight or UV-rays within the previous month;
- Subject refusing sun avoidance;
- Subject enrolled in another clinical trial during the study period (concerns the studied zones);
- Subject who does not meet the Ministry of Health guidelines for Covid-19 at the time of the visit.

2.1.2 Study requirements and constraints

DURING THE STUDY, THE SUBJECTS		
HAVE TO	**MUST NOT**	**ARE ALLOWED TO USE*** (except on visiting days)
• respect dates and hours of evaluation visits; • follow the conditions of use of the investigational product at home; • complete the daily-log and bring it back with the investigational product/packaging at the end of the study; • avoid excessive UV exposure (including artificial UV); • wear mask and disinfect hands during the visits at the laboratory.	• apply any product to test areas the days of the visits* to the investigation center; • apply any other similar product (shampoo) to test areas during the study; • modify their usual hygiene or care products and/or use new products; • allow the use of the study product by another person than herself/himself.	• usual care products (conditioner, hair mask).

** a hair wash with the usual or tested product is allowed the day before the visit to the investigation center.*

2.1.3 Compliance assessment

The compliance is controlled by checking the daily log.

+ See **Appendix 7.2**.

2.1.4 Protocol deviations

A protocol deviation can be defined as any non-adherence to the final protocol, including:

- wrong inclusion (inclusion criteria or non-inclusion criteria not fulfilled);
- start of a prohibited concomitant treatment;
- non-adherence of the subjects to the study schedule (missed or postponed visit);
- missing data for one or several evaluation criteria;
- low compliance of the subject to the study product(s) application;
- premature study end or untraceable subject;
- no respect of the constraints envisaged by the protocol.

Deviations to the protocol should be classified as:

- **minor** if they don't impact the rights, safety or well-being of the subjects. They do not increase the risk for the subject and/or do not have a significant effect on the integrity of the data collected,
- **major (or protocol violations**) if they affect the rights, safety or well-being of participants. They increase the risk for the subject and/or have a significant effect on the integrity of the study data,
- **critical:** any protocol violations as mentioned above necessarily requiring the suspension or the termination of the study.

In case of minor protocol deviation, the technician or the investigator repeats the instructions and reminds the subject to follow protocol requirements / study procedures. In case of persistent or major protocol violations, the subject is declared non-compliant and withdrawn from the study because of non-compliance.

The non-adherences observed are presented in the following table:

Subject#	Description of the non-adherence	Type of non-adherence (minor / major)	Data kept in the analysis (yes/no)
1	Last product application was done on D26 instead of D27.	minor	yes
5	Last product application was done on D26 instead of D27.	minor	yes
6	The subject used the product eight times a week instead of maximum seven times in week 1, 2 and 3 of the study.	minor	yes
8	The subject returned on D32 instead of D28.	minor	yes
9	The subject returned on D32 instead of D28.	minor	yes
17	**The subject used the product before the visit on D27 instead of D26.**	minor for tolerance and questionnaire evaluations **major for efficacy evaluations**	yes for tolerance and questionnaire evaluations **no for efficacy evaluations**
18	**The subject used the product before the visit on D27 instead of D26.**	minor for tolerance and questionnaire evaluations **major for efficacy evaluations**	yes for tolerance and questionnaire evaluations **no for efficacy evaluations**
20	Subject used the product twice instead of minimm three times a week in week 1.	minor	yes
	Last product application was done two days before the visit (D27 instead of D28).	minor	yes
22	Subject used the product twice instead of minimm three times a week in week 3.	minor	yes

- The protocol non-adherence of the subjects #1, 5, 6, 8, 9, 20 and 22 did not invalidate the data obtained for these subjects.
- The protocol non-adherence of the subjects #17 and 18 invalidated the data obtained for these subjects.

2.1.5 Concomitant treatments

- **None of the concomitant medications started after the beginning of the study invalidated the data obtained for any subject.**

  + See the concomitant medications table in **Appendix 7.3.**

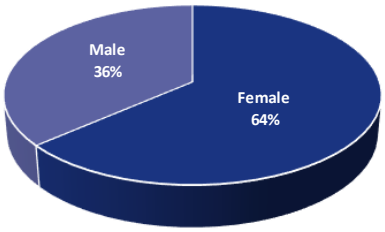
2.1.6 Follow-up

	Number of SUBJECTS				
	INCLUDED	COMPLETING THE STUDY	ANALYZED	NOT COMPLETING THE STUDY	NOT ANALYZED
Cutaneous acceptability/ Subjective evaluation	22	22	22	/	
Auto-score / Clinical score / IGIS	22	22	20	/	2 Subject 17 and 18: used the product on the day of the visit (D27) instead of the day before (D26).

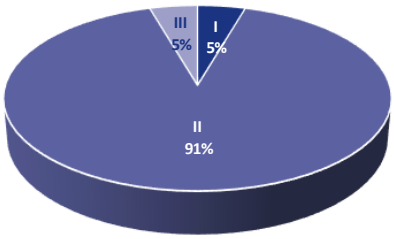
2.1.7 Demographic data

ANALYZED SUBJECTS (included in at least one analysis)	SEX	AGE (IN YEARS)			Scalp type	Phototype	Sensitive skin on the face	Mild to moderate scalp psoriasis	COMMENTS AND DETAILED DATA
		Mean ± SEM	Min.	Max.					
22	Female: 14 Male: 8	45±3	19	66	Normal: 1 Dry: 11 Greasy: 10	I: 1 II: 20 III: 1	Yes: 18 No: 4	Mild: 15 Moderate: 7	See **Appendix 7.1**

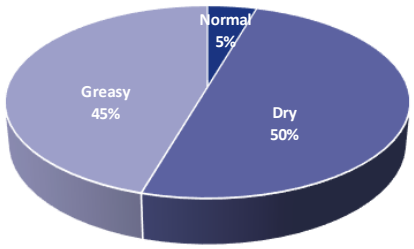
SEX



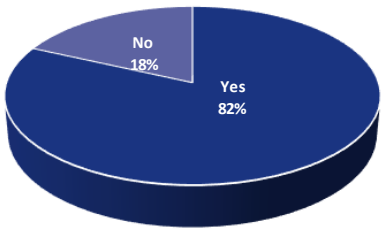
PHOTOTYPE



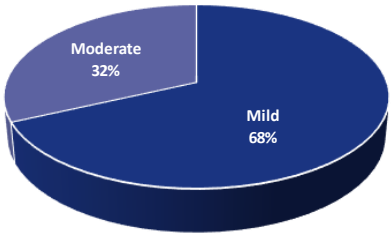
SCALP TYPE



SENSITIVE SCALP



SCALP PSORIASIS



2.2 INVESTIGATIONAL PRODUCT

2.2.1 Description

Reference	Batch#	Form	Packaging	Confidentiality procedure	Storage temperature
VIHREÄ TEE & KAMOMILLA SHAMPOO	TO1172	Dark green bar of shampoo	50 x 1 unit	Encoded	Room temperature

2.2.2 Application

Zone	Frequency	Directions for use
Scalp	3-7 times per week	Use on wet hair and scalp. Foam the shampoo bar in your hands and then scrub it to your hair to get some foam on them. You can also foam the shampoo bar directly on your hair. Then scrub thoroughly the scalp and hair with foam, rinse well.

2.2.3 Labelling

Example of labelling of each product by EUROFINS Dermscan/Pharmascan and translation:

DERMSCAN Badanie n°	DERMSCAN Study #
Nr Ochotnika: ..... Nr Dermscan: ..... W nagłej potrzebie:	Subject#:..... Dermscan ref.: ..... Emergency telephone number: .....
Warunki przechowywania:	Conservation: .....
Przechowywać z dala od dzieci i ich zasięgu wzrokowego. Stosować pod kontrolą medyczną tylko dla potrzeb badania.	Keep out of reach and sight of children. To be used only under strict medical supervision for clinical trial.

2.2.4 Storage

Until the beginning of the study, products are kept at room temperature in a dedicated air-conditioned room, which is locked and access controlled.

2.2.5 Attribution to the subjects

➔ *Product*

All the subjects receive the same product reference.

➔ *Application zones*

Not applicable. All the subjects apply the product to the same zone.

2.2.6 Handing-out

The products are delivered to the subjects by the investigator with an explanation of the application conditions.

2.2.7 Future

As far as possible, one sample of the study product is kept by the investigation center for a period of six months after its receipt.

- **By default, the products (used and not used) are destroyed at the end of the study according to the current internal EUROFINS Dermscan/Pharmascan procedures.**

2.3 STUDY STAGES

ON D0:

Subjects:

- come to the investigation center without having applied any product on the scalp;
- are informed about the trial objectives, the procedures and the risks of the study with the information sheet;
- sign two copies of the Consent Form;
- perform the auto-score of itching and dandruff.

Dermatologist:

- conducts an epidemiological interview;
- verifies inclusion and non-inclusion criteria;
- performs a clinical examination of the scalp;
- asks the subjects about their usual unpleasant sensations (cutaneous level);
- assesses the clinical score of the rash (psoriasis area) on the scalp for product's efficacy evaluation;
- gives to the subjects:
  - the **product** to be used according to the instructions in 2.2.1 and 2.2.2,
  - the **daily log** to write down their possible unpleasant sensations or medications.

+ See **Appendix 7.2**.

ON D28 (±1) (last application being done the day before the visit – D27):

Subjects:

- return to the investigation center without having applied any product to the studied zone since the previous day;
- bring back their daily log and study product/packaging;
- perform the auto-score of the itching and dandruff;
- fill in the subjective evaluation questionnaire.

+ See **Appendix 7.6**.

Dermatologist:

- conducts an epidemiological interview;
- performs a new clinical examination of the scalp;
- asks the subjects about the unpleasant sensations they felt during the study to assess the cutaneous acceptability of the study product;
- assesses the scalp state for global efficacy evaluation;
- performs the clinical score of the rash (psoriasis area) on the scalp for the product's efficacy evaluation;
- collects possible adverse events.

2.4 DATA ANALYSIS

The following data are analyzed:

	Parameter(s)	Unit(s)	Variation(s) DX/D0 Kinetics	Statistical analysis (tick if yes)	Expected result(s)
Cutaneous acceptability	Clinical signs observed Functional and physical signs reported by the subjects	/	D28/D0	/	No worsening
Global efficacy score	7-point scale	%	D28	% improvement	
Efficacy clinical score	Item	/	D28/D0	X	↘
Auto-score	Items	/	D28/D0	X	↘
Subjective evaluation	Questionnaire	%	D28	Statistically significant proportion of positive answers	

Individual data are presented in raw value tables. These tables also show the descriptive statistics: means, medians, minima, maxima, standard errors of the means (SEM) and confidence intervals of 95% (95% CI).

2.4.1 Calculation formulas

The variations (Δ) and in percentage on the mean (Δ%) are calculated according to the following formulas:

$$\Delta = TZ_{ti} - TZ_{t0}$$

with: TZ: value obtained on the zone treated by the tested product
t0: before product application
ti: at each measurement time after product application

2.4.2 Statistical method

NORMALITY OF THE DIFFERENCES

Determined by: **SHAPIRO-WILK TEST** (α=0.01)

According to the result of the normality test, we perform either:

PAIRED STUDENT T-TEST(1)	**WILCOXON SIGNED RANK TEST**(2)

Analysis conditions	p-value	H0	Conclusion
Type I error (α) = 5% in bilateral / unilateral mode	**p ≤ 0.05**	Rejected	Statistically significant difference
Null hypothesis (H0)= no difference between means(1) or medians(2)	**p > 0.05**	Not rejected	No statistically significant difference

Moreover, to evaluate the significance of the answers to the subjective evaluation questionnaire, the 95% confidence interval is determined according to the Wilson method and compared to the theoretical proportion of 50%:

Statistical hypotheses	p-value	H0	Conclusion
Null hypothesis (H0): Proportion of positive answers ≤50%	**p ≤ 0.05**	Rejected (α= 5%)	**Proportion of positive answers is significantly superior to 50%**
Alternative hypothesis (H1): Proportion of positive answers > 50%	**p > 0.05**	Not Rejected	Proportion of positive answers is not significantly superior to 50%

2.4.3 Statistical software

The software used is Excel and SAS 9.4.

2.5 AUDIT AND TRIAL MONITORING VISIT

An audit and/or trial monitoring visit may be carried out at the Sponsor's request or by the appropriate regulatory authority. The aim of the monitoring visit is to verify that the study is conducted according to the determined protocol and current regulations.

- **No monitoring visit occurred for this study.**

3 PRINCIPLES AND RESULTS

3.1 UNDESIRABLE EFFECTS / ADVERSE EVENTS

No Undesirable Effects was observed during the study.

No Serious Adverse Event was reported during the study.

3.2 CUTANEOUS ACCEPTABILITY

3.2.1 Principle

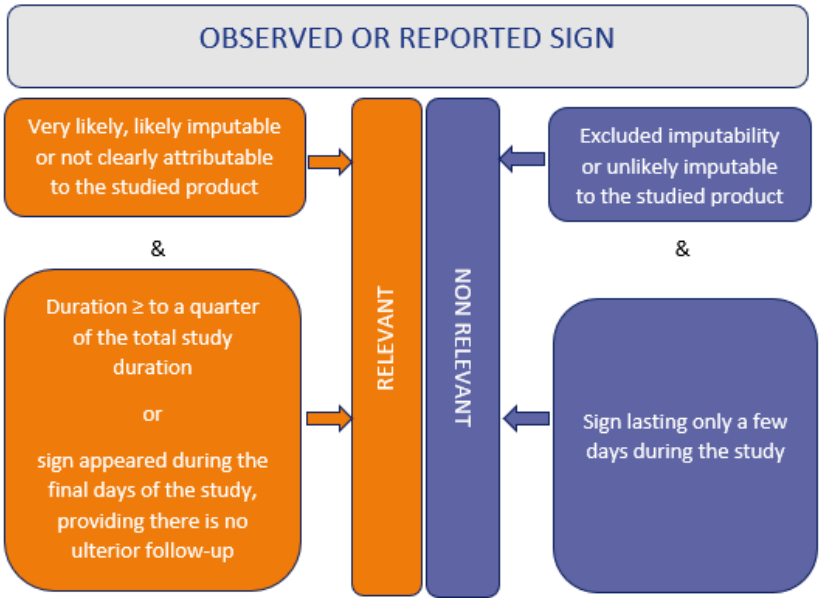
Before (D0) and after 28 days of the product use, the subject's scalp is examined by the dermatologist in charge of study to assess each of the following parameters:

	NONE	VERY MILD	MILD	MODERATE	SEVERE
Dandruff state	☐	☐	☐	☐	☐
Greasy scalp	☐	☐	☐	☐	☐
Erythema	☐	☐	☐	☐	☐
Desquamation	☐	☐	☐	☐	☐
Dryness	☐	☐	☐	☐	☐
Others	☐	☐	☐	☐	☐
Please define:	.....				

On D0, the subjects are also asked about their usual functional and physical signs (usual ones and felt on D0):

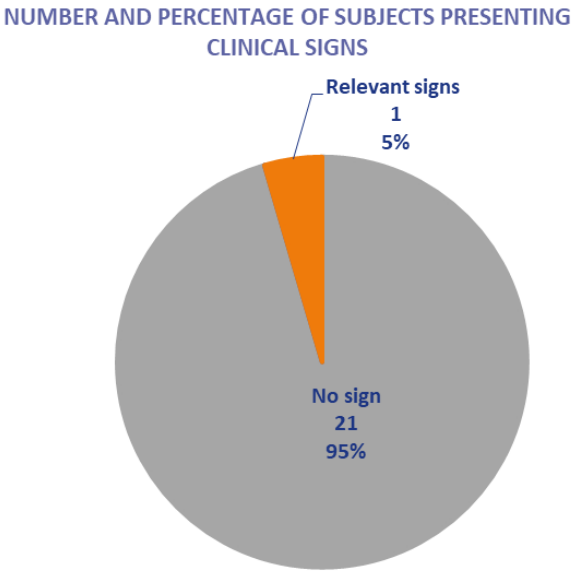
	NONE	VERY MILD	MILD	MODERATE	SEVERE
Tightness	☐	☐	☐	☐	☐
Stinging	☐	☐	☐	☐	☐
Itching / Pruritus	☐	☐	☐	☐	☐
Warm, burning sensation	☐	☐	☐	☐	☐
Dandruff state	☐	☐	☐	☐	☐
Greasy scalp	☐	☐	☐	☐	☐
Redness / Erythema	☐	☐	☐	☐	☐
Desquamation	☐	☐	☐	☐	☐
Dryness	☐	☐	☐	☐	☐
Others	☐	☐	☐	☐	☐
Please define:	.....				

At the end of the study, the cutaneous acceptability of the product is assessed by taking into account the relevant elements reported by the subject (functional and physical signs) as well as those noted during the examination (clinical signs).
The confrontation of these signs is used to conclude on the final cutaneous acceptability of the studied product.



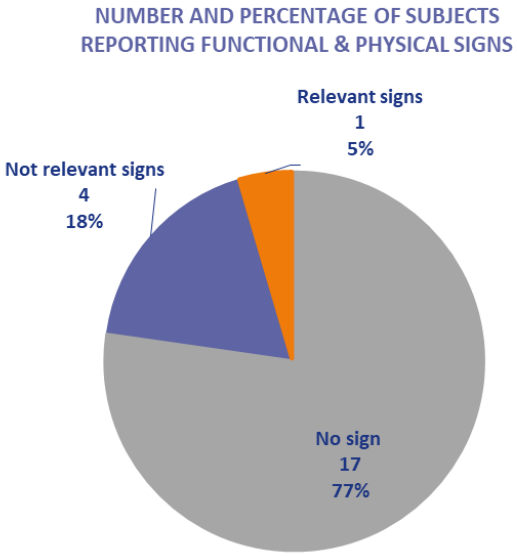
3.2.2 Summary of the results

❖ *Clinical signs*



Observed clinical signs		
SUBJECT NUMBER	TYPE OF SIGNS	RELEVANCE
1	Moderate dandruff state on the parietal and temporal areas on D28 (likely imputable, usual sign). Mild erythema on the parietal area on D28 (likely imputable, usual sign). Moderate desquamation on parietal and temporal areas on D28 (likely imputable, usual sign).	Relevant

❖ *Functional and physical signs reported by subjects*



Functional & physical signs reported by the subjects

SUBJECT NUMBER	FUNCTIONAL SIGNS	PHYSICAL SIGNS	RELEVANCE
1	Moderate itching on the whole scalp just after the product application from one hour up to whole day from D0 to D2 and on D4, D6, D8, D10, D12, D14, D16, D18, D20, D22, D24, D26. (likely imputable, usual sign).	None	Not relevant
4	Very mild tightness on back on the occipital area after hair drying (10-15 minutes after product application) during ten minutes on D1, D3 and D25 (likely imputable, usual sign).	None	Not relevant
17	Mild itching on the forhead 15 minutes after the product application during one hour on D3 (likely imputable). Moderate burning sensation around the left eye one hour after application during whole day on D25 (likely imputable).	None	Not relevant
19	Mild tightness on the cheeks one hour after the product application during ten minutes on D0 (likely imputable, usual sign). Mild tightness on the scalp one hour after the product application during ten minutes on D1 (likely imputable).	Mild dandruff state on the scalp one hour after the product application during whole day on D2 (likely imputable, usual sign). Very mild dryness on the cheeks one hour after the product application during less than five minutes on D3 (likely imputable, usual sign). Very mild dryness on the scalp one hour after the product application during whole day on D4 (likely imputable, usual sign). Moderate hair roughness on the head just after the product application during whole day on D5 (it is not a sign of product intolerance).	Not relevant
20	None	Moderate hair dryness just after the product application during less than five minutes on D1 (likely imputable). **Mild hair dryness just after the product application during less than five minutes on D8, D10, D13, D15, D17, D20, D22, D25, D27 (likely imputable).** Moderate hair roughness just after the product application during less than five minutes on D5 (it is not a sign of product intolerance).	Relevant

Four subjects (#1, 4, 17 and 19) reported functional signs and one of them (#19) reported also physical signs. Moreover one subject (#20) reported only physical signs. Signs reported by subject #20 was judged as relevant.
Clinical signs (worsened in comparison to D0 state) was observed in one subject (#1) on D28 and was judged as relevant.
Under these study conditions, after 28 days of three to seven times per week use the Investigator judged the product "VIHREÄ TEE & KAMOMILLA SHAMPOO" as well-tolerated on the cutaneous level.

3.3 GLOBAL EFFICACY EVALUATION

3.3.1 Principle

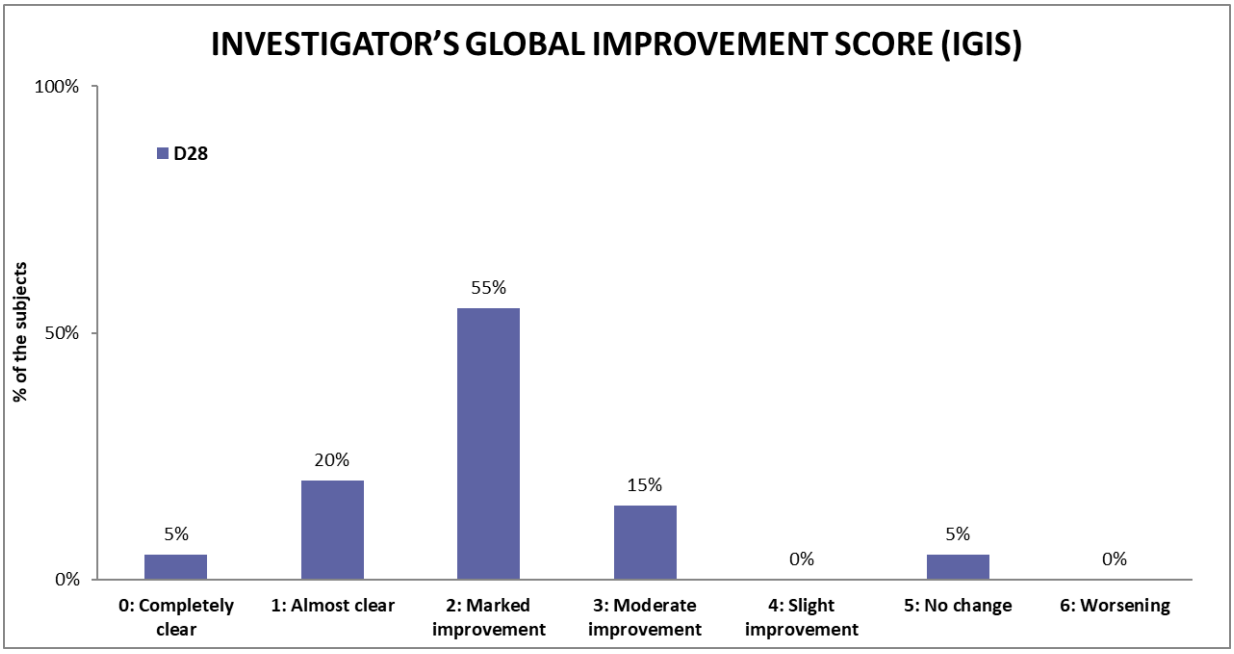
The investigator assesses on a 7-point scale evaluation of global improvement on D28 with structured scales from 0 to 6.
The scales are presented below:

Investigator's Global Improvement Score (IGIS)	
Score	**Description**
0	**Completely clear.** Except for possible residual discoloration.
1	**Almost Clear**. Very significant clearance (about 90%); however, slight degree of scaling and elevation as well as some erythema may be present.
2	**Marked improvement.** Significant improvement (about 75%); however, some disease remaining.
3	**Moderate improvement.** Intermediate between slight and marked, representing about 50% improvement.
4	**Slight improvement.** Some improvement (about 25%); however, significant disease remaining.
5	**No change.**
6	**Worsening.**

3.3.2 Summary of the results

The individual results are presented in **Appendix 7.5.**
A synthesis of the results obtained is presented below:

	D28
0: Completely clear	5%
1: Almost clear	20%
2: Marked improvement	55%
3: Moderate improvement	15%
4: Slight improvement	0%
5: No change	5%
6: Worsening	0%



After 28 days of three to seven times a week of use, of the product: "VIHREÄ TEE & KAMOMILLA SHAMPOO":

- presented a global improvement of the scalp skin state, characterized by Investigator's Global Improvement Score (IGIS) assessed by the dermatologist:

Investigator's Global improvement Score (IGIS):

- completely clear of 5%,
- almost clear of 20%,
- marked improvement of 55%,
- moderate improvement of 15%,
- no change of 5%;

3.4 CLINICAL SCORE BY THE DERMATOLOGIST

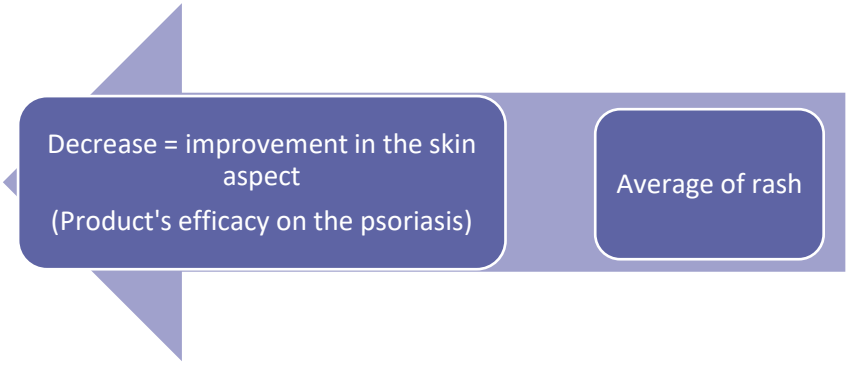
3.4.1 Principle

The investigator assesses the clinical score of the rash (visible psoriasis area) on scalp on D0 and D28 with structured 11-point scale from 0 to 10.
The scales are presented below:

Rash

☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
0	1	2	3	4	5	6	7	8	9	10

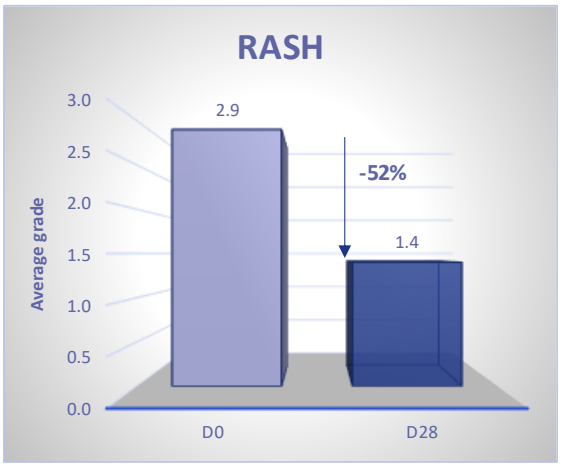
No rash Severe rash



3.4.2 Summary of the results

A synthesis of the results obtained is presented below:

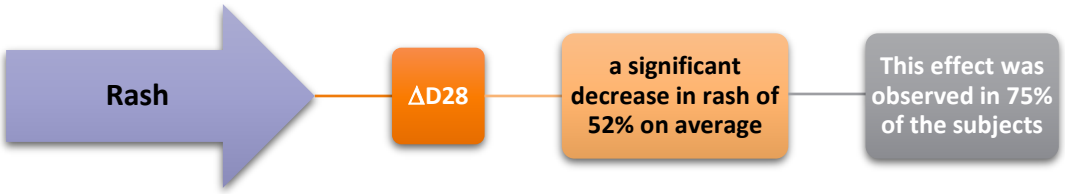
								Statistical analysis			
	Number of subjects	D0 mean ± SEM	Dx mean ± SEM		Δ Dx-D0 (mean ± SEM)		Δ% on mean	p	significant	Test	% of subjects with the expected effect
Rash	20	2.9 ± 0.5	D28	1.4 ± 0.3	Δ D28	-1.5 ± 0.3	-52%	<0.0001	Yes	t-test	75%



Less rash on the scalp: significant decrease in the average grade of rash in 52%
⇨ 75% of the subjects on D28

After 28 days of three to seven times a week of use, of the product: "VIHREÄ TEE & KAMOMILLA SHAMPOO":

- presented an improvement of the scalp rash state (psoriasis area), characterized by clinical score assessed by the dermatologist:



3.5 AUTO-SCORE BY THE SUBJECT

3.5.1 Principle

The subject will assess on a 11-point scale from 0 to 10 the efficacy of the investigational product on itching and dandruff on D0 and after 28 days of use.
The scales are presented below.

1. Itching

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10
No itching Severe itching

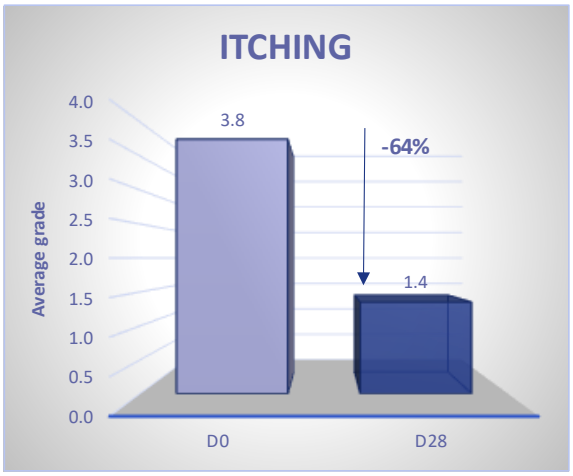
2. Dandruff

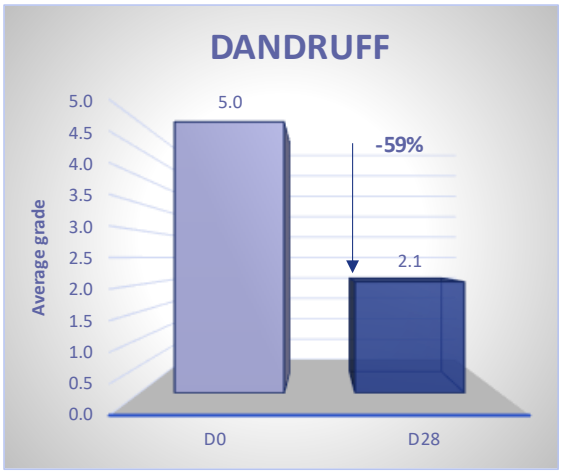
☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10
No dandruff Severe dandruff

3.5.2 Summary of the results

A synthesis of the results obtained is presented below:

	Number of subjects	D0 mean ± SEM	Dx mean ± SEM	Δ Dx-D0 (mean ± SEM)	Δ% on mean	Statistical analysis p	significant	Test	% of subjects with the expected effect
Itching	20	3.8 ± 0.5	D28 1.4 ± 0.4	Δ D28 -2.4 ± 0.4	-64%	<0.0001	Yes	t-test	85%
Dandruff	20	5.0 ± 0.4	D28 2.1 ± 0.4	Δ D28 -3.0 ± 0.3	-59%	<0.0001	Yes	Wilcoxon	95%





Less itching on the scalp: significant decrease in the average grade of itching in 64%
⇨ 85% of the subjects on D28

Less dandruff: significant decrease in the average grade of dandruff in 59%
⇨ 95% of the subjects on D28

After 28 days of three to seven times a week of use, of the product: "VIHREÄ TEE & KAMOMILLA SHAMPOO":

- presented an improvement of the itching, characterized by auto-score assessed by the subjects:

Itching → **ΔD28** → **a significant decrease in itching of 64% on average** → **This effect was observed in 85% of the subjects**

- presented an improvement of the dandruff state, characterized by auto-score assessed by the subjects:

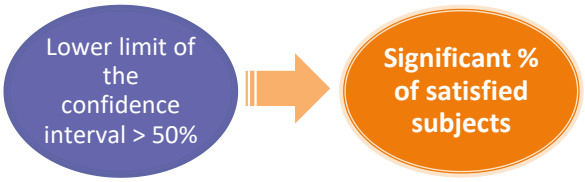
Dandruff → **ΔD28** → **a significant decrease in dendruff of 59% on average** → **This effect was observed in 95% of the subjects**

3.6 SUBJECTIVE EVALUATION QUESTIONNAIRE

3.6.1 Principle

A subjective evaluation questionnaire, prepared by the clinical trial centre and submitted to the sponsor, is filled in by the subjects at the end of the study (D28) to subjectively evaluate the properties of the studied product, its global efficacy and its future use.

To evaluate the significance of the answers, the 95% confidence interval is determined according to the Wilson method and compared to the theoretical proportion of 50% (see § 1.4.2)

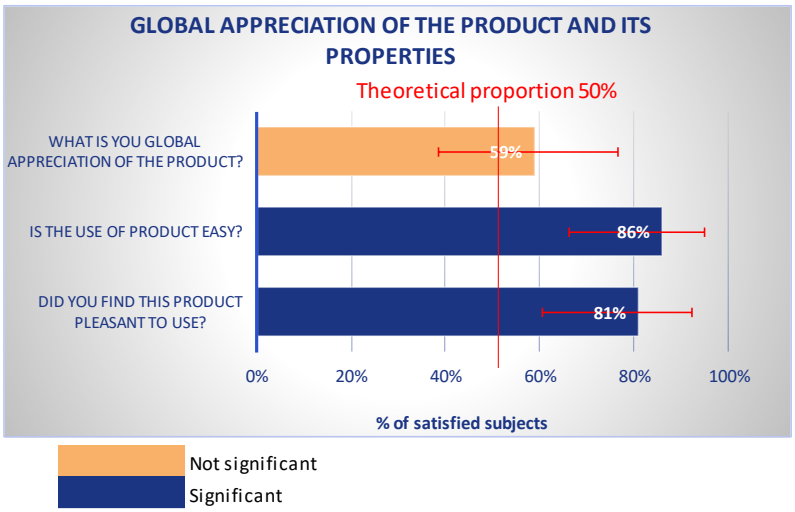


3.6.2 Summary of the results

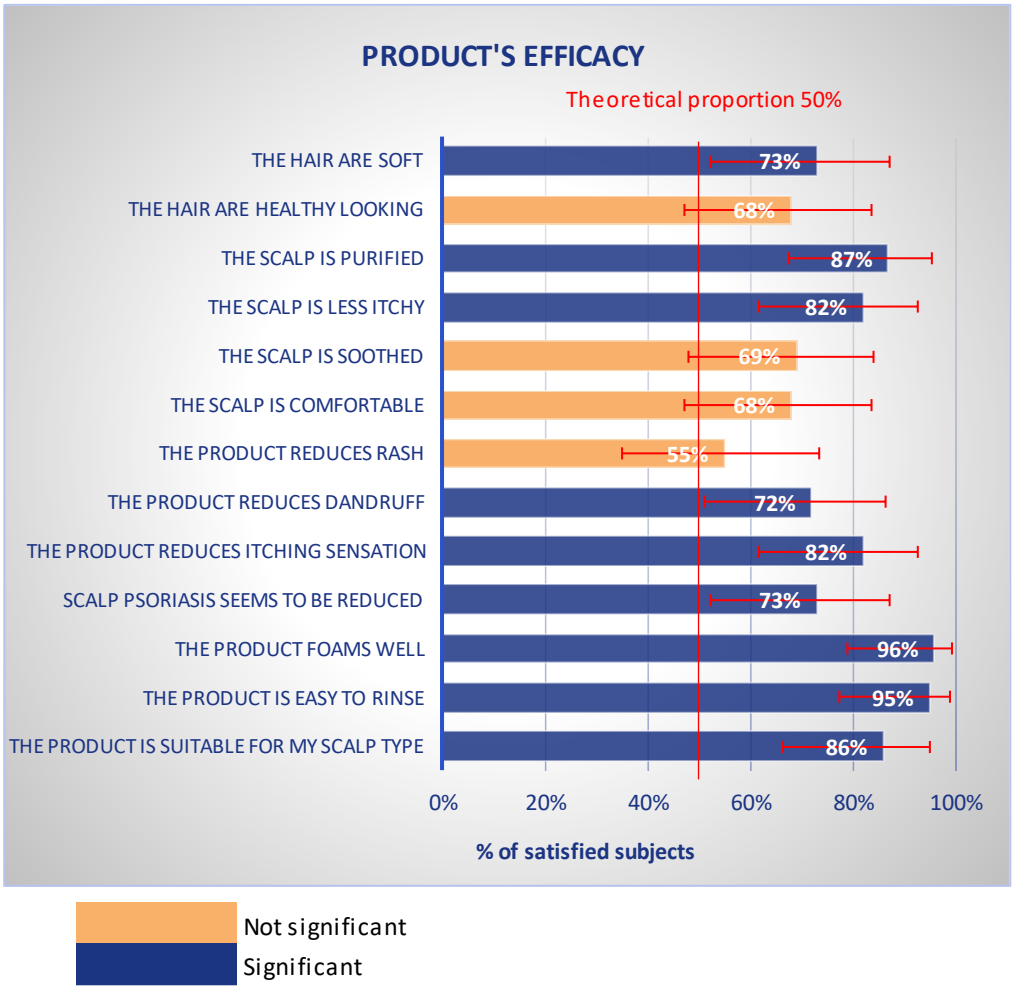
The subjects' answers to the subjective evaluation questionnaire are presented in **Appendix 7.6.**

To be easier to read, the percentages are rounded off. The sum of these percentages may be different from 100%.
In this study (n=22), one subject represents 4.5%.

GENERAL APPRECIATION OF THE PRODUCT AND ITS PROPERTIES	After 28 days			
			Significativity	
	% of positive answers	very pleasant / pleasant	Lower limit > 50%	95% CI
What is you global appreciation of the product?	59%	(14% / 45%)	No	(39% - 77%)
			Significativity	
	% of positive answers	agree /somewhat agree	Lower limit > 50%	95% CI
Is the use of product easy?	**86%**	(59% / 27%)	Yes	(66% - 95%)
Did you find this product pleasant to use?	**81%**	(36% / 45%)	Yes	(61% - 92%)

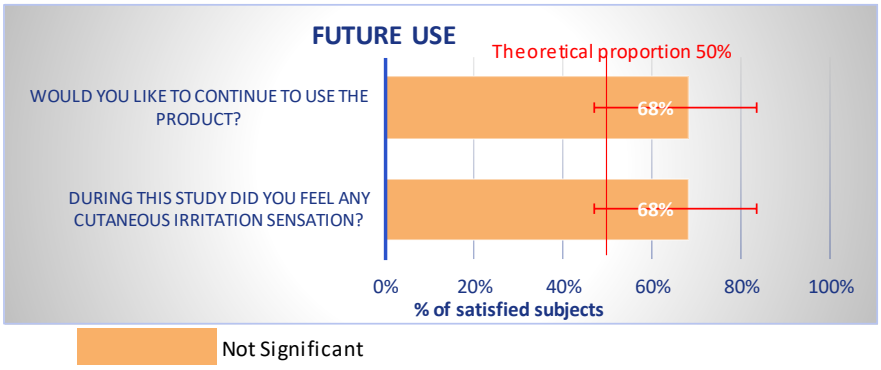


PRODUCT'S EFFICACY	After 28 days			
			Significativity	
	% of positive answers	agree /somewhat agree	Lower limit > 50%	95% CI
The hair are soft	**73%**	(18% / 55%)	Yes	(52% - 87%)
The hair are healthy looking	68%	(32% / 36%)	No	(47% - 84%)
The scalp is purified	**87%**	(64% / 23%)	Yes	(67% - 96%)
The scalp is less itchy	**82%**	(68% / 14%)	Yes	(62% - 93%)
The scalp is soothed	69%	(55% / 14%)	No	(48% - 84%)
The scalp is comfortable	68%	(50% / 18%)	No	(47% - 84%)
The product reduces rash	55%	(41% / 14%)	No	(35% - 73%)
The product reduces dandruff	**72%**	(45% / 27%)	Yes	(51% - 86%)
The product reduces itching sensation	**82%**	(59% / 23%)	Yes	(62% - 93%)
Scalp psoriasis seems to be reduced	**73%**	(32% / 41%)	Yes	(52% - 87%)
The product foams well	**96%**	(64% / 32%)	Yes	(79% - 99%)
The product is easy to rinse	**95%**	(68% / 27%)	Yes	(78% - 99%)
The product is suitable for my scalp type	**86%**	(36% / 50%)	Yes	(66% - 95%)



ACCEPTABILITY	After 28 days			
			Significativity	
	% of positive answers	No	Lower limit > 50%	95% CI
During this study did you feel any cutaneous irritation sensation?	**82%**	(82%)	Yes	(62% - 93%)

FUTURE USE	After 28 days			
			Significativity	
	% of positive answers	yes	Lower limit > 50%	95% CI
Would you like to continue to use the product?	68%	(68%)	No	(47% - 84%)
At the end of this study would you like to buy this product (regardless of the price)?	68%	(68%)	No	(47% - 84%)



Vol	Q4 What did you LIKE about this product?
1	Product is easy to use. Leaves hair soft and shiny.
2	None
3	Easy to use.
4	Reduces the inflammation of the scalp and the amount of scales/dandruff.
5	None
6	Pleasant fragrance.
7	Easy to use.
8	Easy to use.
9	Easy to use.
10	None
11	Easy to spread.
12	Form of the product.
13	Foams and spreads easily.
14	Foams easily and it is very efficient.
15	Efficient product, brings effect quickly. Reduces itching, foams nice.
16	Applies and rinses easily. It is efficient and has delicate fragrance.
17	None
18	None
19	None
20	Foams richly after application.
21	It foams "just right" - not too much, not too little.
22	Fragrance.

Vol	Q5 What did you DISLIKE about this product?
1	Leaves scalp itchy.
2	None
3	No fragrance.
4	Hair was more rough and dry.
5	None
6	Bar form of the product could be replaced with liquid form.
7	Soap after use sticks to every surface.
8	None
9	Fragrance
10	None
11	Stiff and dry hair after wash.
12	Square bar of the soap.
13	Cube bar - could be more oval.
14	Cube bar form is not comfortable to use.
15	None
16	None
17	None
18	None
19	None
20	My hair were unpleasant to touch after the wash.
21	Eyes stinging during application.
22	The feeling of coarse hair.

4 CONCLUSION

Under these study conditions, after 28 days of once or twice daily use, we observed that:

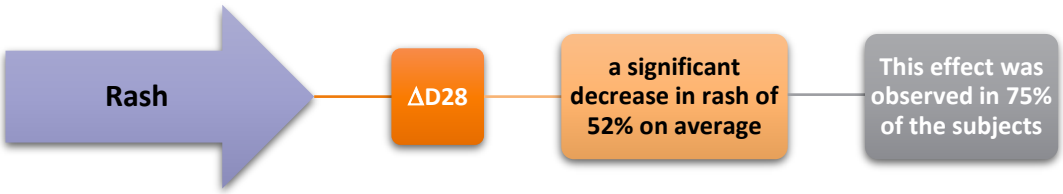
Under these study conditions, after 28 days of three to seven times a week use, the product "VIHREÄ TEE & KAMOMILLA SHAMPOO":

- **was assessed by the dermatologist as having a good tolerance on the cutaneous level;**
- **presented a global improvement of the scalp skin state, characterized by Investigator's Global Improvement Score (IGIS) assessed by the dermatologist:**

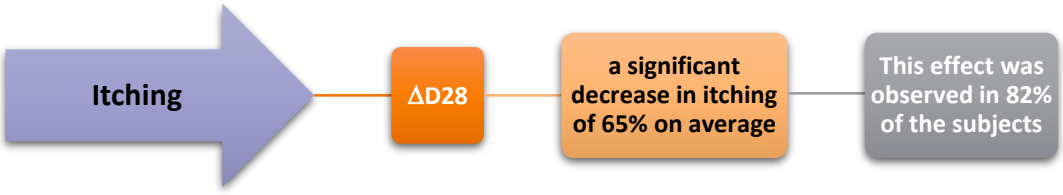
Investigator's Global improvement Score (IGIS):

- completely clear of 5%,
- almost clear of 20%,
- marked improvement of 55%,
- moderate improvement of 15%,
- no change of 5%;

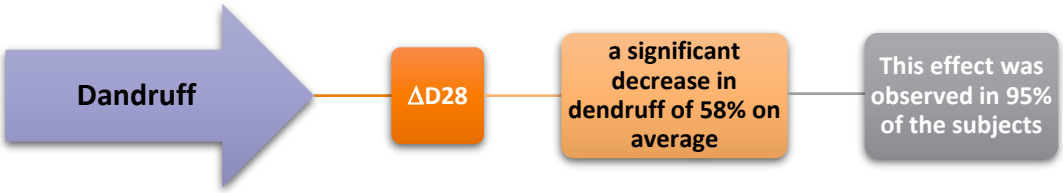
- **presented an improvement of the scalp rash state (psoriasis area), characterized by clinical score assessed by the dermatologist:**



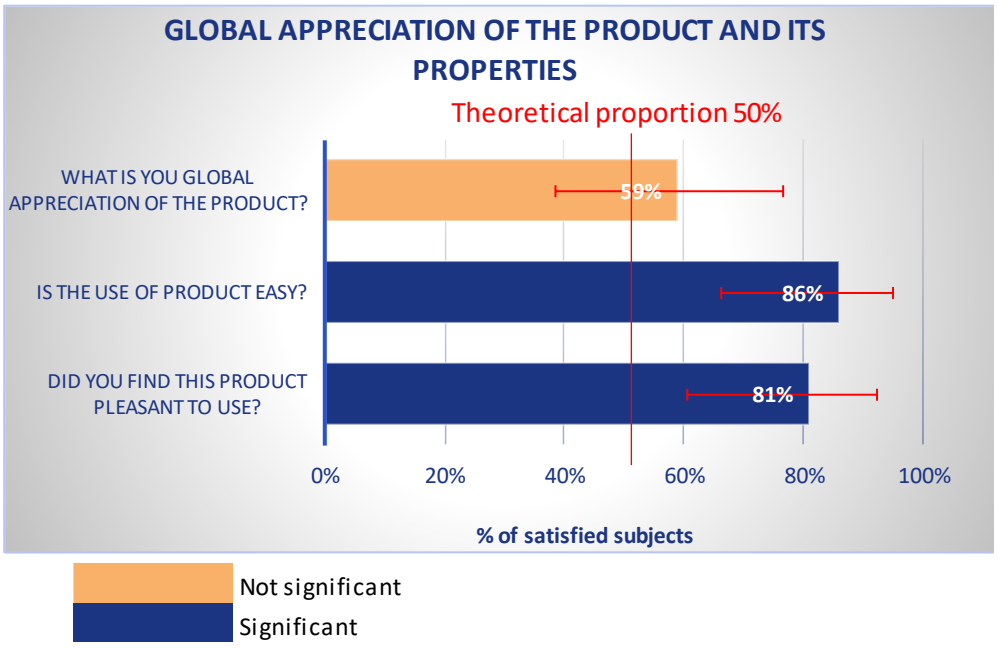
- **presented an improvement of the itching, characterized by auto-score assessed by the subjects:**

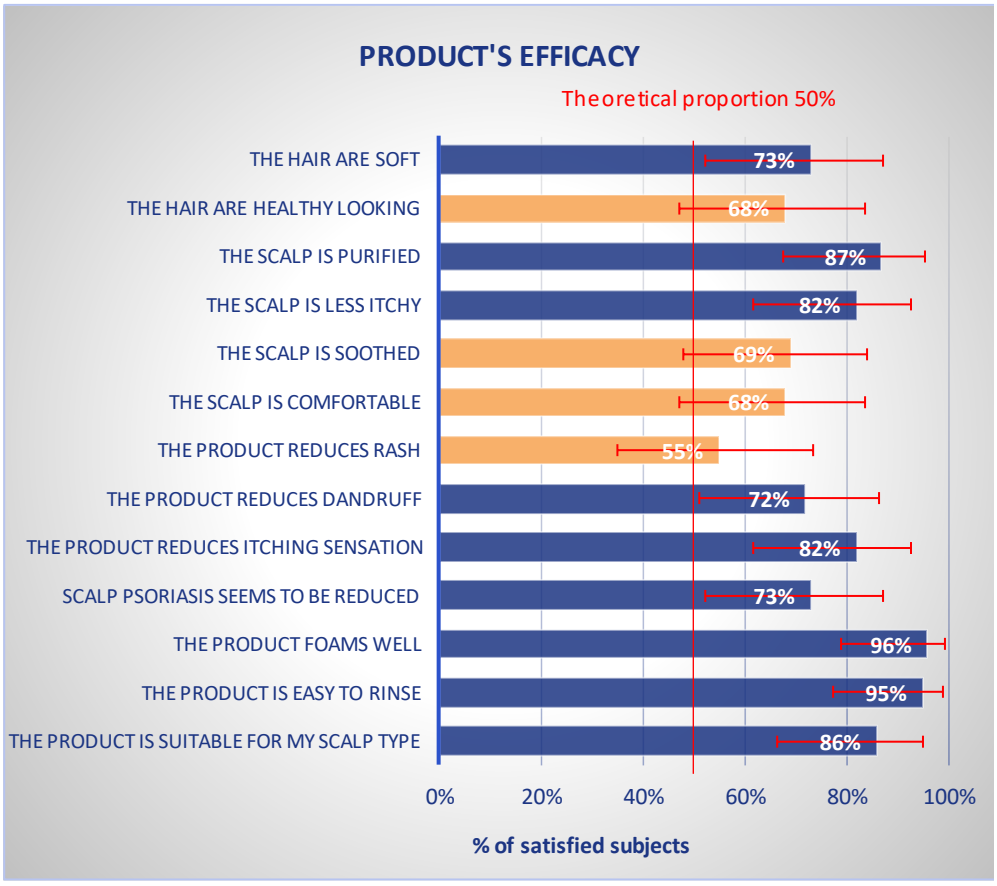


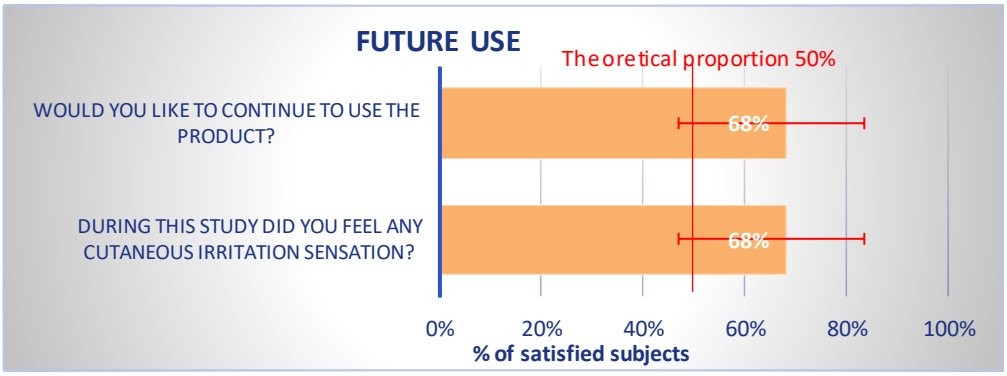
- **presented an improvement of the dandruff state, characterized by auto-score assessed by the subjects:**



➢ **was appreciated by majority of subjects for its properties and efficacy:**







The product "VIHREÄ TEE & KAMOMILLA SHAMPOO" can claim "TOLERANCE TESTED UNDER DERMATOLOGICAL CONTROL"

5 CERTIFICATION

The study is conducted according to Helsinki Declaration (1964) and its successive updates. Data are obtained using the study protocol, current internal procedures and as closely as possible to the guidance on Good Clinical Practice CPMP / ICH / 135 / 95 (R2).

This study is totally performed under the responsibility of EUROFINS Dermscan/Pharmascan.

All the observations and numerical data collected throughout the study are reported in this document and are in accordance with the obtained results.

	INVESTIGATOR - dermatologist	PROJECT MANAGER ASSISTANT
Name	Ewa KARAMON	Karina KUPPER
Date	01/12/2022	01/12/2022
Signature		

Any modifications are the sole responsibility of the author of the modification, whether he/she is acting for the Sponsor or independently.

The on-line publishing, on the Internet, of this study report with the names and signatures is strictly prohibited.

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APPENDICES:

STUDY DOCUMENTS, DETAILED RESULTS
&
ETHICAL REQUIREMENTS AND REGULATORY STANDARDS

7 APPENDICES – STUDY DOCUMENTS/ DETAILED RESULTS

7.1 SUBJECTS' CHARACTERISTICS

Subject #	Last name	First name	Age	Sex	Phototype	Scalp type	Sensitive scalp	Mild to moderate scalp psoriasis	Comments	D0 date	D28 date
1	MA	K	53	F	II	G	Yes	Mild	Protocol non-adherence	2022-08-29	2022-09-27
2	LE	M	34	F	II	G	YES	Mild	None	2022-08-30	2022-09-27
3	WĄ	J	65	F	II	G	Yes	Mild	None	2022-08-30	2022-09-27
4	BI	S	31	F	II	G	Yes	Moderate	None	2022-08-30	2022-09-27
5	PY	J	58	M	II	G	No	Mild	Protocol non-adherence	2022-08-30	2022-09-27
6	LI	K	28	F	II	G	No	Mild	Protocol non-adherence	2022-08-30	2022-09-27
7	WĄ	W	31	M	II	G	Yes	Mild	None	2022-08-30	2022-09-27
8	CI	I	57	F	II	D	Yes	Mild	Protocol non-adherence	2022-09-01	2022-10-03
9	SZ	M	32	F	II	D	Yes	Moderate	Protocol non-adherence	2022-09-01	2022-10-03
10	TO	E	44	F	II	D	Yes	Moderate	None	2022-09-06	2022-10-04
11	KO	L	55	F	II	D	Yes	Mild	None	2022-09-06	2022-10-04
12	GO	E	37	F	II	D	Yes	Mild	None	2022-09-06	2022-10-04
13	MA	C	54	M	II	D	Yes	Moderate	None	2022-09-06	2022-10-04
14	RA	K	19	M	II	G	Yes	Mild	None	2022-09-07	2022-10-05
15	MA	P	31	M	I	D	Yes	Moderate	None	2022-09-07	2022-10-05
16	MA	R	30	M	II	D	Yes	Moderate	None	2022-09-07	2022-10-05
17	JU	B	66	F	II	N	Yes	Mild	**Protocol non-adherence**	2022-09-12	2022-10-10
18	SK	M	64	F	II	D	Yes	Mild	**Protocol non-adherence**	2022-09-12	2022-10-10
19	SK	M	65	F	II	D	Yes	Mild	None	2022-09-12	2022-10-11
20	BR	A	56	F	II	D	Yes	Mild	Protocol non-adherence	2022-09-12	2022-10-11
21	FI	J	60	M	III	G	No	Moderate	None	2022-09-21	2022-10-19
22	MA	M	22	M	II	G	No	Mild	Protocol non-adherence	2022-09-21	2022-10-19

Mean	**45**	**F**	14	**I**	1	**N**	1	**Yes**	18	**Mild**	15
Median	49	**M**	8	**II**	20	**D**	11	**No**	4	**Moderate**	7
Minimum	*19*			**III**	1	**G**	10				
Maximum	*66*			**IV**	0						
SEM	**3**										
95% CI	7										

Legend: F: female
M: male
N: normal
D: dry
G: greasy

7.2 DAILY LOG (TRANSLATION)

eurofins | Dermscan Pharmascan

KARTA BIEŻĄCEJ OBSERWACJI (miejscowo)

PONIŻSZA TABELA MUSI BYĆ WYPEŁNIANA KAŻDEGO DNIA **długopisem (nie ołówkiem).** Jeśli produkt nie był aplikowany, należy wpisać "0" w polu "Ilość"

Badany produkt | Przypomnienie warunków stosowania produktu

DZIEŃ	DATA	ILOŚĆ DZIENNYCH APLIKACJI	ODCZUWALNY DYSKOMFORT I/LUB OZNAKI NIETOLERANCJI	RODZAJ REAKCJI SKÓRNYCH LUB DYSKOMFORTU (np.: zaczerwienienie, obrzęk, suchość, pieczenie, mrowienie, swędzenie, ściąganie ...)	MIEJSCE (np.: policzki, czoło...)	CZAS WYSTĄPIENIA REAKCJI OD MOMENTU APLIKACJI/ZASTOSOWANIA PRODUKTU (np.: zaraz po aplikacji, po x minutach, itd...)	CZAS TRWANIA (np.: kilka minut, przez cały czas, itd...)	INTENSYWNOŚĆ 1 bardzo lekkie 2 lekkie 3 średnie 4 ostre	NORMALNY OBJAW PO ZASTOSOWANIU TEGO TYPU PRODUKTU (tak lub nie)	UŻYCIE LEKÓW		
										Użycie?	Jaki?, dlaczego?	Jaka dawka? Jak długo?
Np.	*10/12/2020*	1	☒Tak ☐ Nie	*Zaczerwienienie*	*Czoło*	*5 minut po aplikacji*	*10 minut*	*2*	*tak*	☒Tak ☐ Nie	*Paracetamol, ból głowy*	*500 mg x 1*
D0		Rano Wieczorem ☐ ☐	☐ Tak ☐ Nie							☐ Tak ☐ Nie		
D1			☐ Tak ☐ Nie							☐ Tak ☐ Nie		
D2			☐ Tak ☐ Nie							☐ Tak ☐ Nie		
D3			☐ Tak ☐ Nie							☐ Tak ☐ Nie		
D4			☐ Tak ☐ Nie							☐ Tak ☐ Nie		
D5			☐ Tak ☐ Nie							☐ Tak ☐ Nie		
D6			☐ Tak ☐ Nie							☐ Tak ☐ Nie		

..../.....
D28

7.3 CONCOMITANT TREATMENTS

Subject #	Medication (sales name)	Indication	Beginning of treatment (compared to the kinetics)	End of treatment (compared to the kinetics)
4	Paracetamol	Headache	D 8	D 8
	Ibuprom®	Stomach ache	D 12	D 12
5	Sinupret® Extra	Runny nose	D 14	D 18
6	Apap®	Headache	D 2	D 2
		Menstual pain	D 2	D 4
7	Apap®	Headache	D 18	D 18
			D 25	D 25
10	Paracetamol	Headache	D 13	D 14
11	Aglan®	Spine pain	D 4	D 8
17	Pyralgina®	Headache	D 22	D 22
18	Diclac®	Spine pain	D 4	D 4
			D 23	D 23
19	Solpadeine®	Headache	D 0	D 0
	Naproxen®		D 2	D 2
		Knee pain	D 5	D 5
20	Persen® Forte	Neurosis	D 1	D 1
			D 8	D 8
			D 10	D 10
			D 15	D 15
			D 17	D 17
	Clonazepamum®		D 2	D 2
			D 5	D 5
			D 22	D 22

7.4 CUTANEOUS ACCEPTABILITY- INDIVIDUAL RESULTS

Cutaneous acceptability

SCALP

Subject#	Signs reported by the subjects		Clinical signs observed on D28
	Functional signs	Physical signs	
1	Moderate itching on the whole scalp just after the product application from one hour up to whole day from D0 to D2 and on D4, D6, D8, D10, D12, D14, D16, D18, D20, D22, D24, D26. (likely imputable, usual sign).	None	**Moderate dandruff state on the parietal and temporal areas on D28 (likely imputable, usual sign).** **Mild erythema on the parietal area on D28 (likely imputable, usual sign).** **Moderate desquamation on parietal and temporal areas on D28 (likely imputable, usual sign).**
2	None	None	None
3	None	None	None
4	Very mild tightness on back on the occipital area after hair drying (10-15 minutes after product application) during ten minutes on D1, D3 and D25 (likely imputable, usual sign).	None	None
5	None	None	None
6	None	None	None
7	None	None	None
8	None	None	None
9	None	None	None
10	None	None	None
11	None	None	None
12	None	None	None
13	None	None	None
14	None	None	None
15	None	None	None
16	None	None	None
17	Mild itching on the forhead 15 minutes after the product application during one hour on D3 (likely imputable). Moderate burning sensation around the left eye one hour after application during whole day on D25 (likely imputable).	None	None
18	None	None	None
19	Mild tightness on the cheeks one hour after the product application during ten minutes on D0 (likely imputable, usual sign). Mild tightness on the scalp one hour after the product application during ten minutes on D1 (likely imputable).	Mild dandruff state on the scalp one hour after the product application during whole day on D2 (likely imputable, usual sign). Very mild dryness on the cheeks one hour after the product application during less than five minutes on D3 (likely imputable, usual sign). Very mild dryness on the scalp one hour after the product application during whole day on D4 (likely imputable, usual sign). Moderate hair roughness on the head just after the product application during whole day on D5 (it is not a sign of product intolerance).	None
20	None	Moderate hair dryness just after the product application during less than five minutes on D1 (likely imputable). **Mild hair dryness just after the product application during less than five minutes on D8, D10, D13, D15, D17, D20, D22, D25, D27 (likely imputable).** Moderate hair roughness just after the product application during less than five minutes on D5 (it is not a sign of product intolerance).	None
21	None	None	None
22	None	None	None

7.5 GLOBAL EFFICACY EVALUATION – INDIVIDUAL RESULTS

INVESTIGATOR'S GLOBAL IMPROVEMENT SCORE (IGIS)

Subject #	Score value on D28
1	5
2	2
3	2
4	1
5	1
6	1
7	0
8	2
9	2
10	2
11	3
12	2
13	3
14	1
15	2
16	2
*(17)**	*(1)**
*(18)**	*(2)**
19	2
20	2
21	3
22	2
Mean	**2.0**
Median	2
Minimum	*0*
Maximum	*5*
SEM	**0.2**
Subjects %	
0: Completely clear	**5%**
1: Almost clear	**20%**
2: Marked improvement	**55%**
3: Moderate improvement	**15%**
4: Slight improvement	**0%**
5: No change	**5%**
6: Worsening	**0%**

Legend:
0: Completely clear. Except for possible residual discoloration.
1: Almost clear. Very significant clearance (about 90%); however, slight degree of scaling and elevation as well as some erythema may be present
2: Marked improvement. Significant improvement (about 75%); however, some disease remaining.
3: Moderate improvement. Intermediate between slight and marked, representing about 50% improvement.
4: Slight improvement. Some improvement (about 25%); however, significant disease remaining.
5: No change.
6: Worsening.

7.6 CLINICAL SCORE BY THE DERMATOLOGIST – INDIVIDUAL RESULTS

Rash

0 = no rash
10 = severe rash

Subject#	D0	D28	Variations Δ D28
1	1	1	0
2	0	0	0
3	3	1	-2
4	6	2	-4
5	1	0	-1
6	1	1	0
7	1	0	-1
8	1	1	0
9	3	2	-1
10	5	3	-2
11	2	1	-1
12	4	1	-3
13	6	3	-3
14	3	0	-3
15	7	5	-2
16	7	4	-3
*(17)**	*(1)**	*(0)**	*(-1)**
*(18)**	*(2)**	*(2)**	*(0)**
19	1	0	-1
20	0	0	0
21	4	3	-1
22	2	0	-2
Mean	**2.9**	**1.4**	**-1.5**
Median	2.5	1.0	-1.0
Minimum	*0.0*	*0.0*	*-4.0*
Maximum	*7.0*	*5.0*	*0.0*
SEM	**0.5**	**0.3**	**0.3**
95% CI	1.1	0.7	0.6
Nb of subjects	20	20	20
	Δ%		**-52%**
	Statistical analysis p =		**<0.0001**
	Statistical test		**t-test**

% of subjects with the expected effect	**75%**

Legend: ( )*: data non included in the analysis

7.7 AUTO-SCORE BY THE SUBJECTS – INDIVIDUAL RESULTS

Itching

0 = no itching
10 = severe itching

Subject#	D0	D28	Variations Δ D28
1	6	7	1
2	2	0	-2
3	3	1	-2
4	5	0	-5
5	3	0	-3
6	2	0	-2
7	2	0	-2
8	2	0	-2
9	4	2	-2
10	6	2	-4
11	2	1	-1
12	7	1	-6
13	7	4	-3
14	4	1	-3
15	8	4	-4
16	7	4	-3
*(17)**	*(1)**	*(0)**	*(-1)**
*(18)**	*(2)**	*(0)**	*(-2)**
19	3	0	-3
20	2	0	-2
21	0	0	0
22	0	0	0
Mean	**3.8**	**1.4**	**-2.4**
Median	3.0	0.5	-2.0
Minimum	*0.0*	*0.0*	*-6.0*
Maximum	*8.0*	*7.0*	*1.0*
SEM	**0.5**	**0.4**	**0.4**
95% CI	1.1	0.9	0.8
Nb of subjects	20	20	20
	Δ%		**-64%**
	Statistical analysis p =		**<0.0001**
	Statistical test		**t-test**

% of subjects with the expected effect	**85%**

Dandruff

0 = no dandruff
10 = severe dandruff

Subject#	D0	D28	Variations Δ D28
1	5	6	1
2	4	1	-3
3	4	1	-3
4	8	2	-6
5	4	0	-4
6	4	1	-3
7	2	0	-2
8	5	2	-3
9	6	2	-4
10	6	3	-3
11	4	1	-3
12	6	1	-5
13	7	4	-3
14	2	0	-2
15	7	4	-3
16	7	4	-3
*(17)**	*(4)**	*(2)**	*(-2)**
*(18)**	*(4)**	*(2)**	*(-2)**
19	4	2	-2
20	4	1	-3
21	6	4	-2
22	5	2	-3
Mean	**5.0**	**2.1**	**-3.0**
Median	5.0	2.0	-3.0
Minimum	*2.0*	*0.0*	*-6.0*
Maximum	*8.0*	*6.0*	*1.0*
SEM	**0.4**	**0.4**	**0.3**
95% CI	0.8	0.8	0.6
Nb of subjects	20	20	20
	Δ%		**-59%**
	Statistical analysis p =		**<0.0001**
	Statistical test		**Wilcoxon**

% of subjects with the expected effect	**95%**

Legend:
()*: data not included in analysis

7.8 SUBJECTIVE EVALUATION QUESTIONNAIRE

GENERAL APPRECIATION OF THE PRODUCT AND ITS PROPERTIES

What did you think about this product?

		very pleasant	pleasant	neither pleasant nor unpleasant	unpleasant	very unpleasant
1	What is you global appreciation of the product?	14%	45%	41%	0%	0%

		agree	somewhat agree	neither agree nor disagree	somewhat disagree	disagree
2	Is the use of product easy?	59%	27%	5%	9%	0%
3	Did you find this product pleasant to use?	36%	45%	18%	0%	0%
4	What did you LIKE about this product? (open question)					
5	What did you DISLIKE about this product? (open					

PRODUCT'S EFFICACY

What did you think about the product's efficacy after 28 days of use?

		agree	somewhat agree	neither agree nor disagree	somewhat disagree	disagree
6	The hair are soft	18%	55%	9%	9%	9%
7	The hair are healthy looking	32%	36%	27%	5%	0%
8	The scalp is purified	64%	23%	9%	0%	5%
9	The scalp is less itchy	68%	14%	14%	0%	5%
10	The scalp is soothed	55%	14%	23%	5%	5%
11	The scalp is comfortable	50%	18%	23%	5%	5%
12	The product reduces rash	41%	14%	32%	9%	5%
13	The product reduces dandruff	45%	27%	18%	5%	5%
14	The product reduces itching sensation	59%	23%	14%	0%	5%
15	Scalp psoriasis seems to be reduced	32%	41%	23%	0%	5%
16	The product foams well	64%	32%	5%	0%	0%
17	The product is easy to rinse	68%	27%	0%	5%	0%
18	The product is suitable for my scalp type	36%	50%	9%	0%	5%
19	During this study did you feel any cutaneous irritation sensation?	18%	82%	0%	0%	0%

ACCEPTABILITY

		yes	no
20	Would you like to continue to use the product?	68%	32%

FUTURE USE

		yes	no
21	At the end of this study would you like to buy this product (regardless of the price)?	68%	32%

8 APPENDICES - ETHICAL REQUIREMENTS AND REGULATORY STANDARDS

8.1 ADVERSE EVENT

8.1.1 Adverse Event (AE)

Any noxious symptom, occurring in a subject taking part in a clinical trial, whether or not this symptom is related to the study or the study product(s) (e.g. flu, headache, abnormal biological analysis…).

8.1.2 Undesirable Effect (UE) / Adverse Reaction (AR)

For a cosmetic product, an **undesirable effect** is defined as an adverse reaction for human health attributable to the normal or reasonably foreseeable use of the cosmetic product(s).
There are 5 levels of imputability: very likely, likely, not clearly attributable, unlikely and excluded (ANSM methodology).

The severity/intensity of undesirable effects/adverse events can be graded on a three-point scale:

- **mild**: discomfort noted, that does not disturb normal daily activities;
- **moderate**: discomfort sufficient to reduce or affect normal daily activities;
- **severe**: inability to work or have normal daily activities.

8.1.3 Serious Adverse Event (SAE) / Serious Undesirable Effect (SUE)

Any event that:

- results in death (note: death is the outcome, not the event);
- is life threatening;
- requires in-patient hospitalization (at least one night) or prolongation of existing hospitalization (does not include hospitalization scheduled before the inclusion);
- results in temporary or permanent functional incapacity or disability;
- is a congenital anomaly;
- is considered like by the investigator.

8.1.4 Documentation

All concomitant treatments are reported in the CRF (Case Report Form); only those started after the beginning of the study are reported in the study report.

All Undesirable Effects are reported in the CRF and the study report.
If it requires the temporary or definitive termination of the study product, the need for a corrective treatment or the withdrawal of the subject, an Adverse Event form is completed.

All SAE/SUE are reported in the CRF and the study report.

8.1.5 Notification

The investigator declares to the Sponsor, by e-mail, the occurrence of adverse reactions according to their severity and their unexpectedness (according to the investigator's advice).

All SAE/SUE are transmitted by e-mail to the Sponsor without delay, at the latest 24 hours after knowledge of their occurrence.
A SAE/SUE declaration form signed by a physician is sent, within 48 hours, by e-mail with acknowledgement of receipt.

8.1.6 Follow-up

When an adverse event linked to the investigational product or the protocol persists at the end of the study, the Investigator ensures that the subject is followed up until total resolution of the event or stabilization of the symptoms without releasing the Sponsor of any obligation or responsibility.

8.1.7 Occurrence of pregnancy

The occurrence of a pregnancy (reported or diagnosed) after inclusion in the study is considered as an intercurrent event not related to the study product(s) nor the protocol and induces the immediate dropping out of the subject.
Any pregnancy that occurs during the study period is reported by e-mail to the Sponsor within 24 hours following its discovering.
A follow-up is done according to the current internal procedures until the completion/termination of the pregnancy or its interruption.

8.2 PREMATURE TERMINATION OF SUBJECT PARTICIPATION

In compliance with the Helsinki Declaration (1964) and its successive updates, subjects have the right to exit from the study at any time and for any motive.

The investigator can also interrupt the subject participation in the study prematurely in the case of a disease occurrence, a pregnancy or the occurrence of an adverse reaction.

The Sponsor can demand that any subject be excluded from the study for major infringements to the protocol, for administrative reasons or any other motive however this would need to be clearly documented with a rationale as to why.

Nevertheless, premature removal of a high percentage of subjects from the study can make it difficult or impossible to interpret. Consequently, any premature exit without valid motives should be avoided as much as possible and is carefully documented in the case report form, the final report and, if necessary, in the Adverse Event form.

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

- presence of a non-inclusion criteria;
- Undesirable Effect / Adverse Event occurrence;
- Serious Adverse Event / Serious Adverse Effect occurrence;
- withdrawal of consent;
- lost to follow-up;
- appearance of non-inclusion criteria;
- non-adherence to the protocol;
- other reason.

No replacement is foreseen as 10% additional subjects are planned to be included in the study.

8.3 CONFIDENTIALITY AND GENERAL DATA PROTECTION REGULATION

In this study, EUROFINS Dermscan/Pharmascan processes personal data of subjects on behalf of the Sponsor, in accordance with the rules on the protection of personal data and, in particular, the Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data. For this purpose, EUROFINS Dermscan/Pharmascan limits the collection and use of personal data to that which is needed for analysis and control purposes, by ensuring their security and integrity and by guaranteeing their confidentiality.

EUROFINS Dermscan/Pharmascan makes sure beforehand and throughout the duration of the data-processing:
- of the compliance with the obligations of the applicable data protection law,
- to inform subjects of their personal data-processing after obtaining their consent,
- to implement and maintain appropriate technical and organisational measures.

An identification code is attributed to each subject for the purpose to keep his/her identity confidential. This code consists of the first two letters/first letter of the subject's name and the first letter of his/her first name.

According to Article 14 of GDPR, the concerned subject must be informed of the identity and the contact details of the Controller and, where applicable, of the controller's representative. However, considering the objective of the study, to avoid any bias in the investigational product evaluation, the identity of the Sponsor is not revealed to the subject participating.

8.4 DATA COLLECTION AND VALIDATION

The personnel in charge of the study collects data into individual case report forms in electronic (e-CRF CleanWEB™ internet platform) or paper format and/or directly from measurement software.
When information is collected in paper format, the simple/double data entry is then done from these supports by the designed operator(s), without any interpretation, in specific MS EXCEL databases.
The Project Manager or assistant checks the double data entry by comparing both databases.

Then the coherence of the whole data set is checked as well as formulas used in the EXCEL tables (calculation formulas, selected data…).
When all the controls are done, the database is locked.

8.5 QUALITY MANAGEMENT

In order to ensure that the clinical trials are in compliance with the Sponsor's requirement, EUROFINS Dermscan/Pharmascan has implemented a quality management system which has been certified ISO 9001: 2015.
This quality assurance system includes appropriate Good Clinical Practices (GCP) and regulation requirements.

Each study report is subjected to a quality inspection by a member of the EUROFINS Dermscan/Pharmascan Proofreading Committee. The proofreader is chosen because he(she) is not involved in the audited study. The inspection of the study report allows to confirm that the results reflect exactly the study raw data and that the study fulfils any standard and regulatory requirements.
A certificate of quality inspection signed by the person who checked the report is enclosed in each study.

8.6 ARCHIVES OF STUDY DOCUMENTS

<table>
<tr><td>STUDY DOCUMENTS AND DATA</td><td colspan="3">TIME AFTER DISPATCH OF THE FINAL REPORT:
 

0 1 (maximum) 10 YEARS</td></tr>
<tr><td>Paper</td><td>Stored at the investigation center</td><td>Securely archived at an approved service provider</td><td rowspan="2">Destruction of the archives unless otherwise stipulated in writing by the Sponsor</td></tr>
<tr><td>Digital</td><td colspan="2">Securely archived</td></tr>
</table>