ASSESSMENT OF THE SKIN PRIMARY AND ACCUMULATED IRRITATION POTENTIAL AND SKIN SENSITIZATION, PHOTOALLERGY AND PHOTOTOXICITY POTENTIAL OF A PRODUCT TO BE APPLIED TO THE SKIN, UNDER CONTROLLED AND MAXIMIZED CONDITIONS

FINAL REPORT

PRODUCT NAME: FAGRON TRICHOFOAM ESPUMA CAPILAR

PRODUCT CODE: 058870-03
STUDY CODE: All-S-RIPT-FA-FT- 058870-03-10-16
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ASSESSMENT OF THE SKIN PRIMARY AND ACCUMULATED IRRITATION POTENTIAL AND SKIN SENSITIZATION, PHOTOALLERGY AND PHOTOTOXICITY POTENTIAL OF A PRODUCT TO BE APPLIED TO THE SKIN, UNDER CONTROLLED AND MAXIMIZED CONDITIONS

SUMMARY

Product Name:	FAGRON TRICHOFOAM ESPUMA CAPILAR
Product Code:	058870-03
Study Code:	All-S-RIPT-FA-FT- 058870-03-10-16
Report Code:	All-S-RIPT-FA-FT- 058870-03-10-16-RFV01-Rev01
Report Copy Code:	All-S-RIPT-FA-FT- 058870-03-10-16-RETI01-Rev01

STUDY OF PRIMARY AND ACCUMULATED IRRITATION AND SENSITIZATION

STUDY OBJECTIVE	To prove the absence of the skin primary and accumulated irritation potential and skin sensitization potential of a product to be applied to the skin under maximized conditions, with controlled product quantity and application site, supervised by a dermatologist.
METHODOLOGY	Both the test-product and control were applied to patch test filter paper discs and then applied to the right or left back (scapular area) of the study subjects. The applications were performed on Mondays, Wednesdays and Fridays, during 3 consecutive weeks. Forty-eight hours (48h) after the application, the patch test was removed by trained technicians and, approximately 30 minutes after the patch test removal, the site was assessed in order to check the presence of possible clinical signs. After this period (induction) there was a, minimum, 10 day-period when no patch was applied to the study subjects' back (rest period). Then, the challenge period started. A single application of the patch test was performed, followed by readings after 48h and 72h. The study subjects were assessed by a dermatologist at the start and at the end of the study and supervised all along the study.
INVESTIGATOR IN CHARGE	Vivian Pessoto Rosa.
STUDY LENGTH	6 weeks.
FREQUENCY OF APPLICATION	9 applications on the 3 first weeks (induction period). 1 application on the last week (challenge period).
APPLICATION SITE	Back (Scapular area).
NUMBER OF SUBJECTS	59 study subjects.
POPULATION DESCRIPTION	Female and male, age range from 18 to 69 years old, phototype II to IV (Fitzpatrick).
ETHICS	This study was conducted in conformance with the Declaration of Helsinque principles, the applicable regulatory requirements, including Resolution CNS no. 466/12, and in spirit of the Good Clinical Practices (Document of the Americas and ICH E6: Good Clinical Practice).
RESULTS	During the study, no subjects presented skin clinical signs related to the product.
CONCLUSION	The product did not induce primary and accumulated skin irritation and sensitization process in the study group. The product was considered safe under the study conditions.

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PHOTOALLERGY AND PHOTOTOXICITY STUDY

STUDY OBJECTIVE	To prove the absence of the skin photoallergy and phototoxicity potential of a product to be applied to the skin, under maximized conditions, with controlled product quantity and application site, supervised by a dermatologist.
METHODOLOGY	Both the test-product and control were applied to patch test filter paper discs and then applied to the right or left back (scapular area) of the study subjects. The applications were performed on Mondays and Wednesdays, during 3 consecutive weeks. Twenty-four hours (24h) after the application of the patch test, it was removed by trained technicians and approximately 30 minutes after the patch test removal the application site received ultraviolet A and B irradiation. The application site was assessed after each irradiation. On Fridays, only readings were performed. After this period (induction) there was a, minimum, 10 day-period when no patch was applied to the study subjects' back (rest period). Then, the challenge period started. The product was applied again, remaining for a 24-hour period. After 30 minutes of its removal, the area received ultraviolet. A irradiation and was assessed immediately and 24, 48 and 72 hours after the removal. The study subjects were assessed by a dermatologist at the start and at the end of the study and supervised all along the study.
INVESTIGATOR IN CHARGE	Vivian Pessoto Rosa.
STUDY LENGTH	6 weeks.
FREQUENCY OF APPLICATION	6 applications on the 3 first weeks (induction period). 1 application on the last week (challenge period).
APPLICATION SITE	Back (Scapular area).
NUMBER OF SUBJECTS	32 study subjects.
POPULATION DESCRIPTION	Female and male subjects, age range from 20 to 70 years old, phototype II to III (Fitzpatrick).
ETHICS	This study was conducted in conformance with the Declaration of Helsinque principles, the applicable regulatory requirements, including Resolution CNS no. 466/12, and in spirit of the Good Clinical Practices (Document of the Americas and ICH E6: Good Clinical Practice).
RESULTS	During the study, no subjects presented skin clinical signs related to the product.
CONCLUSION	The product did not induce skin photoallergy and phototoxicity processes in the study group. The product was considered safe under the study conditions.

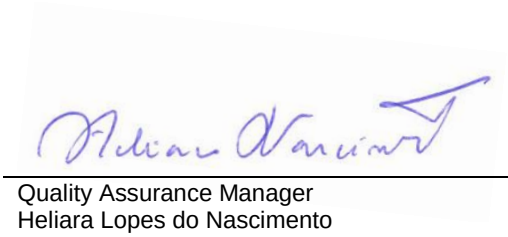
QUALITY ASSURANCE

The study was conducted according to the Resolution CNS no. 466/2012, in the spirit of Good Clinical Practices and in conformity with the Standard Operating Procedures of Allergisa.

Data quality is assured, considering that our personnel is trained according to the study to be carried out, our equipment is always duly calibrated and the methods used are recognized and/or validated.

The Quality Assurance Department is in charge of auditing the Management System; and is fully available for any specific study monitoring carried out by the sponsor.

The signature representing the Quality Assurance System means that the study was conducted as described above.



Quality Assurance Manager
Heliara Lopes do Nascimento
01/26/2017

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CONTENTS

1. ABBREVIATION LIST

ICH E6:	Good Clinical Practice.
GCP	Good Clinical Practices
ICH	International Conference on Harmonisation
ANVISA	Agência Nacional de Vigilância Sanitária (National Health Surveillance Agency).
CNS	Conselho Nacional de Saúde (National Health Council)
IC	Informed Consent

2. INTRODUCTION

Over the last few years, the cosmetic industry has grown considerably, same as its concern in developing safe and effective products. The creation of the Consumer Defense Code, the requirements of the National Agency of Sanitary Surveillance of the Ministry of Health and the competition itself have lead the companies to adopt more careful attitudes concerning the action and benefits of their products by trying to associate their claims to scientific works.

Industry awareness and consumer's and regulatory agencies requirements caused cosmetic manufacturers to adopt procedures that lead them to know better their products: to conduct clinical tests on safety and efficacy, which are coordinated by expert physicians, before marketing a product. These procedures provide cosmetic companies with greater safety, credibility and reliability among their consumers.

Once the cosmetic product becomes freely available for the consumer, it must be safe when applied under normal or reasonably foreseeable conditions of use (ANVISA guide for the Safety Evaluation of Cosmetic Products). For this, the raw materials used in the product formulation must be raw materials with proved safety and with established use in the cosmetic industry. In addition, the safety of the final formulation must be tested before it is marketed, as required in the ANVISA guide for the Safety Evaluation of Cosmetic Products.

According to the Good Clinical Practices, an adverse event is any untoward medical occurrence in a patient or clinical investigation subject using a product that does not necessarily have a causal relationship with the treatment (International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use – ICH).

The contact of the skin with topical products, such as cosmetic products, may trigger different types of reactions. Among these adverse reactions, we can point out eczematous contact dermatitis, urticaria, acne and spots (SAMPAIO & RIVITTI, 2000). In general, the contact dermatitis results from two mechanisms: the primary irritation, through the action of irritant substances; or the sensitization, in the presence of an allergenic ingredient.

In order to evaluate the irritation and sensitization potential of a product, a series of variables must be taken into account: components used in the formulation, ingredient concentration, absorption, amount applied, skin condition, application directions and frequency, as well as the cumulative effect (DOOMS-GOOSSENS, 1993).

Skin permeability varies according to the area of the body, where skin folds and face are areas of higher absorption. When applied to the skin, a product will have greater or smaller percutaneous absorption depending on its concentration, type of vehicle used, skin surface area and contact time with the skin (ZATZ, 1993). Therefore, some body areas are more susceptible to the occurrence of irritation than others are.

Tests conducted with humans are governed by very strict laws in order to protect and safeguard people. These laws vary from country to country. In Brazil, these studies are allowed, if they comply with the precepts of the Declaration of Helsinque and the CNS 466/12 Resolution (NATIONAL HEALTH COUNCIL, 2013).

The objective of cosmetics safety assessment studies is to confirm the absence of risks associated with the use of the cosmetic product.

Compatibility studies, performed with patch tests, aim to prove the absence of adverse events during the first application of a cosmetic product to the skin, proving that the product is safe for use. They consist of repeated applications of the product to the skin, assessing the non-occurrence of irritation or sensitization (KLIGMAN & WOODING, 1967; FISHER, 1995). The absence of photo-sensitization or photo-irritant potential can also be proved.

Differently, the acceptance studies evaluate the safety of the products under real-use conditions, which allows knowing the product under the same-marketed conditions. Therefore, in-use studies are performed with the finished product, before it is introduced into the market. (BARAN & MAIBACH, 1994).

Besides safety, this research can also assess sensory characteristics of the product, and detect additional complaints and comments as to its "performance".

By performing clinical studies, the company has the opportunity to know in advance the possible considerations and complaints that may arise when the product is marketed, being able to develop strategies, such as specific training for its Consumer Service Staff before launching the product (BARAN & MAIBACH, 1994).

3. OBJECTIVE

The objective of this study was to prove the absence of the skin primary and accumulated irritation potential and the skin sensitization, photoallergy and phototoxicity potential of a product to be applied to the skin under maximized conditions, with controlled product quantity and application site, supervised by a dermatologist.

4. INVESTIGATIONAL PRODUCT

Product information, as declared by the Sponsor, is described in Appendix 3. A sample of the product was cataloged and will be stored in our files for one-month period.

4.1. Identification

Table 1. Test product identification

Product Name	Product Code
FAGRON TRICHOFOAM ESPUMA CAPILAR	058870-03

4.2. Product Application

The test-product was applied neat and distributed in the patch test filter paper disc, which was duly identified. A sterile physiological solution (NaCl 0.9%) was used as the control, duly identified in another patch test filter paper disc.

4.3. Storage

All products sent by the sponsor were initially stored in the samples room at the study center, with controlled temperature and restricted access. Products release was controlled by the Investigator In Charge or by a previously designated technical staff.

5. APPLICABLE ETHICAL REMARKS

This study was conducted in conformance with the Declaration of Helsinque principles, the applicable regulatory requirements, including Resolution CNS no. 466/12, in the spirit of Good Clinical Practice principles (Document of the Americas and ICH E6: G*ood Clinical Practice*).

Subjects were informed about the study objective, its methodology and length, and about the possible expected benefits and the constraints related to the study. Those who confirmed their interest in participating in the study signed an Informed Consent form (Appendix 1).

The study technical documentation is in Allergisa´s files, where it will be stored for a 5-year period.

6. STUDY PERIOD

Study of primary and accumulated irritation and sensitization:

The study lasted a total of 6 weeks.

- **Medical Assessment:** 11/04/2016.
- **First Application:** 11/07/2016;
- **End Date:** 12/16/2016.

Photoallergy and Phototoxicity Study:

The study lasted a total of 6 weeks.

- **Medical Assessment:** 10/28/2016.
- **First Application:** 10/31/2016;
- **End Date:** 12/09/2016.

7. STUDY SUBJECTS

7.1. Study subjects Recruitment

The study subjects were recruited by the recruitment department of the Study Center that has a computerized and updated register system. The subjects registered into this system are interested in participating in clinical trials. They were contacted and asked to take part in the selection process and if they met all required criteria, they would be included in the study.

7.2. Selection and Admission of Study Subjects

During the subjects' selection for the study, the physician in charge certified that the subjects had no pathologies that could interfere with the study results. The physician is also responsible for all information contained in the subject's assessment form, by checking all inclusion and exclusion criteria for admission of the subject in the study.

7.3. Population Description

Study of primary and accumulated irritation and sensitization:

A total of 87 study subjects were recruited for this study (Appendix 2). Out of those, 17 subjects (001, 003, 011, 012, 015, 016, 022, 029, 039, 047, 048, 061, 063, 065, 076, 082 and 085) did not meet the inclusion criteria or presented any of the exclusion criteria.

The study was initiated with 70 subjects, being 57 female and 13 male subjects, aged from 18 to 69 years.

Photoallergy and Phototoxicity Study:

A total of 36 study subjects were recruited for this study (Appendix 2).

One subject (027) gave up the study for personal reasons, before the initial evaluation.

The study was initiated with 35 subjects, being 32 female and 03 male subjects, aged from 20 to 70 years.

The study had the objective of obtaining at least 50 and 25 responses, respectively, at its ending, according to the Guide for Safety Evaluation of Cosmetics Products from the National Health Surveillance Agency – ANVISA.

7.4. Inclusion Criteria

Study of primary and accumulated irritation and sensitization:

- Healthy study subjects;
- Intact skin on test site;
- Agreement to adhere to the procedures and requirements of the study and to report to the institute on the day(s) and at the time(s) scheduled for the assessments;
- Ability to consent to participate in the study;
- Any gender;
- Aged from 18 to 70 years old;
- Phototype (Fitzpatrick): I to IV.

- Photoallergy and Phototoxicity Study:
- Healthy study subjects;
- Intact skin on test site;
- Agreement to adhere to the procedures and requirements of the study and to report to the institute on the day(s) and at the time(s) scheduled for the assessments;
- Ability to consent to participate in the study;
- Any gender;
- Aged from 18 to 70 years old;
- Phototype (Fitzpatrick): II to III.

7.5. Non Inclusion Criteria

- Any skin marks on the test site that might interfere with the assessment of possible skin reactions (pigmentation disorders, vascular malformations, scars, increased pilosity, and great amounts of ephelides and nevus, sunburns).
- Active dermatosis (local or disseminated) that might interfere with the results of the study;
- Pregnancy or breastfeeding;
- Previous history of allergic reactions, irritation or intense feelings of discomfort to topical-use products, cosmetics or medication;
- Subjects with history of allergy to the material used in the study;
- Previous history of atopy;
- History of pathologies aggravated or triggered by ultraviolet radiation;
- Subjects suffering from immunodeficiencies;
- Intense exposure to sunlight or to sun tanning sessions up to 15 days before the initial evaluation;
- Intention of being intensely exposed to sunlight or to sun tanning sessions during the study period;
- Intention of sea bathing, going to the pool or sauna during the study;
- Subjects who practice water sports;
- Dermographism;
- Use of the following topical or systemic medications: immunosuppressive drugs, antihistamines, non-hormonal anti-inflammatory drugs, and corticosteroids within two weeks before the selection process;
- Oral or topical treatment with vitamin A acid and/or its derivatives up to 1 month before the study start;
- Aesthetic and/or dermatological treatment performed on the body within 03 weeks before selection;
- Be currently taking part or have already participated in another clinical study which was concluded less than 07 days before selection, if the previous study is an in-use research study, or less than 21 days if the previous study was a Compatibility study or an Adverse Reaction Investigation;
- Intention of being vaccinated during the study period or up to 3 weeks before the study;
- Any conditions which the investigator finds compromising to the evaluation of the study;
- History of lack of adherence or unwillingness to adhere to the study protocol;
- Professionals who are directly involved in the performance of the current protocol as well as their relatives.

7.6. Injunction and Constraint

- No excessive exposure to sunlight or artificial tanning;
- No sea bathing, pool or sauna during the study;
- No contact of the patch test with water;

- No use the following medication: Non-hormonal anti-inflammatory drugs of continuous use*, corticosteroids, anti-histamines, immunosuppressive drugs, acid A vitamin and derivatives. In case any therapeutic use was required, the subject could be excluded from the study.
- During the study, any aesthetic, cosmiatric or dermatological treatment on the body was also forbidden.

8. METHODOLOGY

8.1. Study Design

Comparative, single-blind, controlled and clinical study.

8.2. Materials and Equipment

- Adhesive hypoallergenic card for patch testing with duly identified 1.0-cm^2 filter paper discs;
- Semi-occlusive hypoallergenic tape;
- 0.9% sterile physiological solution (NaCl 0.9%);
- Gloves, masks and caps;
- Surgical marker;
- Cotton swab;
- Distilled water;
- Beaker;
- Dropper bottle;
- Transparent bottle;
- Protective fabric.
- System of Irradiators ((A- EM-310 and A-EM-311);

8.3. Test Site

The product was applied to the study subjects back (scapular area).

8.4. Population Size

Study of primary and accumulated irritation and sensitization:

This study was conducted with 70 approved subjects with the objective of obtaining at least 50 responses at the end of the study.

Photoallergy and Phototoxicity Study:

This study was conducted with 35 approved subjects with the objective of obtaining at least 25 responses at the end of the study.

The study complied with the Guide for Safety Evaluation of Cosmetics Products from the National Health Surveillance Agency – ANVISA.

*Sporadic use should be assessed by the investigator regarding excluding from the study.

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8.5. Study of primary and accumulated irritation and sensitization:

At first, the study subjects were assessed by a dermatologist in order to verify the inclusion and exclusion criteria.

The patch test methodology (KLIGMAN & WOODING, 1967), also known as contact test or epicutaneous test, was used.

The product (0.05g/cm²) was distributed on the duly identified patch test filter paper disc and the 0.9% sterile physiological solution, used as control, was distributed on another duly identified disc.

The patch test containing both the test-product and control was then attached to the scapular area of the right or left back of the subjects.

Induction Period: the applications were performed three times a week, for three consecutive weeks, remaining in contact with the skin for 48 hours during the week and for 72 hours during weekends.

Rest Period: There was a rest period of at least 10 days following the induction period, when no *patches* were applied.

Challenge period: After the rest period, a patch with the test product and control was applied to the right or left back of the subjects on a virgin area, that is, where no patches had been applied before.

The patch was removed by the investigators after approximately 48 hours of contact with the skin.

The assessments (readings) were performed approximately 30 minutes (48h reading) and 24 hours (72h reading) after *patch test* removal.

The subjects were assessed at the end of the study by a dermatologist and supervised all along the study.

8.6. Photoallergy Assessment

At first the study subjects were assessed by a dermatologist in order to verify the inclusion and exclusion criteria.

The patch test methodology (KLIGMAN & WOODING, 1967), also known as contact test or epicutaneous test, was used.

The product (0.05g/cm²) was distributed on the duly identified patch test filter paper disc and the 0.9% sterile physiological solution, used as control, was distributed on another duly identified disc.

The patch test containing both the test-product and control was then attached to the scapular area of the right or left back of the subjects.

Induction Period: The sample was always applied to the same duly protected area (right or left back of the subjects). The subjects' eyes were protected from incidence of light.

The product and control applications were performed twice a week (Mondays and Wednesdays) for three weeks, totaling six applications.

The patch test was removed by the investigators 24 hours after application, and after approximately 30 minutes the area was irradiated with a A and B ultraviolet lamp (UVA/UVB), immediately after the completion of the irradiation, the reading was performed and it will be recorded in a specific form. Before irradiation there is no record of reading, however, if during the cleansing of the contact area with the product or when the subject undergo the irradiation any clinical sign is observed by the trained

technician, the irradiation will not be performed and the adverse event investigation will be started, according to the institute standard procedure

The subjects were instructed to protect the irradiated area of their skin from sunlight. The assessments (readings) in the induction period were performed after the irradiation and approximately 24 hours after the last irradiation. The area adjacent to the site of test application and the disc of the control patch (with sterile physiological solution 0.9%) were irradiated and used as control (without product).

The energy dose applied was inferior to the study subjects' MED.

Rest Period: There was a rest period of at least 10 days following the induction period, during which no *patches* were applied.

Challenge period: After the rest period, a patch containing the test product and control was applied to the right or left back of the subjects on a virgin area, that is, where no patches had been applied before.

The patch was removed after 24 hours of contact with the skin. After approximately 30 minutes of the patch test removal, the test site was irradiated with UVA lamp.

The subjects were instructed to protect the irradiated area of their skin from sunlight. The area adjacent to the site of test application and the disc of the control patch (with saline solution) were irradiated and used as control (without product).

Before irradiation there is no record of reading, however, if during the cleansing of the contact area with the product or when the subject undergo the irradiation any clinical sign is observed by the trained technician, the irradiation will not be performed and the adverse event investigation will be started, according to the institute standard procedure

Assessments (readings) were performed right after the irradiation and also 24, 48 and 72 hours after the last irradiation. If any subject presented clinical signs in the challenge period, an investigation would be performed with this subject with the objective of identifying whether it was an irritation/photoirritation response or sensitization/photosensitization. In this case, after the treatment and remission of the clinical sign, the challenge phase would be repeated through an application of 2 identical patches, with six patch tests containing the product with different concentrations (100%, 50%, 20%, 10%, 5% and 2%) and only one of them would be irradiated, under the same conditions described in the previous paragraph.

If the investigation presented negative result, the dermatologist could close the event with negative nexus and the clinical signs seen in the first patch possibly occur due to a nonspecific reaction. The assessment is very individual and the dermatologist in charge takes into account the reaction history.

If the investigation presented positive result, the positivity of each concentration would be assessed, as well as the clinical signs intensity and the remission throughout the readings in order to confirm the hypothesis of photo-sensitization or photoirritation. The responses and the reaction history would be assessed by the dermatologist in charge for the definition of the diagnostic and the causal relation with the test-product. The dermatologist assess the clinical sign type, the time of appearance and remission of those signs and if there was relapse after re-exposure to the product. The investigation procedure of the adverse events is described in the internal procedure of the institute. The study subjects were assessed at the end of the study by a dermatologist and supervised all along the study.

8.7. Phototoxicity Assessment

The patch-test containing the test-product and control was applied to duly protected right or left back area of the subjects. The subjects' eyes were protected from incidence of light. The product application was executed only once, and it happens the same day as the challenge phase application of the photosensitization method described above.

The patch was removed after 24 hours of contact with the skin. After removal, the test site was assessed and irradiated with UVA lamp.

The area adjacent to the site of test application and the disc of the control patch (with sterile physiological solution 0.9%) were irradiated and used as control (without product).

The subjects were instructed to protect the irradiated area of their skin from sunlight.

Assessments (readings) were performed right after the irradiation and also 24, 48 and 72 hours after the last irradiation.

8.8. Irradiations Aspect

8.8.1. Light Source Used

A Solar Simulator was used, which is equipped with two ultraviolet 300-Watt radiation lamps (Ultra Vitalux) manufactured by Osram with digital control of irradiation time, automatic opening and closing function for light application and separation of ultraviolet radiation through a transparent glass. The radiation was controlled by an optical power meter, manufactured by Solar Light Co. Inc.

For the irradiation of the challenge period, which is only performed with UVA irradiation, a filter is placed to block the UVB radiation, using the same device.

8.8.2. Energy Density

The lamp output is 4.57mW/cm2 @20cm (UVA) and 0.013 MED/min @20cm (UVB).

Total irradiation: 11-15 joules.

8.8.3. Working Conditions – Induction Period

UVA+UVB

Distance of the Lamp: 38 cm

Irradiation area of the test product: 1,0 cm^2

Lamp Output: 0.575 MED//cm^2.min

11.25-11.51 mW/ cm^2

Irradiation period: 1.5 minutes / session

Total irradiation: 6.1 – 6.2 joules

8.8.4. Working Conditions – Challenge Period

UVA

Distance of the Lamp: 38 cm

Irradiation area of the test product: 1,0 cm^2

Lamp Output: 10.49 – 10.73 mW/ cm^2

Irradiation period: 10 minutes

Total irradiation: 6.3 – 6.4 joules.

8.9. Assessment of Clinical Signs (Readings)

In case any subject presented any clinical sign during the readings, the assessment scale published by the International Contact Dermatitis Research Group - ICDRG (FISHER, 1995) would be used.

Table 2. Scale published by the International Contact Dermatitis Research Group - ICDRG

REACTION	RESULT
0 – Absent	Negative (-)
1 - Mild Erythema	Doubtful (?)
2 - Clear Erythema	Positive (+)
3 - Erythema + Edema + Papules	Positive (++)
4 - Erythema + Edema + Papules + Vesicles	Positive (+++)

8.10. Procedure Schedule

Table 3. Study Schedule (Study of primary and accumulated irritation and sensitization)

			Stages				
			Sign Informed Consent	Clinical Assessment by the Dermatologist	Patch test Application	Patch test Removal	Assessments (Readings)
		Visit 1	X	X	-	-	-
Induction Period	Week 1	Visit 2	-	-	X	-	-
		Visit 3	-	-	X	X	X
		Visit 4	-	-	X	X	X
	Week 2	Visit 5	-	-	X	X	X
		Visit 6	-	-	X	X	X
		Visit 7	-	-	X	X	X
	Week 3	Visit 8	-	-	X	X	X
		Visit 9	-	-	X	X	X
		Visit 10	-	-	X	X	X
		Visit 11	-	-	-	X	X
Rest period - weeks 4 and 5 – no visits performed							
Challenge Period	Week 6	Visit 12	-	-	X	-	-
		Visit 13	-	-	-	X	X
		Visit 14	-	X	-	-	X

Table 4. Study Schedule (Photoallergy and phototoxicity study)

			Stages					
			Sign Informed Consent	Clinical Assessment by the Dermatologist	Patch test Application	Patch test Removal	Irradiation	Assessments (Readings)
		Visit 1	X	X	-	-	-	-
Induction Period	Week 1	Visit 2	-	-	X	-	-	-
		Visit 3	-	-	-	X	X	X
		Visit 4	-	-	X	-	-	X
		Visit 5	-	-	-	X	X	X
		Visit 6	-	-	-	-	-	X
	Week 2	Visit 7	-	-	X	-	-	-
		Visit 8	-	-	-	X	X	X
		Visit 9	-	-	X	-	-	X
		Visit 10	-	-	-	X	X	X
		Visit 11	-	-	-	-	-	X
	Week 3	Visit 12	-	-	X	-	-	-
		Visit 13	-	-	-	X	X	X
		Visit 14	-	-	X	-	-	X
		Visit 15	-	-	-	X	X	X
		Visit 16	-	-	-	-	-	X
Rest period - weeks 4 and 5 – no visits performed								
Challenge Period	Week 6	Visit 17	-	-	X	-	-	-
		Visit 18	-	-	-	X	X	X
		Visit 19	-	-	-	-	-	X
		Visit 20	-	-	-	-	-	X
		Visit 21	-	X	-	-	-	X

8.11. Criteria and Procedures for Study Subjects Withdrawal

The exclusion of a study subject by the investigator may occur due to the following reasons:

- Study subjects not included: subjects who signed the IC, but who did not meet the inclusion and exclusion criteria of the study,
- Subjects who presented - at the Investigator's discretion - any problem that could prevent product applications from continuing, at any time during the study,
- Consent withdrawal by the study subject, regardless of the reason,
- Lack of adhesion of the study subject to the study. A significant lack of adhesion would be recorded if the subject did not visit the study center for assessments,
- Serious Adverse Event,
- Concurrent disease or treatment: any pathological process or treatment that occurred during the study period and that could interfere with the study product, such as a medication interaction or masking of results.

Those subjects removed from the study by the investigator would be assessed in case they presented any event possibly related to the study, even after their removal. Those subjects removed due to occurrence of an adverse event would be continually assessed until the case is completely resolved.

Those subjects who are removed from study after the inclusion stage, will not be replaced.

9. ADVERSE EVENTS

An adverse event is any untoward medical occurrence in a patient or clinical investigation subject administered a product and that does not necessarily have a causal relationship with this treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of the investigational product (adapted from ICH, 1996).

According to the Good Clinical Practices (ICH, 1996), a Serious Adverse Event is any untoward medical occurrence that at any dose:

- Results in death;
- Is life-threatening;
- Requires inpatient hospitalization or prolongation of existing hospitalization;
- Results in persistent or significant disability/incapacity;
- Is a congenital anomaly/birth defect.

Thus any new sign, symptom or disease, or clinically significant worsening compared to the condition at the first visit, should be considered an Adverse Event. Lack of clinical or self-perceived efficacy of a cosmetic product or drug is not considered an Adverse Event.

Clinical signs and dermatological or systemic diseases observed during the selection process of the study subjects are not considered as Adverse Events. This information is recorded on the medical assessment form as a reason for non-inclusion and the subjects are then not included in the study.

The adverse events occurred as a result of incorrect product use (either cosmetics or drugs products) - such as inappropriate frequency or incorrect application - will be considered as adverse events that do not interfere with the product evaluation, since the subject- in this situation - does not follow the correct use directions stated on the product label.

An Adverse Event Form is completed for all events occurred. The study sponsor is notified of an adverse event through a Notification of Occurrence form sent by electronic mail or in the Final Study Report.

In case there is an adverse event with doubtful causal nexus, an investigation process is initiated in order to determine if such event is or is not related to the study or investigational product.

The procedures adopted during the event investigation are defined by the physician in charge, based on the nature of the reaction, the subject's medical history and on factors that may interfere with the occurrence of the event, such as medication or other concomitant disorders.

When closing a final diagnosis, the relationship of an Adverse Event to the study or study products can be defined by using one of the following expressions:

- Negative Nexus or Not Related – The existence of a positive causal relation between the product and the adverse event observed is not possible.

- Improbable – The existence of a positive causal relation between the product and the adverse event observed is improbable.
- Possible – The existence of a positive causal relation between the product and the adverse event observed is possible, but there are no means of certifying this.
- Probable – The existence of a positive causal relation between the product and the adverse event observed is probable, although the relation is not completely proved.
- Positive Nexus or Certainly Related - according to the physician in charge, there are evidences that allow concluding the causal relation as being positive between the occurrence of the event and the application/use of the cosmetic or drug product.

10. RESULTS

10.1. Study of primary and accumulated irritation and sensitization

10.1.1. Adherence to the Study

A total of 59 subjects completed the study.

A total of 11 subjects withdrew from the study due to personal reasons unrelated to the test product (subjects 031, 033, 040, 054, 056, 057, 072, 079, 080, 084 and 087).

10.1.2. Dermatological Clinical Assessment

During the study, no subjects presented any clinical signs in the test product application site.

The data obtained from the assessments of the site in contact with the product is recorded in Table 5.

No subjects presented clinical signs in the control site.

Table 5. Patch test assessments: Test-product

Subject No	Application	Reading + Application	Reading + Application	Reading + Application	Reading + Application	Reading + Application	Reading + Application	Reading + Application	Reading + Application	Reading	Application	Reading	Reading
002	0	0	0	F	0	0	0	0	0	0	0	0	0
004	0	0	0	F	0	0	0	0	0	0	0	0	0
005	0	0	0	0	0	0	0	0	0	0	0	0	0
006	0	0	0	F	0	0	0	0	0	0	0	0	0
007	0	0	0	F	0	0	0	0	0	0	0	0	0
008	0	0	0	F	0	0	0	0	0	0	0	0	0
009	0	0	0	F	0	0	0	0	0	0	0	0	0
010	0	0	0	F	0	0	0	0	0	0	0	0	0
013	0	0	0	F	0	0	0	0	0	0	0	0	0
014	0	0	0	F	0	0	0	0	0	0	0	0	0
017	0	0	0	F	0	0	0	0	0	0	0	0	0
018	0	0	0	F	0	0	0	0	0	0	0	0	0
019	0	0	0	F	0	0	0	0	0	0	0	0	0
020	0	0	0	F	0	0	0	0	0	0	0	0	0
021	0	0	0	F	0	0	0	0	0	0	0	0	0
023	0	0	0	F	0	0	0	0	0	0	0	0	0
024	0	0	0	F	0	0	0	0	0	0	0	0	0
025	0	0	0	F	0	0	0	0	0	0	0	0	0
026	0	0	0	F	0	0	0	0	0	0	0	0	0
027	0	0	0	F	0	0	0	0	0	0	0	0	0
028	0	0	0	F	0	0	0	0	0	0	0	0	0
030	0	0	0	F	0	0	0	0	0	0	0	0	0
031	F/R	R	R	R	R	R	R	R	R	R	R	R	R
032	0	0	0	0	0	0	0	0	0	0	0	0	0
033	F/R	R	R	R	R	R	R	R	R	R	R	R	R
034	0	0	0	0	0	0	0	0	0	0	0	0	0
035	0	0	0	F	0	0	0	0	0	0	0	0	0
036	0	0	0	F	0	0	0	0	0	0	0	0	0
037	0	0	0	F	0	0	0	0	0	0	0	0	0
038	0	0	0	F	0	0	0	0	0	0	0	0	0
040	0	0	0	0	0	0	0	0	0	0	F/R	R	R
041	0	0	0	F	0	0	0	0	0	0	0	0	0
042	0	0	0	F	0	0	0	0	0	0	0	0	0
043	0	0	0	F	0	0	0	0	0	0	0	0	0
044	0	0	0	F	0	0	0	0	0	0	0	0	0
045	0	0	0	F	0	0	0	0	0	0	0	0	0

Caption:

X = Not Applied / Reading Not Performed
F = Absence
R = Removed from the Study
DK = Darkening
DY = Dryness
F/R = Absence / Removed from the Study

0= No reaction
1 = Mild Erythema
2 = Clear Erythema
3 = Erythema + Edema + Papules
4 = Erythema + Edema + Papules + Vesicles

Continuing Table 5. Patch test assessments: Test-product

Subject No	Application	Reading + Application	Reading + Application	Reading + Application	Reading + Application	Reading + Application	Reading + Application	Reading + Application	Reading + Application	Reading	Application	Reading	Reading
046	0	0	0	0	0	0	0	0	0	0	0	0	0
049	0	0	0	F	0	0	0	0	0	0	0	0	0
050	0	0	0	F	0	0	0	0	0	0	0	0	0
051	0	0	0	0	0	0	0	0	0	0	0	0	0
052	0	0	0	F	0	0	0	0	0	0	0	0	0
053	0	0	0	0	0	0	0	0	F	0	0	0	0
054	F/R	R	R	R	R	R	R	R	R	R	R	R	R
055	0	0	0	F	0	0	0	0	0	0	0	0	0
056	F/R	R	R	R	R	R	R	R	R	R	R	R	R
057	0	F/R	R	R	R	R	R	R	R	R	R	R	R
058	0	0	0	F	0	0	0	0	0	0	0	0	0
059	0	0	0	F	0	0	0	0	0	0	0	0	0
060	0	0	0	F	0	0	0	0	0	0	0	0	0
062	0	0	0	F	0	0	0	0	0	0	0	0	0
064	0	0	0	F	0	0	0	0	0	0	0	0	0
066	0	0	0	F	0	0	0	0	0	0	0	0	0
067	0	0	0	0	0	0	0	0	0	0	0	0	0
068	0	0	0	F	0	0	0	0	0	0	0	0	0
069	0	0	0	F	0	0	0	0	0	0	0	0	0
070	0	0	0	F	0	0	0	0	0	0	0	0	0
071	0	0	0	F	0	0	0	0	0	0	0	0	0
072	0	0	0	F	0	F/R	R	R	R	R	R	R	R
073	0	0	0	F	0	0	0	0	0	0	0	0	0
074	0	0	0	F	0	0	0	0	0	0	0	0	0
075	0	0	0	F	0	0	0	0	0	0	0	0	0
077	0	0	0	F	0	0	0	0	0	0	0	0	0
078	0	0	0	0	0	F	0	0	0	0	0	0	0
079	0	0	0	F	0	F/R	R	R	R	R	R	R	R
080	0	0	0	0	0	F	F/R	R	R	R	R	R	R
081	0	0	0	F	0	0	0	0	0	0	0	0	0
083	0	0	0	F	0	0	0	0	0	0	0	0	0
084	0	0	0	F	0	F/R	R	R	R	R	R	R	R
086	0	0	0	F	0	0	0	0	0	0	0	0	0
087	0	F/R	R	R	R	R	R	R	R	R	R	R	R

Caption:

X = Not Applied / Reading Not Performed
F = Absence
R = Removed from the Study
DK = Darkening
DY = Dryness
F/R = Absence / Removed from the Study

0= No reaction
1 = Mild Erythema
2 = Clear Erythema
3 = Erythema + Edema + Papules
4 = Erythema + Edema + Papules + Vesicles

10.2. Photoallergy and Phototoxicity Study

10.2.1. Adherence to the Study

A total of 32 subjects completed the study.

A total of 03 subjects withdrew from the study due to personal reasons not related with the test product (subjects 013, 019 and 036).

10.2.2. Dermatological Clinical Assessment

During the study, no subjects presented any clinical signs in the test product application site.

The data obtained from the assessments of the site in contact with the product is recorded in Table 6.

No subjects presented clinical signs in the control site.

Table 6. Patch test assessments: Test-product

Subject No	Application	Irradiation + Reading	Reading + Application	Irradiation + Reading	Reading	Application	Irradiation + Reading	Reading + Application	Irradiation + Reading	Reading	Application	Irradiation + Reading	Reading + Application	Irradiation + Reading	Reading	Application	Irradiation + Reading	Reading	Reading	Reading
001	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
002	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0	0
003	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
004	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
005	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0	0
006	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
007	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
008	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
009	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0	0
010	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
011	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
012	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
013	0	0	0	0	0	0	0	0	0	F	F/R	R	R	R	R	R	R	R	R	R
014	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
015	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
016	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
017	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
018	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
019	F/R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R
020	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
021	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
022	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
023	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
024	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
025	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0	0
026	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
028	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0	0
029	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0	0
030	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0	0
031	0	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0
032	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0	0
033	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0	0	0	0
034	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0	0	0	0
035	0	0	0	0	0	0	0	0	0	0	F	0	0	0	0	0	0	0	0	0
036	F/R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R

Caption:

L = Not Applied / Reading Not Performed
F = Absence
R = Removed from the Study
DK = Darkening
DY = Dryness
F/R = Absence / Removed from the Study

0= No reaction
1 = Mild Erythema
2 = Clear Erythema
3 = Erythema + Edema + Papules
4 = Erythema + Edema + Papules + Vesicles

11. CONCLUSION

According to the methodology used to assess the skin primary and accumulated irritation potential and the skin sensitization, photoallergy and phototoxicity potential of the product **FAGRON TRICHOFOAM ESPUMA CAPILAR**, submitted by the company **WNF INDUSTRIA E COMERCIO LTDA**, it could be concluded that:

- During the study, no subjects presented skin clinical signs related to the product.
- The product did not induce skin irritation, sensitization, phototoxicity or photoallergy process in the study group.
- The product was considered safe under the study conditions.

Vivian Pessoto Rosa
Investigator in Charge
01/26/2017

Dr. André Luiz Vergnanini
Dermatologist (CRM 45125)
01/26/2017

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APPENDIX 1 INFORMED CONSENT

STUDY OF PRIMARY AND ACCUMULATED IRRITATION AND SENSITIZATION

The ICF attached to this report is regarding all studies that the subject has been clarified and included due to sharing of studies with different sponsors and studies.

- You are being invited to join a study. We ask that you understand all the steps in detail and, if you agree, sign this consent form;
- The objective of the study is to prove the absence of irritation and/or Skin Sensitization potential of cosmetic products (soaps, shampoos, deodorants, powders, bath oils, moisturizers, lotions, perfumes, colognes, sunscreens, insect repellent among others), health care products (dressing, adhesive plasters, hospital-medical use products), topical medications (ointments, gels, for use on the skin) and/or raw materials (individual ingredients that compose a cosmetic product);
- The study will be conducted in the headquarter of ALLERGISA pesquisa dermato-cosmética ltda, located at Av. Dr. Romeu Tórtima Avenue, 452/466 – Barão Geraldo – Campinas – SP;
- The study will be conducted with up to 80 study subjects;
- Your participation in the study will last 1 week for the Primary Irritation Study, 3 weeks for the Cumulative Irritation Study and 6-7 weeks for the Irritation/Sensitization Study;
- You will be previously assessed by a dermatologist at the start and end of the study and supervised all along the study period;
- Skin Irritation and Sensitization are irritation and allergic reactions, which may occur eventually in your skin, after these products application;
- You must attend the institute up to 17 times in total.
- In all return visits, the remaining period will be approximately 3 hours or until the completion of the study procedures;
- The dates you must attend to the study procedure (return visits) are described in the schedule you will receive in the study start;
- For the Primary Irritation Study, the patch test (adhesive tape) containing the evaluated products will be applied once on the right and/or left dorsum (back). After removal, evaluations will be carried (readings);
- For the Cumulative Irritation study, the patch test (adhesive tape) containing the evaluated products will be applied on the right and/or left dorsum (back), during three consecutive weeks. You will have to attend the institute on Mondays, Wednesdays and Fridays for applications and readings;
- For the Cumulative Irritation and/or Sensitization Study, the patch test (adhesive tape) containing the evaluated products will be applied on the right and/or left dorsum (back), during three or four consecutive weeks. You will have to attend the institute on Mondays, Wednesdays and Fridays for application and reading. After this period, called "induction", you will remain in rest for 10 days, as minimum, and you must return to apply again the patch test, which must be removed by the technical responsible after approximately 48 hours or by yourself at home, after approximately 24 hours (on that case, you will be informed) and you must attend the institute for the readings;

- We ask you to take care and do not wet the patch test during the whole period of the study;
- During the study, any dermatological treatment is forbidden; If the treatment is required, notify immediately the institute.
- Communicate to the institute the use of any kind of topical medication (external/skin use) or systemic (pills and liquids (solutions and syrups) of oral use or injections), such as cortisone, anti-allergic or any other;
- After signing the Informed Consent, you could be dismissed either by the specialist physician in case you present any of the exclusion criteria of the study or in case all available vacancies have been previously filled;
- You commit yourself to not join any other research during this study;
- If you are a female, you state that you are not pregnant or breast feeding and commit yourself to not become pregnant during the study period;
- Your consent does not exempt the institute organizers from their responsibilities;
- You are aware that, on occasions, a representative of the sponsor company may be present to observe the study;
- You accept that, in this study context, your data will be collected and may be subject to electronic processing. In case any of your register data change (e.g. telephone number, address etc), please ask the study organizers to have them updated;
- In general, these products topically applied products present a good risk/benefit relation; however, they may cause sensitization and local irritation - especially after long-term use. In case any reaction occurs, you will be assessed and supervised by a dermatologist;
- All raw materials used in the product are approved for topical use and are not toxic. However, same as with any other products, they might cause unexpected reactions such as “redness”, “swelling”, “itching” and “burning” in the product application sites.
- As a benefit of the study you will be assessed by an expert physician before the study start, and, if observed any problem, on the assessed area, you will be alerted and instructed. In addition, your participation will contribute to warrant the release/marketing of a safe topical use (on the skin) products;
- Any doubts you might have during or after the study will be promptly solved;
- Your participation in the study is entirely voluntary;
- You will not be paid for being part of this study, but you will receive a compensation at the end of the study for the costs related to food expenses;
- You can withdraw from the study at any time, if you wish; however, you should inform the institute of your withdrawal;
- You can be removed from the study in case you do not fulfill your responsibilities, according to the study protocol;
- You could be removed of the study according to investigator's discretion. In this conditions, you will receive by the end of the study, the compensation regarding the expenses with food;
- Your voluntary cooperation will be of great importance to the study. Therefore, we ask you to report to the trial site on the days and times scheduled throughout the study;

- If you change any of your habits, we ask that you please keep us informed, so we can better interpret the results;
- Do not make use of any products (e.g.: deodorants or antiperspirants, talcum powder, bath oil, creams, lotions, perfumes, colognes and topical medications) in areas close to the test sites. If you use any of these products or if you are taking any medication, please, let us know;
- In case of intense, persistent or moderate itching sensation or other signs of irritation, please inform us at once, coming to the trial place or contacting us via telephone 19-3517-6800 (working hours) or 19-99778-0204 (until 10 p.m);
- We warrant you that any adverse reactions (reactions, skin irritation or skin discomfort sensations) will be supervised by the dermatologist and/or specialist in charge of the project until resolved and, if so required, suitable medication will be provided for the treatment;
- If you present an adverse reaction with clinical sign (reaction that is able to be observed to the naked eye: redness, swelling, etc), photos will be taken with the single purpose of investigation of the reaction and record of these information;
- You identity will be keep confidential during the procedure and only the study investigator can access these records;
- Eventual indemnifications are insured;
- We ensure that you will be informed of any new relevant information (important information) that may interfere with your consent;
- All information obtained about the study subjects will be kept confidential (secret); however, by signing this informed consent, you will be providing the sponsor and the regulatory authorities (study regulatory agencies) with the permission to conduct audits on all study documents and data;
- In case of any doubts or problems, you can contact the medical team via telephone no. 19-3517-6800 with Vivian Pessoto Rosa (Investigator in Charge).
- One copy of this form will be kept on Allergisa files, and another will be given to you.
- I am aware that the photos taken for the investigation procedure, in case of any reaction, are part of the procedure of this study and I agree with those images capturing.

I agree to join the study **"ASSESSMENT OF THE SKIN PRIMARY AND CUMULATIVE IRRITATION POTENTIAL AND SKIN SENSITIZATION POTENTIAL OF PRODUCTS UNDER CONTROLLED AND MAXIMIZED CONDITIONS"** I declare I have been clarified on all items above.

01	Signature of the Study Subject (as in the ID or Driver's License)	Date
03	Signature of the person in charge of explaining the IC	Date

PHOTOALLERGY AND PHOTOTOXICITY STUDY

- You are being invited to join a study. We ask that you understand all the steps in detail and, if you agree, sign this consent form;
- The objective of the study is to prove the absence of irritation and/or Skin Photoallergy and/or Phototoxicity potential of cosmetic products (soaps, shampoos, deodorants, powders, bath oils, moisturizers, lotions, perfumes, colognes, sunscreens, insect repellent among others), health care products (dressing, adhesive plasters, hospital-medical use products), topical medications (ointments, gels, for use on the skin) and/or raw materials (individual ingredients that compose a cosmetic product);
- The study will be conducted in the headquarter of ALLERGISA pesquisa dermato-cosmética ltda, located at Av. Dr. Romeu Tórtima Avenue, 452/466 – Barão Geraldo – Campinas – SP;
- The study will be conducted with up to 40 study subjects;
- You will participate in the study for 1 week for the Phototoxicity study and for 6 weeks for the Photoallergy/Phototoxicity study;
- You will be previously assessed by a dermatologist at the start and end of the study and supervised all along the study period;
- Skin and Photoallergy and Phototoxicity are reactions which might occur on your skin after using such products in contact with the sun light or similar;
- You must attend the institute up to 21 times in total.
- In all return visits, the remaining period will be approximately 3 hours or until the completion of the study procedures;
- The dates you must attend to the study procedure (return visits) are described in the schedule you will receive in the study start;
- For the Photoallergy/Phototoxicity study, the patch test (adhesive tape) containing the evaluated products will be applied on the right and/or left dorsum (back), during three consecutive weeks: on Mondays, Wednesdays and Fridays. The areas of application will be irradiated with A and B ultraviolet radiation, twice a week, on Tuesdays and Thursdays. After this period, called "induction", you will remain in rest for at least 10 days, and must return to reapplication of patch test, that will be removed after approximately 24 hours. After the patch removal, the area will be assessed, irradiated and new assessments (readings) will be performed after approximately 24h, 48h and 72h;
- For the Phototoxicity study, the patch test (adhesive tape) containing the evaluated products will be applied once on the right and/or left dorsum (back). After the patch removal, the area will be assessed, irradiated with ultraviolet A and new assessments (readings) will be performed after approximately 24h, 48h and 72h;
- We ask you to take care and do not wet the patch test during the whole period of the study;
- During the study, any dermatological treatment is forbidden; If the treatment is required, notify immediately the institute.

- Communicate to the institute the use of any kind of topical medication (external/skin use) or systemic (pills and liquids (solutions and syrups) of oral use or injections), such as cortisone, anti-allergic or any other;
- After signing the Informed Consent, you could be dismissed either by the specialist physician in case you present any of the exclusion criteria of the study or in case all available vacancies have been previously filled;
- You commit yourself to not join any other research during this study;
- If you are a female, you state that you are not pregnant or breast feeding and commit yourself to not become pregnant during the study period;
- Your consent does not exempt the institute organizers from their responsibilities;
- You are aware that, on occasions, a representative of the sponsor company may be present to observe the study;
- You accept that, in this study context, your data will be collected and may be subject to electronic processing. In case any of your register data change (e.g. telephone number, address etc), please ask the study organizers to have them updated;
- In general, these products used topically present a good relation risks/benefits, however, they might cause photoallergy and phototoxicity, meaning that the reactions provoked with the presence of sunlight or similar, especially with the prolonged use. In case any reaction occurs, you will be assessed and supervised by a dermatologist;
- All raw materials used in the product are approved for topical use and are not toxic. However, same as with any other products, they might cause unexpected reactions such as “redness”, “swelling”, “itching” and “burning” in the product application sites.
- As a benefit of the study you will be assessed by an expert physician before the study start, and, if observed any problem, on the assessed area, you will be alerted and instructed. In addition, your participation will contribute to warrant the release/marketing of a safe topical use (on the skin) products;
- Any doubts you might have during or after the study will be promptly solved;
- Your participation in the study is entirely voluntary;
- You will not be paid for being part of this study, but you will receive a compensation at the end of the study for the costs related to food expenses;
- You can withdraw from the study at any time, if you wish; however, you should inform the institute of your withdrawal;
- You can be removed from the study in case you do not fulfill your responsibilities, according to the study protocol;
- You could be removed of the study according to investigator's discretion. In this conditions, you will receive by the end of the study, the compensation regarding the expenses with food;
- Your voluntary cooperation will be of great importance to the study. Therefore, we ask you to report to the trial site on the days and times scheduled throughout the study;
- If you change any of your habits, we ask that you please keep us informed, so we can better interpret the results;

- Do not make use of any products (e.g.: deodorants or antiperspirants, talcum powder, bath oil, creams, lotions, perfumes, colognes and topical medications) in areas close to the test sites. If you use any of these products or if you are taking any medication, please, let us know;
- In case of intense, persistent or moderate itching sensation or other signs of irritation, please inform us at once, coming to the trial place or contacting us via telephone 19-3517-6800 (working hours) or 19-99778-0204 (until 10 p.m);
- We warrant you that any adverse reactions (reactions, skin irritation or skin discomfort sensations) will be supervised by the dermatologist and/or specialist in charge of the project until resolved and, if so required, suitable medication will be provided for the treatment;
- If you present an adverse reaction with clinical sign (reaction that is able to be observed to the naked eye: redness, swelling, etc), photos will be taken with the single purpose of investigation of the reaction and record of these information;
- You identity will be keep confidential during the procedure and only the study investigator can access these records;
- Eventual indemnifications are insured;
- We ensure that you will be informed of any new relevant information (important information) that may interfere with your consent;
- All information obtained about the study subjects will be kept confidential (secret); however, by signing this informed consent, you will be providing the sponsor and the regulatory authorities (study regulatory agencies) with the permission to conduct audits on all study documents and data;
- In case of any doubts or problems, you can contact the medical team via telephone no. 19-3517-6800 with Vivian Pessoto Rosa (Investigator in Charge).
- One copy of this form will be kept on Allergisa files, and another will be given to you.
- I am aware that the photos taken for the investigation procedure, in case of any reaction, are part of the procedure of this study and I agree with those images capturing.

I agree to join the study "ASSESSMENT OF THE SKIN PHOTOALLERGY AND PHOTOTOXICITY POTENTIAL OF PRODUCTS, UNDER CONTROLLED AND MAXIMIZED CONDITIONS" I declare I have been clarified on all items above.

01	Signature of the Study Subject (as in the ID or Driver's License)	Date
02	Signature of the person in charge of explaining the IC	Date

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APPENDIX 2 STUDY GROUP

STUDY OF PRIMARY AND ACCUMULATED IRRITATION AND SENSITIZATION

SUBJECT No	INITIALS (NAME)	AGE (YEARS)	GENDER	PHOTOTYPE	STATUS
001	RPS	30	F	III	I
002	AMLC	35	F	III	I
003	EACVP	55	F	II	I
004	ATM	70	F	II	I
005	MICS	61	F	II	I
006	JMS	34	M	IV	I
007	DKSM	38	F	III	I
008	PSS	45	M	III	I
009	LDA	40	F	IV	I
010	MMG	58	F	III	I
011	RS	41	F	II	I
012	GMP	18	F	III	I
013	MFM	19	F	IV	I
014	GSN	28	F	III	NI
015	ECMS	34	F	III	NI
016	DSPSS	18	F	IV	NI
017	ECSG	25	F	III	I
018	JSJF	35	F	IV	I
019	JLSS	23	F	IV	I
020	SGS	48	F	III	I
021	AMNC	62	F	III	I
022	LDM	52	F	III	I
023	MJA	66	F	IV	I
024	PAO	29	F	III	I
025	EMA	47	F	III	I
026	MMSO	24	F	III	I
027	TSC	34	F	III	I

Caption:
F= Female; M= Male
The phototype of those subjects who withdrew from the study or were rated as being failure in selection was not determined – N/A or NC
Phototype according to Fitzpatrick:
I – The skin gets easily sunburned, never tans
II - The skin gets easily sunburned, tans slightly
III - The skin gets moderately sunburned, tans gradually
IV - The skin gets minimally sunburned, tans well
V - The skin rarely gets sunburned, gets very tanned.
VI - The skin never gets sunburned and it is deeply pigmented
I= included; NI = Not Included (to present any exclusion criteria and/or not present some of the inclusion criteria)
FS= Failure in Selection; D= Withdrawn

Study Group (continuation) - Primary and accumulated irritation and sensitization study

SUBJECT No	INITIALS (NAME)	AGE (YEARS)	GENDER	PHOTOTYPE	STATUS
028	PSH	32	F	III	I
029	MHC	40	M	III	I
030	LCPS	41	F	III	I
031	JJO	51	F	II	I
032	MHOS	44	F	III	I
033	MCC	58	F	III	NI
034	SFS	48	F	III	I
035	FMB	55	F	IV	NI
036	DCS	39	M	III	I
037	RRMS	32	F	IV	I
038	ACC	18	F	III	NI
039	FF	44	F	III	NI
040	SSA	18	F	III	I
041	LSOA	46	F	III	I
042	AMC	55	F	II	I
043	JAF	69	M	III	I
044	SRC	51	F	III	NI
045	ZMAB	68	F	III	I
046	NBF	20	F	III	I
047	SAC	69	F	III	I
048	JLDL	22	M	IV	I
049	CLL	59	F	III	I
050	CJP	45	M	III	I
051	RPC	36	F	III	I
052	AMR	35	M	IV	I
053	MJCC	61	F	II	I
054	AOA	39	F	III	I

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Study Group (continuation) - Primary and accumulated irritation and sensitization study

SUBJECT No	INITIALS (NAME)	AGE (YEARS)	GENDER	PHOTOTYPE	STATUS
055	DRS	53	M	III	I
056	RCSO	57	F	IV	I
057	IRO	44	F	IV	NI
058	NSBM	28	F	II	NI
059	MGN	53	F	III	I
060	GQSN	31	F	IV	NI
061	MS	58	F	IV	NI
062	SRS	30	F	III	I
063	LS	18	F	IV	I
064	RRD	51	F	III	I
065	KAMS	39	F	II	I
066	VCDJ	55	F	IV	I
067	VSSP	34	F	IV	NI
068	MLSS	34	F	III	I
069	FRC	32	F	III	I
070	VSC	25	F	IV	I
071	NAM	26	F	II	I
072	LASS	33	F	IV	I
073	AMGS	25	F	II	I
074	MMMP	50	F	II	I
075	JJS	28	M	IV	I
076	MAAS	64	F	III	I
077	ALLL	36	F	IV	I
078	EAMS	56	F	II	I
079	RCS	50	M	II	I
080	HCPF	30	F	II	I
081	RZ	62	F	II	I
082	MAS	32	F	III	I
083	PHF	46	M	III	I

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ALLERGISA

PHOTOALLERGY AND PHOTOTOXICITY STUDY

SUBJECT No	INITIALS (NAME)	AGE (YEARS)	GENDER	PHOTOTYPE	STATUS
001	MM	60	F	III	I
002	ESRI	30	F	III	I
003	EGP	64	F	III	I
004	CBS	69	F	II	I
005	GOS	68	F	II	I
006	SSMC	52	F	II	I
007	ICSM	55	F	III	I
008	ACS	70	F	III	I
009	JCSQ	42	F	III	I
010	AMR	59	F	II	I
011	AEB	63	F	II	I
012	FBA	31	M	III	I
013	RZS	32	F	III	I
014	JZSA	33	F	III	I
015	ER	37	F	III	I
016	ST	63	F	II	I
017	MBCF	51	F	II	I
018	VVA	58	M	III	I
019	FB	42	F	II	I
020	KCB	42	F	II	I
021	SAS	49	F	II	I
022	VLCD	61	F	III	I
023	IACP	54	F	III	I
024	JSO	60	M	III	I
025	NOI	20	F	III	I
026	FABS	65	F	III	I
027	DCP	57	F	III	D
028	HRPS	68	F	III	I
029	ALS	41	F	III	I
030	MMC	64	F	II	I
031	IMRPS	51	F	III	I
032	RSO	33	F	III	I
033	TSM	45	F	II	I
034	RSL	41	F	III	I
035	AGAE	36	F	III	I
036	BJS	57	F	III	I

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