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ASSESSMENT OF THE SKIN PRIMARY AND CUMULATIVE IRRITATION POTENTIAL AND SKIN SENSITIZATION POTENTIAL OF A PRODUCT, UNDER CONTROLLED AND MAXIMIZED CONDITIONS IN SUBJECTS WITH SENSITIVE SKIN

FINAL REPORT

INVESTIGATIONAL PRODUCT TYPE: Conditioner
INVESTIGATIONAL PRODUCT NAME: No. 5 – Bond Maintenance Conditioner

INSTITUTE PRODUCT CODE: 096954-05
STUDY CODE: All-S-02/14/2022-BURGUNDY-GROUP-IRRITATION-SENSITIZATION
REPORT CODE: All-S-RIPT-096954-05-02-22-RFV01-Rev01

REPORT DATE: 04/19/2022

SPONSOR: OLAPLEX INC.
1187 Coast Village Road, 1-520 - Santa Barbara
California - United States

STUDY CENTER: ALLERGISA PESQUISA DERMATO-COSMÉTICA LTDA.
[redacted]

Investigator in Charge: [redacted]

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ASSESSMENT OF THE SKIN PRIMARY AND CUMULATIVE IRRITATION POTENTIAL AND SKIN SENSITIZATION POTENTIAL OF A PRODUCT, UNDER CONTROLLED AND MAXIMIZED CONDITIONS IN SUBJECTS WITH SENSITIVE SKIN

SUMMARY

Investigational Product Name	No. 5 – Bond Maintenance Conditioner
Product Code of the Institute	096954-05
Study Code	All-S-02/14/2022-BURGUNDY-GROUP-IRRITATION-SENSITIZATION
Report Code	All-S-RIPT-096954-05-02-22-RFV01-Rev01
Sponsor	OLAPLEX INC.
OBJECTIVE OF THE STUDY	To prove the absence of primary and cumulative irritation potential and skin sensitization potential of a product under maximized conditions, with controlled product amount and application site in subjects with sensitive skin, supervised by a dermatologist.
METHODOLOGY	Both the test-product and control were applied to patch test filter paper discs and, then, attached to the right or left back (scapular area) of the study subjects. Induction Period: The applications were performed during 3 consecutive weeks. Forty-eight hours (48h), or 72h (on weekends) after the application, the product was removed by expert technicians and the site was assessed in order to check the presence of possible clinical signs. Rest Period: After the induction there was a minimum 10 day-period when no product was applied to the study subjects' dorsum. Challenge Test: Then, the challenge period started. One single application was made, followed by readings after 48h and 72h of it being attached to the subject's dorsum. The dermatological clinical assessment was made in the beginning and end of the study and the subjects were supervised by a dermatologist throughout the study.
INVESTIGATOR IN CHARGE	[redacted]
STUDY LENGTH	6 weeks.
APPLICATION SITE	Back (Scapular area)
FREQUENCY OF APPLICATION	9 applications on the first 3 weeks (induction period). 1 application on the last week (challenge period).
INCLUDED STUDY POPULATION DESCRIPTION	Male and female subjects, aged between 18 and 59 years old (mean age: 36 years old), phototypes II to IV.
NUMBER OF SUBJECTS	A total of 91 study subjects were included in the study and a total of 51 subjects completed the study.

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ÉTICA	This study was conducted in conformity with the Declaration of Helsinki principles and according to the demands of applicable regulations, including CNS Resolution No. 466/12, and according to the Good Clinical Practices (Document of the Americas and ICH E6: Good Clinical Practices).
RESULTS / CONCLUSION	• The product has no *irritant and sensitizing potential*. • The product was considered safe under the study conditions.

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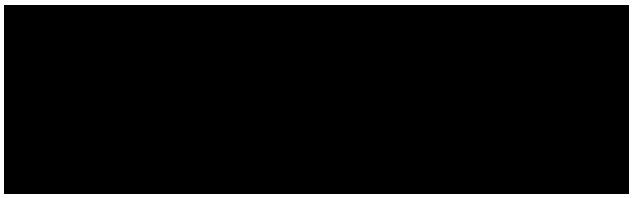
QUALITY ASSURANCE

The study was conducted according to the Resolution CNS 466/12, the Good Clinical Practices and in conformity with the Standard Operating Procedures of the Institute.

Data quality is assured, considering that our personnel is trained according to the requirements of 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 responsible by the Management System auditory; and it is completely available for any specific study monitory performed by the Sponsor.

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



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1. ABBREVIATION LIST

Ave.	Avenue
Cm	Centimeter
CNS	Brazilian Health Council
CRM	Regional Council of Medicine
Dr.	Doctor
Etc.	*Et Cetera*
G	Gram
H	Hour
i.e.	*Id Est*
ICDRG	International Contact Dermatitis Research Group
ICF	Informed Consent Form
ICH	International Conference on Harmonization
ID	Identification (Brazilian General Registration)
LTDA	Limited
ml	Milliliter
No.	Number
SP	São Paulo
Tx	Study Assessment Time-Points

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2. INTRODUCTION

Industry awareness and consumer's and regulatory agencies requirements caused personal hygiene, household, cosmetic and perfume products 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 personal hygiene, household, cosmetic and perfume products become freely available for the consumer, it must be safe when applied under normal or reasonably foreseeable conditions of use. For this, the raw materials used in the product formulation must be raw materials with proved safety and with well-established use in the industry. In addition, the safety of the final formulation must be tested before it is marketed.

The contact of the skin with topical products, such as personal hygiene, cosmetic and perfumes products, may trigger different types of reactions. Among these adverse reactions, we can point out eczematous contact dermatitis, urticaria, acne and blemishes (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).

The objective of studies for safety assessment of personal hygiene, household, cosmetic and perfume products is to confirm the absence of risk associated with the product use.

Compatibility studies performed through patch test aim to prove the absence of adverse events during the contact of personal hygiene, household, cosmetic and perfume products for the first time on the skin, proving that they are 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 photoirritant or photoallergy potential can also be proved.

2.1. Sensitive Skin

The expression "Sensitive Skin" is used to describe individuals who present reduced tolerance to frequently-used or prolonged-use cosmetic products. Such tolerance may be expressed through a range of symptoms varying from subjective complaints such as itching, burning and stinging sensations to visible clinical signs, such as erythema, desquamation and others.

Mechanisms in charge of the development of "sensitive skin" comprise increased immune response, blood and sensorineural hyperreactivity, altered inflammatory mechanisms, psychological susceptibility, as well as reduced barrier epidermic function.

Even though data from the literature are still preliminary, "sensitive skin" can be evidenced by complaints from subjects who report intense and frequent sensory adverse events when using cosmetics and personal care products (FARAGE and MAIBACH, 2010).

Studies from cosmetics manufacturers have shown that 1% to 10% of facial cosmetic products users have already presented subjective sensations such as tingling, stinging and itching. Such symptoms may emerge immediately after product application or some minutes or hours after application. They can also emerge after a product cumulative application or in combination with the use of other products concurrently (AMIN and MAIBACH HI, 1996).

For people with sensitive skin, this number rises to 50% of users with complaints of discomfort sensation with visible signs of inflammation (SIMION and RAU, 1994).

3. OBJECTIVE

The objective of this study was to prove the absence of the primary and cumulative skin irritation and sensitization potential of a product, under maximized conditions, with controlled product quantity and application site in subjects with sensitive skin, supervised by a dermatologist.

4. STUDY DESIGN

Comparative single-blind controlled clinical study.

5. TEST SITE

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

6. INVESTIGATIONAL PRODUCT

The investigational product was provided by the Sponsor and was labeled with adequate codes. All products sent by the sponsor were initially stored in the sample room at the study center, with controlled temperature and restricted access. The products release was controlled by the principal investigator or by a previously designated technical staff.

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Product information, as declared by the Sponsor, are described in APPENDIX 3. One sample of the product was cataloged and can be found in the Institute's archive, for a period of one month after the end of the study.

6.1. Identification

Table 1. Investigational product identification

Type of Product	Product Name	Product Code
Conditioner	No. 5 – Bond Maintenance Conditioner	096954-05

6.2. Investigational Product Application Directions

The investigational product (in the amount of 0.05g/cm²) was applied in the concentration of 100%, i.e., as it is found.

The investigational product was distributed over the filter paper disc of the patch test, duly identified, with the alphabet letter corresponding to the product. Sterile saline solution (NaCl 0.9%) was used as the control, being distributed on another patch test filter paper disc.

The investigational product and control were applied always to the same alphabet letter and always attached to the same dorsum area of the subjects throughout the induction period of the study.

7. STUDY PERIOD

The total duration of the study was 6 weeks for each subjects.

Group 1

- **Clinical Assessment and First Application:** 02/14/2022;
- **End Date:** 03/25/2022.

Group 2

- **Clinical Assessment and First Application:** 02/21/2022;
- **End Date:** 04/01/2022.

So that the study could be finished with the number of subjects required by protocol, new subjects were screened, forming groups 1 and 2. These groups had the adequate procedure schedule to the start date, ensuring compliance with the methodology proposed by protocol, as in item 9.2.

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8. STUDY SUBJECTS

8.1. Study Subjects Recruitment

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

The study was performed in one of Allergisa's facilities and the subjects were informed about the address/site when they were contacted.

8.2. Selection and Admission of Study Subjects

During the subjects selection to this study, the physician in charge ensured that that the subjects did not present pathologies that could interfere on the study results and the physician is also responsible for the information on the study subject evaluation form, verifying all the inclusion and non-inclusion criteria for the subjects admission.

8.3. Study Population

The sample size of the population to be recruited predicted by Protocol was up to 150 subjects, with the objective of completing the study with 50 responses.

8.4. Inclusion Criteria

- Healthy 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 of giving consent for participation in the study;
- Aged from 18 to 70 years old;
- Phototype (Fitzpatrick): I to IV;
- Any gender.

8.5. Non-Inclusion Criteria

- Pregnancy or breastfeeding;

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- 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;
- Antecedents of allergic reactions or intense discomfort sensations to topical products: cosmetics, health products or medications;
- History of atopy (atopic dermatitis, allergic rhinitis, allergic bronchitis, allergic conjunctivitis, etc.);
- Discomfort sensation with temperature changes (too hot/too cold) and/or when you are in the air conditioner;
- Subjects with history of allergy to the materials used in the study;
- 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 assessment;
- Intention of being intensely exposed to sunlight or to sun tanning sessions during the study period;
- Forecast of sea bathing, of going to the pool or bathtub during the study;
- Subjects who practice water sports;
- Dermographism;
- Aesthetic and/or dermatological treatment performed on the body within 03 weeks before selection;
- Use of the following topical or systemic medications: immunosuppressant drugs, anti-histaminic drugs, non-hormonal anti-inflammatory drugs, and corticosteroids up to 2 weeks before selection; in case of deposit corticosteroids, up to 1 month before selection;
- Oral or topical treatment with acid vitamin A and/or its derivatives up to 01 month before the study started;
- Forecast of vaccination during the study or up to 03 weeks before the study.
- 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 study;
- Be currently taking part or have already participated in another clinical study which was concluded less than 21 days if the previous study was a Compatibility study or an Adverse Reaction Investigation;
- Any conditions not mentioned above 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.

8.6. Study Requirements

- Not to apply any other product to the test site (dorsum);
- Not to change any cosmetic habits, including personal hygiene;
- Not to have body aesthetic or dermatological treatments performed;
- Not to change food habits;
- Not to change hormone treatment;
- If female, do not change the contraception method;
- Not to wet the patches: during shower, in swimming pools on the sea, sauna or excessive sweat;
- Not to remove the plasters;
- Not to wear tight clothes which can remove the plaster through friction or cause redness;
- Not to expose yourself to prolonged intense sunlight and not to submit yourself to artificial tanning;
- Not to use the medication described below.

8.7. Medications and Prohibited concomitant treatments

Do not use any of these medications and/or perform any of the treatments prohibited during the study. (In case the therapeutic use of any medication mentioned below is necessary, the subject would be excluded from the study).

- Non-hormonal anti-inflammatory drugs of continuous use (the sporadic use should be evaluated by the investigator, concerning the non-inclusion in the study);
- Corticoids;
- Antihistamines;
- Immunosuppressant drugs;
- Acid vitamin A and oral and topical derivatives (e.g.: Isotretinoin);
- Antibiotics;
- Tetracyclines;
- Topical medications of acne treatments, such as benzoyl peroxide;
- Anti-androgenics;
- Halogens;
- Vitamins B12, B6, B1 and D2;
- Isoniazid, rifampicin, ethionamide (treatment for tuberculosis and leprosy);

- Phenobarbiturics, trimethadione, hydantoin, lithium, chloral hydrate (neurological and psychiatric treatment);
- Quinine;
- Disulfiram;
- Thiouracil;
- Thiourea;
- During the study, any aesthetic, cosmetic or dermatological treatment was also forbidden.

9. METHODOLOGY

9.1. Materials and Equipment

- Semi-occlusive hypoallergenic adhesive tape for the patch test with paper filter discs with 1.0 cm^2, duly identified;
- 0.9% sterile saline solution (NaCl 0.9%);
- Distilled water;
- Mineral oil or petrolatum;
- Gloves, masks and caps;
- Beaker;
- Dropper bottle;
- Transparent bottle;
- Surgical marker pen;
- Cotton swab;
- Absorbent cotton;
- Alcohol.
- Repipettor;
- Weight Scale.

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9.2. Procedure Schedule

Table 2. Study Schedule – Groups 1 and 2.

			Phases				
			Sign Informed Consent	Dermatological Clinical Assessment	Product Application	Product Removal	Assessments (Readings)
Induction Period	Week 1	Visit 1	X	X	X	-	-
		Visit 2	-	-	X	X	X
		Visit 3	-	-	X	X	X
	Week 2	Visit 4	-	-	X	X	X
		Visit 5	-	-	X	X	X
		Visit 6	-	-	X	X	X
	Week 3	Visit 7	-	-	X	X	X
		Visit 8	-	-	X	X	X
		Visit 9	-	-	X	X	X
		Visit 10	-	-	-	X	X
Rest Period	Week 4 and 5	No visits made					
Challenge Period	Week 6	Visit 11	-	-	X	-	-
		Visit 12	-	-	-	X	X
		Visit 13	-	X	-	-	X

9.3. Methods and Criteria of Assessment

9.3.1. Dermatological Clinical Assessment

The dermatological clinical assessment of the subjects was made in the initial visit, to check the inclusion and exclusion criteria of the study, and in the final visit to check possible adverse events and discomfort sensations. Subjects were supervised by a dermatologist throughout the study and assessed in case there were any symptoms or clinical signs.

9.3.2. Skin Primary and Cumulative Irritation and Sensitization Assessment

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

Induction Period: The investigational product was always applied to the same duly protected area (right or left back of the subjects). The applications were performed three times a week, for three consecutive weeks with the product 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, during which no products were applied.

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

The product was removed by the trained technicians after approximately 48 hours of contact with the subjects' skin.

The assessments (readings) were performed immediately and, approximately 24 hours (72h reading) after the product removal.

The subjects were instructed to contact the study coordinator at any time, in case they had any complaints. In these cases, they would be sent for evaluation and guidance by the dermatologist in charge, who would evaluate the subjects, then rate the reaction and follow the appropriate procedure (guidance and/or medication and photographic record, when necessary).

The readings (48h after the application) were made right after the investigational product removal, for all cases when no clinical signs were observed. If observed, the readings would be carried after a minimum of 30 minutes and maximum of 60 minutes, so the sign, possibly caused by the act of investigational product removal, would not represent a false positive.

9.3.3. Assessment of Clinical Signs (Readings)

During the study, the areas of product application and control were assessed and, if any clinical signs were verified, they would be classified according to the standardized scale by the International Contact Dermatitis Research Group - ICDRG - (FISHER, 1995).

Table 3. 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 (+++)

The signs described in the table above are considered expected signs for this study, considering mainly the type of maximized exposure to the product, predicted by the methodology. Therefore, they are not considered adverse events.

Every sign observed during the study is supervised by the investigator. In the case of more intense signs (scores 3 and 4), there must be the need of interruption of product application, according to the assessment of the investigator.

9.4. Criteria and Procedures for Study Subjects Withdrawal

The removal of a study subject by the investigator could occur due to the following reasons:

- Study subjects not included: subjects who sign the ICF, but who do not meet the inclusion and non-inclusion criteria of the study;
- Subjects who present complications that affect their eligibility after the study consent;
- Subjects who present - at the Investigator's discretion - any problem that would 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 will be recorded if the subject does not visit the study center for assessments;
- Serious Adverse Event;
- Concurrent disorder or treatment: any pathological process or treatment that occurred during the study period and that might 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 supervised in case they present any event possibly related to the study, even after their removal. Those subjects removed due to occurrence of adverse event were continually supervised until the case is completely resolved.

Those subjects who were removed from study after the inclusion stage were not replaced.

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10. 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 test product use (adapted from ICH, 2016).

According to the Good Clinical Practices (ICH, 2016), 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-assessment 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 evaluation 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 drug products) - such as inappropriate frequency or incorrect application - are 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.

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.

For the conclusion of the final diagnosis, the relation of an Adverse Event can be defined using the decision tree Colipa (2016), according to the following description:

• Very likely: Only cases in which the clinical condition is considered to be evocative are classified as a very likely nexus, the following conditions occurring together: (i) the temporality of the facts is compatible with an adverse reaction to cosmetics and (ii) there is a laboratory test that confirm the relationship with the investigational product (e.g. positive patch test for the investigational product).

• Likely: The cases in which the clinical condition is considered to be evocative are classified as likely causal nexus, occurring with the following conditions together: (i) the temporality of the facts is compatible with an adverse reaction to cosmetics and (ii) there is no laboratory test to confirm the

relationship with the investigational product (e.g. diagnosis of contact dermatitis, without patch test, cosmetic acne - there are no laboratory tests to confirm the relationship with the product).

• Not clearly attributable: Cases in which the clinical scenario is not considered to be evocative or the chronology is not clearly compatible or unknown, are classified as nexus not clearly attributable.

• Unlikely: The following two cases are associated with an unlikely nexus: the clinical scenario is not considered to be evocative; the chronology is not clearly compatible or unknown, and the result of the investigation with the investigational product is negative (patch test or re-exposure).

• Excluded: The cases in which the diagnosis corresponds to a dermatosis of well-known cause and / or known to be caused by the use of products are classified as excluded nexus (e.g. vitiligo, tineas, pityriasis rosea, pityriasis versicolor, psoriasis, folliculitis, solar melanosis, ephelides, among others), when there is no correlation between the subject's complaint and the use of a cosmetic product (for example: muscle pain, lack of appetite, stomach pain, diarrhea, insect bites, among others) or the chronology is clearly incompatible with an adverse reaction to the cosmetic product (for example: there is no improvement in the scenario, even with the interruption of the product; there is relapse of the scenario, without the reintroduction of the product; the signs and symptoms started before the start of the product use).

An Adverse Event Form is completed for all events occurred during the study. During the follow-up of the adverse event, photographs may be taken of the subject after their consent and signature of the Informed Consent for Image Release, always ensuring the preservation of their identity.

11. APPLICABLE ETHICAL REMARKS

This study was conducted in compliance with the Declaration of Helsinki principles, the applicable regulatory requirements, including Resolution CNS no. 466/12, and according to the Good Clinical Practices (Document of the Americas and ICH E6: Good Clinical Practices).

Before the study starts, the subjects were informed about the study objective, its methodology and length, and about the possibly expected benefits and the constraints related to the study. Subjects who agreed to take part in the study signed an Informed Consent Form (ICF) (APPENDIX 1), elaborated according to the Declaration of Helsinki and Resolution CNS No. 466/12. The process of obtaining the ICF confirmed the voluntary nature of subjects participation in the study.

In order to maintain confidentiality of subjects' data, all data collected were identified by a number given to them at the beginning of the study. No personal information was disclosed in all data analyses. If necessary, the investigator in charge must allow the study monitor to access all subjects related records. This includes all documents containing the subject's clinical history for checking suitability for the study, diagnoses and any other document concerning the subject in the study.

All data that were found or proved by the study results are considered as being confidential information and sponsor's property. No information - as well as all documents generated during the study - will be copied or disclosed without a previous written consent of the sponsor. All information was kept confidential until the results were published.

The study technical documentation is in the Institute's archives, where it will be stored for a 5 years period.

12. RESULTS

12.1. Protocol Deviations

Subject 022 was submitted to intense sunlight exposure during the study. Therefore, the subject was removed and her data were not considered in the study.

12.2. Study Population Description and Study Adherence

Ninety-one (91) subjects were included in the study, among them, 51 finished the study. The summarized description of the population and adherence to the study is available in the following table. The detailed description of the population can be found in APPENDIX 2.

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Table 4. Population Included and Adherence to the Study

Population Included									Adherence		
Recruited[1]	**Not Included[2]**	**Withdrawn[3]**	**Included[4]**	**Gender (F)**	**Gender (M)**	**Minimum Age (years)**	**Maximum Age (years)**	**Mean Age (years)**	**Absences[5]**	**Removed[6]**	**Finished the Study[7]**
106	15	00	91	78	13	18	59	36	30	10	51
Subjects									003, 005, 009, 019, 020, 021, 027, 031, 034, 038, 039, 042, 045, 047, 048, 052, 055, 056, 058, 062, 064, 066, 071, 073, 083, 084, 094, 100, 103 and 105	022, 036, 037, 049, 053, 079, 080, 081, 082 and 101	

[1]*subjects who attended the Institute and signed the ICD.*
[2]*Subjects who did not meet the inclusion criteria or presented any of the non-inclusion criteria.*
[3]*subjects who withdrew from the study after the study consent for personal reasons and were not included.*
[4]*subjects who were approved in the study.*
[5]*subjects who were absent in the study for personal reasons unrelated to the study and to the investigational product.*
[6]*subjects removed from the study are characterized as protocol deviations or another reason recorded by the study investigator.*
[7]*subjects considered in the total who finished the study.*
Caption: F=Female; M=Male

Subject 022 was removed from the study for characterizing as protocol deviation as described in the item 12.1.

Subjects 036, 037, 049, 053, 079, 080, 081, 082 and 101 were removed from the study for presenting adverse event according to item 12.3.

The study met the objective of obtaining in the end at least 50 responses.

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12.3. Dermatological Clinical Assessment

Subjects 036, 037, 049, 053, 079, 080, 081, 082 and 101

The study subjects presented irritation after the continuous exposure of the skin to the adhesive tape (adhesive plaster), probably due to individual predisposition, and for this reason the applications were interrupted and their data not used in the study. They were cases of excluded nexus, i.e. unrelated to the product.

During the study, no subjects experienced clinical signs on the investigational product application area (Table 5 and 6).

No subjects presented clinical signs in the control site.

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Table 5. Assessment – Investigational Product – Group 1.

		Induction Period									Rest Period	Challenge Period		
Subject No.	1st Application	Reading + 2nd application	Reading + 3rd application	Reading + 4th application	Reading + 5th application	Reading + 6th application	Reading + 7th application	Reading + 8th application	Reading + 9th application	Reading		10th application	Reading	Reading
002	0	0	0	0	0	0	0	0	0	0	No procedure made	0	0	0
003	0	F/R	R	R	R	R	R	R	R	R		R	R	R
004	0	0	0	0	0	0	0	0	0	0		0	0	0
005	0	0	0	0	0	F	0	0	F	F/R		R	R	R
006	0	0	0	0	0	0	0	0	0	0		0	0	0
007	0	0	0	0	0	0	0	0	0	0		0	0	0
009	0	0	F/R	R	R	R	R	R	R	R		R	R	R
010	0	0	0	0	0	0	0	0	0	0		0	0	0
011	0	0	0	0	0	0	0	0	0	0		0	0	0
013	0	0	0	0	F	0	0	0	0	0		0	0	0
014	0	0	0	0	0	0	F	0	0	0		0	0	0
015	0	0	0	0	0	0	0	0	0	0		0	0	0
016	0	0	0	0	0	0	0	0	0	0		0	0	0
017	0	0	0	0	0	0	0	0	0	0		0	0	0
018	0	0	0	0	0	0	0	0	0	0		0	0	0
019	0	0	0	0	0	F	F/R	R	R	R		R	R	R
020	0	0	0	0	0	0	F	F/R	R	R		R	R	R
021	0	F/R	R	R	R	R	R	R	R	R		R	R	R
022	0	0	0	0	0	0	0	0	0	0		DP/R	R	R
023	0	0	0	0	0	0	0	0	F	0		0	0	0
024	0	0	0	0	0	0	0	0	0	0		0	0	0
025	0	0	0	0	0	0	0	0	0	0		0	0	0
026	0	0	0	0	0	0	0	0	0	0		0	0	0
027	0	F/R	R	R	R	R	R	R	R	R		R	R	R
028	0	0	0	0	0	0	0	0	0	0		0	0	0
029	0	0	0	0	0	0	0	0	0	0		0	0	0
030	0	0	0	0	0	0	0	0	0	0		0	0	0
031	0	0	0	0	0	0	0	0	0	0		F/R	R	R

Caption:
X = Not Applied / Reading Not Performed
F= Absent
R = Removed from the Study
E = Darkening
D = Dryness
F/R = Absent / Removed from the study
EA = Adverse Event
DP = Protocol Deviation

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

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Continuation Table 5. Assessment – Investigational Product – Group 1.

		Induction Period									Rest Period	Challenge Period		
Subject No.	1st Application	Reading + 2nd application	Reading + 3rd application	Reading + 4th application	Reading + 5th application	Reading + 6th application	Reading + 7th application	Reading + 8th application	Reading + 9th application	Reading		10th application	Reading	Reading
033	0	0	0	0	0	0	0	0	0	0	No procedure made	0	0	0
034	0	F/R	R	R	R	R	R	R	R	R		R	R	R
035	0	0	0	0	0	0	0	0	0	0		0	0	0
036	0	0	0	0	0	EA/R	R	R	R	R		R	R	R
037	0	0	0	0	EA/R	R	R	R	R	R		R	R	R
038	0	0	0	F	F/R	R	R	R	R	R		R	R	R
039	0	0	0	0	F	F/R	R	R	R	R		R	R	R
042	0	F/R	R	R	R	R	R	R	R	R		R	R	R
045	0	0	F/R	R	R	R	R	R	R	R		R	R	R
046	0	0	0	0	0	0	0	0	0	0		0	0	0
047	0	0	F/R	R	R	R	R	R	R	R		R	R	R
048	0	F/R	R	R	R	R	R	R	R	R		R	R	R
049	0	0	0	0	0	EA/R	R	R	R	R		R	R	R
051	0	0	0	0	0	0	0	0	0	0		0	0	0
052	0	0	0	0	0	0	0	0	0	0		F/R	R	R
053	0	0	0	0	EA/R	R	R	R	R	R		R	R	R
054	0	0	0	0	0	0	0	0	0	0		0	0	0
055	0	0	F/R	R	R	R	R	R	R	R		R	R	R
056	0	F/R	R	R	R	R	R	R	R	R		R	R	R
057	0	0	0	0	0	0	0	0	0	0		0	0	0
058	0	0	0	0	0	F	F/R	R	R	R		R	R	R
059	0	0	0	0	0	0	0	0	0	0		0	0	0
060	0	0	0	0	0	0	0	0	0	0		0	0	0
062	0	0	0	0	0	0	0	F	F/R	R		R	R	R
063	0	0	0	0	0	F	0	0	0	0		0	0	0
064	0	0	0	0	0	0	0	F	F/R	R		R	R	R
065	0	0	0	0	0	0	0	0	0	0		0	0	0

Caption:
X = Not Applied / Reading Not Performed
F= Absent
R = Removed from the Study
E = Darkening
D = Dryness
F/R = Absent / Removed from the study
EA = Adverse Event
DP = Protocol Deviation

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

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Continuation Table 5. Assessment – Investigational Product – Group 1.

		Induction Period									Rest Period	Challenge Period		
Subject No.	1st Application	Reading + 2nd application	Reading + 3rd application	Reading + 4th application	Reading + 5th application	Reading + 6th application	Reading + 7th application	Reading + 8th application	Reading + 9th application	Reading	No procedure made	10th application	Reading	Reading
066	0	0	0	0	0	0	0	0	0	F		F/R	R	R
067	0	0	0	0	0	0	0	0	0	0		0	0	0
068	0	0	0	0	0	0	0	0	0	0		0	0	0
070	0	0	0	0	0	0	0	0	0	0		0	0	0
071	0	F/R	R	R	R	R	R	R	R	R		R	R	R
072	0	0	0	0	0	0	0	0	0	0		0	0	0
073	0	0	0	0	0	0	F	F/R	R	R		R	R	R
074	0	0	0	0	0	0	0	0	0	0		0	0	0
078	0	0	0	0	0	0	0	0	0	0		0	0	0
079	0	0	0	0	0	EA/R	R	R	R	R		R	R	R
080	0	0	0	0	0	EA/R	R	R	R	R		R	R	R
081	0	0	0	0	0	EA/R	R	R	R	R		R	R	R
082	0	0	0	0	0	0	EA/R	R	R	R		R	R	R
083	0	0	F/R	R	R	R	R	R	R	R		R	R	R
084	0	0	F/R	R	R	R	R	R	R	R		R	R	R

Caption:
X = Not Applied / Reading Not Performed
F= Absent
R = Removed from the Study
E = Darkening
D = Dryness
F/R = Absent / Removed from the study
EA = Adverse Event
DP = Protocol Deviation

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

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Table 6. Assessment – Investigational Product – Group 2.

		Induction Period									Rest Period	Challenge Period		
Subject No.	1st Application	Reading + 2nd application	Reading + 3rd application	Reading + 4th application	Reading + 5th application	Reading + 6th application	Reading + 7th application	Reading + 8th application	Reading + 9th application	Reading		10th application	Reading	Reading
085	0	0	0	0	0	0	0	0	0	0	No procedure made	0	0	0
086	0	0	0	0	0	0	0	0	0	0		0	0	0
087	0	0	0	0	0	0	0	0	0	0		0	0	0
088	0	0	0	0	0	0	F	0	0	0		0	0	0
089	0	0	0	0	0	0	0	0	0	0		0	0	0
090	0	0	0	0	0	0	0	0	0	F		0	0	0
091	0	0	0	0	0	0	0	0	0	0		0	0	0
092	0	0	0	0	0	0	F	0	0	0		0	0	0
093	0	0	0	0	0	0	0	0	0	0		0	0	0
094	0	F/R	R	R	R	R	R	R	R	R		R	R	R
095	0	0	0	0	0	F	0	0	0	0		0	0	0
096	0	0	0	0	0	0	0	0	0	0		0	0	0
097	0	0	0	0	0	F	0	0	0	0		0	0	0
099	0	0	0	0	0	0	0	0	0	0		0	0	0
100	0	F/R	R	R	R	R	R	R	R	R		R	R	R
101	0	0	0	EA/R	R	R	R	R	R	R		R	R	R
102	0	0	0	0	0	0	0	0	0	0		0	0	0
103	0	F/R	R	R	R	R	R	R	R	R		R	R	R
104	0	0	0	0	0	0	0	0	0	0		0	0	0
105	0	F/R	R	R	R	R	R	R	R	R		R	R	R
106	0	0	0	0	0	0	0	0	0	0		0	0	0

Caption:
X = Not Applied / Reading Not Performed
F= Absent
R = Removed from the Study
E = Darkening
D = Dryness
F/R = Absent / Removed from the study
EA = Adverse Event
DP = Protocol Deviation

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

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Table 7 describes the responses observed during the Induction and Challenge periods.

Table 7. Positive responses observed during the study.

No. of Finishing Subjects	No. of Positive Responses during Induction	No. of Positive Responses during Challenge
51	0	0
	Description of the Signs:	**No. of confirmed responses of sensitization**
	-	0

Induction phase: No reactions were observed during the induction phase. The results for this phase indicate the absence of irritation potential for this product.

Challenge phase: no reactions were observed during the challenge phase. The results for this phase indicate the absence of allergenic potential for this product.

13. CONCLUSION

According to the methodology used to assess the skin primary and cumulative irritation potential and skin sensitization potential of the product **No. 5 – Bond Maintenance Conditioner**, submitted by the company **OLAPLEX INC.**, it could be concluded that:

- The product has no *irritant and sensitizing potential*.
- The product was considered safe under the study conditions.

[redacted]

Investigator in Charge
04/19/2022

[redacted]

Dermatologist (CRM: 33685)
04/19/2022

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14. REFERENCES

AMIN, S., LAHTI, A., MAIBACH, H.I. Contact urticaria and the contact urticaria syndrome (immediate contact reactions). In: Marzulli FN, Maibach HI, eds. Dermatotoxicology. 5th ed. Washington: Hemisphere, 1996.

COLIPA Guidelines on the management of undesirable effects and reporting of serious undesirable effects in the European Union. March 2016.

DOOMS - GOOSSENS, A. Cosmetics as causes of allergic contact dermatitis. *Cutis.* 52: 316-320, 1993.

FARAGE M. A, MAIBACH H.I, Sensitive Skin: Closing In On A Physiological Cause. Contact Dermatitis. 2010 Mar; 62(3):137-49. doi: 10.1111/j.1600-0536.2009.01697.x.

FISHER, A.A. Contact Dermatitis, 2ª edition, Philadelphia, Lea & Febiger, 1995.

INTERNATIONAL CONFERENCE FOR HARMONIZATION (ICH) Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance, 2016

KLIGMAN, A.M. & WOODING, W.M. A method for the measurement and evaluation of irritants of human skin. *J. Invest. Derm.* 49: 78-94, 1967.

NATIONAL HEALTH COUNCIL. Resolution 466/12 of the Ministry of Health Federal Official Journal, 06/13/2013.

ORGANIZACIÓN PANAMERICANA DE LA SALUD. BUENAS PRÁCTICAS CLÍNICAS: DOCUMENTO DE LAS AMÉRICAS, 2005

SAMPAIO, S.A.P. & RIVITTI, E.A. Dermatologia Básica, 2ª edição, São Paulo, Artes Médicas, 2000.

SIMION, F.A., RAU, A.H. Cosmet Toilet 109:43, 1994.

WORLD MEDICAL ASSOCIATION. Declaration of Helsinki: Ethical Principles for Clinical Research Involving Humans, 52, 2000. Edinburgh: [s.n.], 2000. Amendment.

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APPENDIX 1 INFORMED CONSENT FORM

Due to sharing the study among different sponsors, the ICF attached regards all studies on which the subject was clarified and included.

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Sub No.: _____

INFORMED CONSENT FORM

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Date: _____/_____/_____ **Group:** _____

TITLE OF THE STUDY PROJECT: ASSESSMENT OF THE PRIMARY AND CUMULATIVE SKIN IRRITATION AND SKIN SENSITIZATION POTENTIAL OF PRODUCTS TO BE APPLIED TO THE SKIN UNDER CONTROLLED AND MAXIMIZED CONDITIONS (HRIPT)

NAME OF THE INVESTIGATOR IN CHARGE [redacted]

STUDY SITE: Allergisa Pesquisa Dermato-Cosmética Ltda.

You are being invited to join a study that will be carried out by Allergisa's staff together with the company that is sponsoring this study.

Before any decision, it is important that you read with attention all information presented, and if you decide to join, you will be requested to sign two originals of this informed consent form and one original will be given to you.

Your participation in this study is completely voluntary and it depends only on your will, and you are also free to withdraw from the study at any time.

Any doubts you might have before, during or after the study will be promptly solved.

This study is being done with all the safety measures necessary to avoid the contamination by coronavirus, which causes the disease COVID-19. If you agree in taking part of this study, please follow the instructions below to keep your own safety.

What are the objectives of this study?

The objective of the study is to prove the absence of skin irritation and/or skin sensitization of cosmetic products (examples: soaps, shampoos, deodorants, powders, bath oils, moisturizers, lotions, perfumes, colognes, sunscreens, insect repellent among others), health care products (examples: dressing, adhesive plasters, hospital-medical use products), topical medications (examples: ointments, gels, for use on the skin), sanitizing products (detergents, soaps, softeners, mutipurpose products among others) and/or raw materials (examples: individual ingredients that compose a cosmetic product).

You may take part in one or more panels (groups of subjects) with up to **150** subjects each, being that these panels may be with subjects who have sensitive skin or not.

Skin Irritation and Sensitization are irritation and allergic reactions, which may occur eventually in your skin, after these products application.

Can I join the study?

To participate in the study, firstly you must present good health and meet other requirements called inclusion and non-inclusion criteria, that will be assessed and discussed by the specialist physician.

You can even be dismissed by the expert physician(s), after signing the informed consent form, if you present any of the non-inclusion criteria of the study, also in case the total amount of subjects was already reached.

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Where will the study be conducted?

The study will be conducted in one of the facilities of ALLERGISA pesquisa dermato-cosmética ltda, head office located at [redacted] with all the necessary precautions for your safety.

What will I have to do?

Your participation in the study will last 06 weeks. During this period, about 13 visits will be made.

At the beginning of the study you will be previously clinically assessed by a dermatologist and you will be supervised all along the study.

You can also call at any time, to clarify any questions or to inform any discomfort sensation you might present during the study. If your discomfort creates the need of an on-site attention care, an appointment will be scheduled according to the urgency of the case, in which all the precautions recommended by experts will be taken to ensure your safety in the first place.

Your adherence to the visits schedule is important for the study results. In case you cannot attend the scheduled date, please, contact the investigator or the study team and check the possibility of returning as soon as possible for the visit.

You commit yourself not to join any other research during this study.

What are the study procedures?

The following procedures will be performed during the study:

• Before the beginning of the study, a technician will clean the counter and the chairs of the room using Gel Alcohol hand sanitizer 70%;

• Before entering or leaving the test room, the technician will put the hand sanitizer on your hands, so that you can sanitize them;

• You will be instructed to sit and get comfortable in the chair of the test room, respecting a minimum distance of 2 meters from other subjects;

• You will be instructed to avoid talking to other subjects to minimize the risk of contamination inside the test room;

• Upon arriving at the Institute, you will receive a mask of mandatory use during the whole time of permanence in the test room;

• You will be instructed to avoid touching your face and mask;

• You will be questioned if your mask is wet; if so, you will get another one for use;

• If you feel the need to go to the toilet, you must wash your hands with water and soap and, then, sanitize them again with the gel alcohol hand sanitizer provided.

• You will be informed about the study objective, its methodology and duration, and about the possibly expected benefits and the constraints related to the study and, if you agree, you will sign this Informed Consent Form;

• You will be clinically assessed by a dermatologist at the beginning and at the end of the study and you will be supervised all along the study;

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INFORMED CONSENT FORM

Date: _____/_____/_____ **Group:** _____

• The "patch tests" (adhesive tape) containing the assessed products will be applied on the right and/or left dorsum (back), always to the same site, three times a week, for three consecutive weeks.

• After this period of "induction", you will remain in rest for, at least, 10 days and should return to apply again the "patch tests" containing the assessed products, which will be removed by the trained technician after 48 hours or by you, at home, after 24 hours. In this case, you will be previously informed. You must come to the Institute for the products application and performance of the readings after the applications.

IMPORTANT!!!

On these returns, all the precautions recommended by our health experts will be taken to ensure your safety and the safety of the study team. Masks will be provided by the Institute for use during your stay at the Institute and during the whole study, and there will be gel alcohol hand sanitizer available. The rooms will be cleaned and disinfected with alcohol 70%, there will be appropriate distancing between people, scheduled and individual appointments and a measurement of your temperature at a distance always when necessary.

We ask you to be at the Institute ONLY at the time informed to you, in order to avoid crowds.

Procedures summary:

PROCEDURES	VISIT	TIME SPENT AT THE INSTITUTE
Signature of the Informed Consent Form Dermatological Clinical Assessment Readings before the Application by the Trained Technician "Patch tests" application (adhesive tape)	1	15 to 30 minutes
"Patch tests" removal (adhesive tape) "Patch tests" application (adhesive tape) Readings by the trained technician	2-10	15 to 30 minutes
"Patch tests" removal (adhesive tape) Readings by the trained technician	11 and 13	15 to 30 minutes
Readings by the trained technician Dermatological Clinical Assessment	13	15 to 30 minutes
Diagnosis for COVID-19 (if applicable)	Any visit, as needed	15 to 30 minutes

What information will be obtained about me?

Personal information such as name, age, usual medications, etc., will be obtained.

For this study, information will be obtained about possible adverse reactions that the product might cause on your skin.

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If you present an adverse reaction with clinical sign on the skin (reaction that is able to be observed to the naked eye: irritation, redness, swelling, etc.), photos will be taken with the single purpose of investigation of the reaction and record of these information. Your identity will be kept confidential during the photographic records performance.

The photographs that need to be sent will be received in a phone number exclusively for the use of the Institute physician and all the information and files sent will be confidential and kept in privacy.

If you present any flu symptoms (headache, fever, shortness of breath, etc.), do not come to the Institute. You must call use so we can schedule a teleconsultation with a physician, we will inform you about the procedures to be followed.

What is a teleconsultation?

The teleconsultation is a remote appointment done by a physician through a telephone call or video conference. During the teleconsultation, you will be ensured of the confidentiality of the medical attention, that is, that it was done in a place where only the physician and the authorized person of the technical department were present during the call.

How will the information be protected, in order to preserve my privacy?

All information obtained about you, from your participation in this study, will be treated confidentially, and your identity will be kept confidential, under all circumstances. The information collected about you will be used only with study purpose.

Your identity will be kept confidential throughout the process and only the study investigator in charge or people from the team delegated will have access to those records.

If the study results are published, your identity will remain confidential.

If it is necessary to perform the teleconsultation, it will be performed with a tool that presents data safety, ensuring confidentiality of the medical attention.

According to Law No. 13.709, of August, 2018, which concerns the General Data Protection Law, Allergisa Pesquisa Dermato-Cosmética LTDA, together with the sponsor, declares to be in compliance with all obligations applicable to the Personal Data Processing (including any and all obligations of information to the Data Subject). Allergisa Pesquisa Dermato-Cosmética LTDA guarantees the continuous monitoring of risks and failures of Information Security that may compromise your personal data (such as name, last name, ID, "CPF", address, etc.), and the sensitive personal data (personal information concerning health, ethnic group, racial origin, political party preferences, among others), through our platforms of digital information storage.

In case any of your register data change (e.g. telephone number, address, etc.), please ask the study organizers to have them updated.

What are my responsibilities in this study?

You should attend the Institute on the days and times determined for each visit. In addition, there are some restrictions that you will follow, such as:

- Wear a mask during the whole study procedure and commute to the Institute;
- Respect the social distancing;

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Date: _____/_____/_____ **Group:** _____

- Frequent cleaning of the hands with soap and/or gel alcohol hand sanitizer;
- Attend only at the times scheduled to avoid crowds;
- Allow temperature measures performed by the technical team on all visits to the Institute, if necessary;
- Do not apply any other product to the test site (dorsum);
- Do not change any cosmetic habits, including personal hygiene;
- Do not have body aesthetic or dermatological treatments performed;
- Do not change food habits;
- Do not change hormone treatment;
- If female, do not change the contraception method;
- Do not wet the patch tests (adhesive tape): during shower, in pools or sea, sauna or excessive sweat;
- Do not remove the "patch tests" (adhesive tape);
- Do not wear tight clothes which can remove the "patch tests" (adhesive tape) through friction or cause redness;
- Do not expose yourself to prolonged intense sunlight and not to submit yourself to artificial tanning;

You cannot perform any dermatological treatment during the study. If the treatment is necessary, immediately inform the study site.

We also ask you to communicate the Institute about any type of medication or external/skin or oral use, tablets and liquids (solutions and syrups) or injections, such as cortisone, anti-allergic or any other and also vitamins.

The dates you must attend to the study procedure (return visits) are described in the schedule you will receive in the study start.

If you change any of your habits, we ask that you please keep us informed, so we can better interpret the results.

We ask you not to 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 products application area. If you use any of these products or are taking any medication, please, let us know.

Can I withdraw from the study at any time?

Yes, you are completely free to withdraw from the study at any time, not having to worry with any negative consequences. You can also remove your data (information given) at any time, if you wish.

In case of new information available that can change your desire to continue your participation in the study, you will be timely communicated by the investigator and study team and you will be completely free to withdraw from the study. Just let us know about your willingness to give up.

What benefits will I have to join the study?

Clinical studies aim to prove the safety and efficacy of the products. By joining this study, you will be contributing that those products are used by the population with much lower risk of skin reactions proven. You will also

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undergo free medical assessments.

Is there any risk related to the study participation?

In general, products topically applied products present a good risk/benefit relation; however, they may cause allergy and irritation - especially after long-term use. In case of any reactions occurs, you will undergo assessments and you will receive all necessary dermatological monitoring.

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" on the product application sites. The risks presented are already known, and if they occur, they will be as minimized as possible. You will be clinically supervised by the study site, until your health clinical conditions are reestablished, regardless of the time that it might take. Any health problems you might have during the study should be informed to the investigator or study team immediately. All immediate or late assistance will be provided.

The risk of contamination by the coronavirus exists independently of your participation in the study. There is a risk of contracting the coronavirus for people who use public collective transportation, due to gatherings of people without the necessary care.

As one more safety measure and risk reduction, the Institute will recruit subjects that do not need this type of transportation, and that live close to the Facility; however, if it is necessary to use this mean of transportation to attend the visits, it is important to follow the safety measures of hands sanitation with gel alcohol hand sanitizer provided and the use of masks, avoiding to the put the hands on the face. The transmission of the coronavirus happens from a sick person to another by close contact through: touch, cough, sneezing, mucus, objects or surfaces contaminated such as cell phones, tables, etc. If you feel sick, with Flu symptoms SUCH AS fever, cough, shortness of breath, loss of sense of smell and taste, among other indispositions, you must avoid physical contact with other people, especially elderly and people with chronic diseases and must stay at home for 14 days.

During the study conduction, a test for diagnosis of COVID-19 (disease caused by the new coronavirus) may be performed, as one more measure of safety taken by the Institute during this period. This test will be done with a manual device, through a small hole in your finger, to collect a small blood sample. The advantage of this test is to obtain a quick and practically painless result. In case of suspect or confirmation by COVID-19, follow the recommendations that the Institute will provide based on the health organs. All immediate or late assistance will be provided and, for cases of possible infections by Covid-19, all the instructions to perform a quarantine or seek hospital attention will be given according to the recommendations of the health organs. The subject will be supervised until his/her health is reestablished.

What if I am pregnant or breastfeeding?

Pregnant or breastfeeding women, or women who are planning to get pregnant are not allowed to take part in this study.

If, despite the orientations given by the physician and the study team, you get pregnant and find out during the study, your participation will be terminated for your safety and the safety of the baby. Please inform the study investigator or study team immediately. They will make sure you get advice on what to do during pregnancy, and you will be

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Date: _____/_____/_____ Group: _____

supervised during the pregnancy until the birth.

Will I have any type of reimbursement for the expenses for participating of this study?

As predicted by Brazilian laws, you will not have any type of financial compensation/payment for your participation in the study; however, you will receive a reimbursement in the end of the study due to expenses of your participation.

If you are removed from the study before its conclusion by the investigator in charge, for example, for safety reasons or non-compliance with the study requirements, you will receive the reimbursement for the expenses regarding the days in which you participated.

How can I know about the study results?

The study results will be assessed by the investigator in charge after it is completed. The results can be published, but your name will not be mentioned.

You can still ask to the investigator about the study results after the conclusion of the study.

If you perform the diagnosis test for COVID-19, you will be informed about the result immediately, in private.

Can I be removed from the study?

Yes, your participation in this study can finish earlier than predicted.

It is duty of the investigator, at any moment, to remove you from the study, if you present any reaction to the products or if your health has been affected for any reason and you are not in conditions to continue as a study subject. You can also be removed from the study in case you do not fulfill your responsibilities, according to the study protocol.

What if my participation in the study cause any harm to any other medication I am currently taking?

It is highly important that you inform the investigator in charge of the study about the use of usual medications, or use of any other different medication when you sign this document and during your participation.

In case you need to take a specific medication, non-mentioned previously, you should communicate the study investigator in charge immediately, because he/she will know how to give you instructions about the best conduct for your case.

With whom will I be able to contact if I do not feel well during the study or present any reactions to the products?

If you do not feel well or in case of any irritation skin signs, immediately communicate, attending to the study site or by telephone: [redacted] (working hours) or [redacted] (from 5 pm to 10 pm). In case of any doubts or problems, you can contact the investigator in charge [redacted] or the medical team by the same telephone numbers.

We assure that for any complications or damages caused by the study, a full assistance will be given to the study subjects together with the sponsors of this study.

Eventual indemnifications for damages caused by the study are assured.

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INFORMED CONSENT FORM

We ask you to call the Institute at any moment if you feel symptoms such as cough, fever, coryza, sore throat or shortness of breath, or if you would like to cancel your participation in the study, through the telephones [redacted] (business hours) or [redacted] (from 5 p.m. to 10 p.m.). Subjects who present these symptoms will not be allowed to participate in the study and if you arrive at the Institute with the symptoms, you will not be allowed inside and will be instructed to go home.

If you have any complaints or any questions about your rights as a subject of this study, you might contact the Independent Ethics Committee INVESTIGA – Instituto de Pesquisas, located at [redacted] by the telephones [redacted] and [redacted]. The hours of operation are on Monday to Friday from 9am to 5pm. The Independent Ethics Committee (IEC) is an agency that has the objective to evaluate and supervise the ethical aspects of all studies involving human beings, aiming to assure the dignity, rights, safety and well-being of the study subject.

Important information!

If you have any questions about the study that was not answered yet, you should ask to the investigator or study team.

Please, keep this document for your information.

Signatures Page – ASSESSMENT OF THE PRIMARY AND CUMULATIVE SKIN IRRITATION AND SKIN SENSITIZATION POTENTIAL OF PRODUCTS TO BE APPLIED TO THE SKIN UNDER CONTROLLED AND MAXIMIZED CONDITIONS (HRIPT)

I read and understood the information provided in this Informed Consent Form. I have obtained the answers for all my questions and I freely decided to join this study. I offer my consent, freely, to join this study, as explained in this document.

I am aware that the photographs and/or videos obtained for the medical attention and investigation are part of the procedure of this study and I agree with the obtaining of these images.

By signing this document, I did not waive from any legal rights I have when I participate in a study, including the indemnification.

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 ICF _____ Date

Subject's Initials: _____ *Initials of the person in charge for applying the ICF:* _____

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APPENDIX 2 STUDY GROUP

SUBJECT	AGE (YEARS)	GENDER	PHOTOTYPE	STATUS
001	45	F	III	NI
002	41	F	II	I
003	38	M	III	I
004	37	F	IV	I
005	23	F	IV	I
006	26	F	IV	I
007	56	F	II	I
008	43	F	IV	NI
009	39	F	IV	I
010	30	M	III	I
011	28	F	II	I
012	26	M	II	NI
013	47	F	III	I
014	43	F	IV	I
015	21	M	IV	I
016	47	F	II	I
017	45	F	III	I
018	33	F	II	I
019	31	F	IV	I
020	18	M	IV	I
021	43	F	IV	I
022	22	F	II	I
023	28	F	III	I
024	33	F	III	I
025	31	F	III	I
026	54	F	II	I
027	42	F	III	I
028	28	F	III	I
029	21	F	III	I
030	18	F	III	I

Caption:
F= Female;
M= Male;
I = Included;
NI = Not Included (present any non-inclusion criteria and/or not present some of the inclusion criteria).

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Study Group: Continuation

SUBJECT	AGE (YEARS)	GENDER	PHOTOTYPE	STATUS
031	41	F	IV	I
032	56	F	IV	NI
033	27	F	III	I
034	27	F	III	I
035	29	F	III	I
036	35	F	III	I
037	52	F	III	I
038	32	M	III	I
039	28	F	IV	I
040	34	F	IV	NI
041	18	F	III	NI
042	23	M	IV	I
043	23	M	III	NI
044	32	F	IV	NI
045	33	F	IV	I
046	42	F	III	I
047	27	F	III	I
048	36	F	III	I
049	41	F	IV	I
050	37	F	IV	NI
051	34	F	IV	I
052	47	F	II	I
053	21	F	II	I
054	40	M	IV	I
055	40	F	IV	I
056	38	F	III	I
057	39	F	IV	I
058	55	F	III	I
059	32	M	III	I
060	43	F	III	I

Caption:
F= Female;
M= Male;
I = Included;
NI = Not Included (present any non-inclusion criteria and/or not present some of the inclusion criteria).

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Study Group: Continuation

SUBJECT	AGE (YEARS)	GENDER	PHOTOTYPE	STATUS
061	23	M	IV	NI
062	21	F	III	I
063	45	M	III	I
064	22	F	III	I
065	23	F	IV	I
066	34	F	IV	I
067	50	F	III	I
068	59	M	IV	I
069	38	F	III	NI
070	47	F	IV	I
071	18	F	III	I
072	55	F	III	I
073	28	F	IV	I
074	29	M	IV	I
075	23	F	III	NI
076	53	F	IV	NI
077	18	F	IV	NI
078	50	F	III	I
079	45	F	IV	I
080	39	F	II	I
081	35	F	IV	I
082	57	F	II	I
083	41	F	III	I
084	20	F	IV	I
085	57	F	III	I
086	30	F	III	I
087	38	F	II	I
088	31	F	III	I
089	47	F	IV	I
090	35	F	III	I

Caption:
F= Female;
M= Male;
I = Included;
NI = Not Included (present any non-inclusion criteria and/or not present some of the inclusion criteria).

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Study Group: Continuation

SUBJECT	AGE (YEARS)	GENDER	PHOTOTYPE	STATUS
091	41	F	III	I
092	24	F	III	I
093	19	F	III	I
094	38	F	II	I
095	30	M	II	I
096	49	F	II	I
097	28	F	III	I
098	32	M	V	NI
099	27	F	III	I
100	25	M	IV	I
101	36	F	III	I
102	41	F	III	I
103	22	F	IV	I
104	46	F	II	I
105	25	F	IV	I
106	56	F	II	I

Caption:
F= Female;
M= Male;
I = Included;
NI = Not Included (present any non-inclusion criteria and/or not present some of the inclusion criteria).

APPENDIX 3 INVESTIGATIONAL PRODUCT INFORMATION

“FORMULA NOT RECEIVED”