ASSESSMENT OF THE SKIN PRIMARY AND CUMULATIVE IRRITATION POTENTIAL AND SKIN SENSITIZATION OF A PRODUCT, UNDER CONTROLLED AND MAXIMIZED CONDITIONS (RIPT)

FINAL REPORT

PRODUCT TYPE: Silicone
PRODUCT NAME: DC-7-0940.

PRODUCT CODE: 080600-01
STUDY CODE: All-S-07/15/2020-TURQUOISE-GROUP-IRRITATION-SENSITIZATION
REPORT CODE: All-S-RIPT-080600-01-07-20-RFV01-Rev01

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ALLERGISA

ASSESSMENT OF THE SKIN PRIMARY AND CUMULATIVE IRRITATION POTENTIAL AND SKIN SENSITIZATION OF A PRODUCT, UNDER CONTROLLED AND MAXIMIZED CONDITION

SUMMARY

PRODUCT NAME	DC-7-0940.
PRODUCT CODE	080600-01
STUDY CODE	All-S-07/15/2020-TURQUOISE-GROUP-IRRITATION-SENSITIZATION
REPORT CODE	All-S-RIPT-080600-01-07-20-RFV01-Rev01
STUDY OBJECTIVE	To prove the absence of the skin primary and cumulative irritation potential and skin sensitization of a product under maximized conditions, with controlled product amount and application site, supervised by a dermatologist.
METHODOLOGY	Both the investigational 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 on Mondays, Wednesdays and Fridays, during 3 consecutive weeks. Forty-eight hours (48h), or 72h (on weekends), after the product application, it was removed by trained technicians and the application 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' back. Challenge Test: Then, the challenge period started. One single application of the investigational product was carried, followed by readings after 48h and 72h of the product being attached to the subjects' 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	Vivian Pessoto Rosa
STUDY DURATION	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	53 subjects completed the study.
POPULATION DESCRIPTION	Female and male subjects, aged from 18 to 58 years old (mean age: 36 years old), phototypes II to IV.
ETHICS	This study was conducted in conformance with the Declaration of Helsinki principles, the applicable regulatory requirements, including Resolution CNS No. 466/12, in spirit of the Good Clinical Practices (*Documento de las Américas* and ICH E6: Good Clinical Practice).
RESULTS / CONCLUSION	• The product did not induce process of skin primary and cumulative irritation in the study group. • The product did not induce process of skin sensitization in the study group. • The product is considered safe in the study conditions. The claim *"Dermatologically tested"* can be supported.

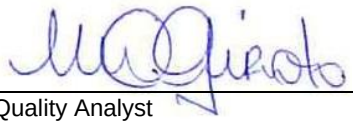
QUALITY ASSURANCE

The study was conducted according to the Resolution CNS No. 466/2012, in the spirit of the 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 below indicates that the study was carried out as described above and that the results were checked against the source documents.



Quality Analyst
Marcella Carla Giroto
09/11/2020

ALLERGISA

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1. ABBREVIATION LIST

Av.	Avenue
cm	Centimeter
CFM	Federal Council of Medicine
CNS	Brazilian Health Council
COVID-19	Coronavirus Disease 2019
CRM	Regional Council of Medicine
Dr.	Doctor
Etc.	*Et Cetera*
g	Gram
GCP	Good Clinical Practice
h	Hour
i.e.	*Id Est*
ICDRG	International Contact Dermatitis Research Group
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ID	Identification (Brazilian General Registration)
LTDA	Limited
ml	Milliliter
No.	Number
SEI	Electronic System of Information
SP	São Paulo

2. INTRODUCTION

Industry awareness and consumer's and regulatory agencies requirements caused personal care products, household cleaning, cosmetics and perfumes 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 companies with greater safety, credibility and reliability among their consumers.

Once the personal care products, household cleaning, cosmetics and perfumes becomes 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 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 care products, cosmetics and perfumes, 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).

Personal care products, household cleaning, cosmetics and perfumes safety studies aims to confirm the absence of risks associated with the product use.

Compatibility studies performed through patch test aim to prove the absence of adverse events during the first contact of a personal care product, household cleaning, cosmetics and perfumes on 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 photoirritant or photoallergy potential can also be proved.

3. OBJECTIVE

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

4. INVESTIGATIONAL PRODUCT

Product information, as declared by the Sponsor, are 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. Investigational product ID

Type of Product	Product Name	Product Code
Silicone	DC-7-0940.	080600-01

4.2. Product Application

The test 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.

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 principal investigator or by a previously designated technical staff.

5. APPLICABLE ETHICAL REMARKS

This study was conducted in conformance with the Declaration of Helsinki principles, the applicable regulatory requirements, including Resolution CNS No. 466/12, and in spirit of the Good Clinical Practices (*Documento de las Américas* and ICH E6: Good Clinical Practice).

Considering the current situation of pandemics of the COVID-19, the decree No. 64.881 of quarantine and its extension restricting agglomeration of people and following the guidelines of the Technical Note No.22/2020/SEI/CETER/GESEF/GGMED/DIRE2/ANVISA for the provision of essential clinical research services, the process of consent was done by telephone, informing the subjects the objective of the study, its methodology and duration, as well as the possibly expected benefits and restrains related to the study. The initial verbal consent was recorded, as described above, and the subject signed the Informed Consent Form (ICF) (Appendix 1), containing the information given by telephone, elaborated according to the Helsinki Declaration and CSN Resolution No. 466/2012.

Extraordinary measures were taken to guarantee the safety of all the people involved in the study (study subjects, technical department and health professionals). The Institute provided and requested all the subjects to wear masks during the whole study; made gel alcohol sanitizers available to hygienize the hands; performed the cleaning and disinfection of the rooms with alcohol 70%; determined adequate distance measures between people and performed the attentions with scheduled and individual appointments.

The research technical documentation is in Allergisa files, where it will be stored for a 5 years period.

5.1. Confidentiality of obtained data

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 is confidential until the results are published.

5.2. Study subjects

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 will be disclosed in all data analysis. If required, the Investigator in charge must have allowed the study monitor to access all subjects' study-related data. This included 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.

The teleconsultation was performed following the guidelines of the CFM RESOLUTION No. 1.643/2002 and according to the LAW No. 13.989, OF APRIL 15, 2020, in full force and effect for the use of this tool. During the teleconsultation, the Institute guaranteed the confidentiality of the medical attention to the subjects, using a device with data safety (cryptography), ensuring the subject's safety.

5.3. Informed Consent Form

The process of obtaining the ICF must confirm the voluntary nature of subjects' participation in the study. All study-related aspects were explained to the subject, before they sign the informed consent form. The Investigator in charge ensured that the informed consent was obtained in conformance with the GCP specifications, the Resolution CNS No. 466/2012 and the international regulatory requirements (ICH).

6. STUDY PERIOD

The study lasted a total of 6 weeks.

- **Clinical Assessment:** Group 1: 07/15/2020; Group 2: 07/21/2020;
- **First Application:** Group 1: 07/20/2020; Group 2: 07/22/2020;
- **Final:** 08/28/2020.

7. STUDY SUBJECTS

7.1. Study Subjects Enrollment

The study subjects were recruited by the recruitment department of the Study Site 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. In this first contact, a process of verbal consent by the subject was done and the subject agreed in performing the teleconsultation and medical assessment of the body. The teleconsultation was done by a physician following the CFM No. 1.643/2002.

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

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 have interfered with the study results through a Teleconsultation, i.e., a remote contact with the study subject, through video conference or telephone call. A complete anamnesis was done through these media, with an assessment of the product application area on the body (scapular area) and, if necessary, a submission of photographs would be requested to evaluate the integrity of the skin, to ensure the safety of the subjects and a complete assessment. The video call was done with a device with data safety (cryptography) and the photographs were sent for a telephone contact exclusively for use of the Institute's physician, using a device with data safety (cryptography).

The physician is also responsible for all information contained in the subject's evaluation form, by checking all inclusion and non-inclusion criteria for the admission of the subject in the study.

7.3. Population Description

A total of 102 study subjects was recruited for this study (Appendix 2). Among those, 12 subjects (008, 016, 017, 024, 031, 035, 060, 071, 072, 073, 088 and 089) did not meet the inclusion criteria or presented some of the non-inclusion criteria.

The study was initiated with 90 subjects, being 80 female and 10 male, aged from 18 to 58 years old (mean age: 36 years old).

The study complied the objective of obtaining, at least, a minimum of 50 responses.

7.4. Inclusion Criteria

a) Subjects who have cell phone with Internet access with instant messages and voice and video calls applications (WhatsApp);
b) Healthy subjects;
c) Intact skin on test site;

d) 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;
e) Ability of giving a consent for his/her participation;
f) Aged from 18 to 70 years old;
g) Phototype (Fitzpatrick): I to IV;
h) Any gender.

7.5. Non-Inclusion Criteria

a) Pregnancy or breastfeeding;
b) 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);
c) Active dermatosis (local or disseminated) that might interfere with the results of the study;
d) Antecedents of allergic reactions or sensation of intense discomfort to topical products: cosmetics, health products or medications;
e) Atopy antecedents, (atopic dermatitis, allergic rhinitis, allergic bronchitis, allergic conjunctivitis, etc.);
f) Discomfort sensation with temperature changes (too hot / too cold) and/or when you are in the air conditioner;
g) Subjects with history of allergy to the materials used in the study;
h) History of pathologies aggravated or triggered by ultraviolet radiation;
i) Subjects suffering from immunodeficiencies;
j) Intense exposure to sunlight or to sun tanning sessions up to 15 days before the initial assessment;
k) Intention of being intensely exposed to sunlight or to sun tanning sessions during the study period;
l) Forecast to sea bathe, to go to the pool or bathtub during the study;
m) Subjects who practice water sports;
n) Dermographism;
o) Aesthetic and/or dermatological treatment performed on the body within 03 weeks before selection;
p) Use of the following topical or systemic medications: immunosuppressants, antihistamines, non-hormonal anti-inflammatory drugs and corticosteroids up to 2 weeks before selection; in case of deposit corticosteroids, up to 1 month before selection;
q) Oral or topical treatment with vitamin A acid and/or its derivatives up to 1 month before the study started;
r) Forecast of vaccination during the study or up to 03 weeks before the study;

s) 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;
t) 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;
u) Any conditions which the investigator finds compromising to the evaluation of the study;
v) History of lack of adherence or unwillingness to adhere to the study protocol;
w) Professionals who are directly involved in the performance of the current protocol as well as their relatives.

7.6. Study Requirements

a) Do not apply any other product to the test site (dorsum);
b) Do not change any cosmetic habits, including personal hygiene;
c) Do not have body aesthetic or dermatological treatments performed;
d) Do not change food habits;
e) Do not change hormone treatment;
f) If female, do not change the medicamentous contraception method;
g) Do not wet the patches: during shower, in pools or sea, sauna or excessive sweat;
h) Do not remove the plasters;
i) Do not wear tight clothes which can remove the plaster through friction or cause redness;
j) Do not expose to excessive sunlight or artificial tanning;
k) Do not use the medication described below.

7.7. Medications and Prohibited Concomitant Treatments

Did the subject used any of these medications and/or performed 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).

a) Non-hormonal anti-inflammatory drugs of continuous use that interfere with the study, in the opinion of the investigator (the sporadic use must be evaluated by the investigator);
b) Corticoids;
c) Anti-histaminic drugs;
d) Immunosuppressant drugs;
e) Acid vitamin A and oral and topical derivatives (e.g. Isotretinoin);
f) Antibiotics;
g) Tetracyclines;
h) Topical medications of acne treatments, such as benzoyl peroxide;
i) Anti-androgenic agents;

j) Halogens;
k) Vitamins B12, B6, B1 and D2;
l) Isoniazid, rifampicin, ethionamide (treatment of tuberculosis and leprosy);
m) Phenobarbiturics, trimethadione, hydantoin, lithium, chloral hydrate (neurological and psychiatric treatment);
n) Quinine;
o) Disulfiram;
p) Thiouracil;
q) Thiourea;
r) During the study, any aesthetic, cosmetic or dermatological treatment on the body was also forbidden.

8. METHODOLOGY

8.1. Study Design

Comparative, single-blind and controlled clinical study.

8.2. Materials and Equipment

- Adhesive hypoallergenic semi-occlusive tape for patch testing with duly identified 1.0 cm^2 filter paper discs;
- 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;
- Cotton;
- Alcohol;
- Repipettor;
- Weighing Scale.

8.3. Test Site

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

8.4. Methods and Criteria of Assessment

8.4.1. Dermatological Clinical Assessment

A dermatological clinical assessment was performed trough a teleconsultation by a dermatologist through a telephone call or video conference to verify the inclusion and non-inclusion criteria of the study. In addition to the telephone call, the submission of a photograph of the subject's back, the site of application of the products, was requested. The photograph or the video image provided should be done with the aid of a person present in the subject's house at the moment of the teleconsultation, with their previous complete authorization and consent. During the teleconsultation, the confidentiality of the medical attention was ensured, 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. Subjects were supervised by a dermatologist throughout the study and assessed in case there were any symptoms or clinical signs.

8.4.2. 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 made three times a week for three consecutive weeks and the product remained 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 test product and control were applied to the right or left back of the subjects on a virgin area, that is, where no products 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 (48h reading) and 24 hours (72h reading) after product removal.

Subjects were instructed to contact the study coordinator at any time, in case they presented 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 (48 hours after application) were performed soon after the removal of the test product, in all cases in which no clinical signs were observed. If it were observed, the readings would be performed after, at least, 30 minutes and, at most, 60 minutes so that the signs, possibly caused by the removal of the test product, did not represent a false positive result.

8.4.3. Assessment of Clinical Signs (Readings)

During the study, the areas of product and control applications were evaluated and in case of any clinical sign, it was classified according to a scale recommended by the International Contact Dermatitis Research Group - ICDRG - (FISHER, 1995).

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

REACTION	RESULT
0 – None	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 maximized exposure to the product expected to this methodology. Therefore, these signs are not considered as adverse events.

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

8.5. Procedure Schedule

Table 3. Schedule of the Study – Group 1

			Phases				
			Sign Informed Consent	Dermatological Clinical Assessment	Product Application	Product Removal	Assessments (Readings)
		Recruitment	X (verbal)	-	-	-	-
		Teleconsultation	-	X	-	-	-
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 (presential)	-	-	X

Table 4. Schedule of the Study – Group 2

			Phases				
			Sign Informed Consent	Dermatological Clinical Assessment	Product Application	Product Removal	Assessments (Readings)
		Recruitment	X (verbal)	-	-	-	-
		Teleconsultation	-	X	-	-	-
Induction Period	Week 1	Visit 1	-	-	-	-	-
		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
	Week 4	Visit 10	-	-	X	X	X
		Visit 11	-	-	-	X	X
Rest Period	Week 5	No visits made					
Challenge Period	Week 6	Visit 12	-	-	X	-	-
		Visit 13	-	-	-	X	X
		Visit 14	-	X (presential)	-	-	X

8.6. Criteria and Procedures for Study Subjects Withdrawal

The removal of a study subject by the investigator could have occurred due the following reasons:

- Study subjects not included: subjects who signed the ICF, but who did not meet the inclusion and non-inclusion criteria of the study;
- Subjects who would 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: For this study, only two absences, on alternate days, would be allowed, provided they did not coincide with the first day of study and with the challenge

period. Consecutive absences or more than two absences would also cause the exclusion of the subject;

- Subjects presenting intercurrences that affect their eligibility in the meantime between the ICF signature and the beginning of the study;
- 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 supervised 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 was completely resolved.

Those subjects who are removed from study after the inclusion stage, would 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 investigational product use (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;
- Life-threatening;
- Inpatient hospitalization or prolongation of existing hospitalization;
- Persistent or significant disability / incapacity;
- 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 of an investigational product 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 investigational product use - 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.

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.

For the conclusion of the final diagnosis, the relation of an Adverse Event was 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 will be 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 test product (e.g. positive patch test for the test product).
- Likely: The cases in which the clinical condition is considered to be evocative will be 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 test 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, will be classified as nexus not clearly attributable.
- Improbable: The following two cases are associated with an improbable 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 test 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 cosmetics will be classified as excluded nexus (e.g. vitiligo, tineas, pityriasis rosea, pityriasis versicolor, psoriasis, folliculitis, solar melanose, 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).

10. RESULTS

10.1. Protocol Deviations

It was checked, after the beginning of the study, that the subjects 051, 055, 056, 063 and 082 present a non-inclusion criterion: subjects 051, 056, 063 and 082 had skin marks on the test site (spots) and subject 055 had sun tanning. It was a screening failure (FS), the subjects were excluded from the study and their data were not considered in the study.

10.2. Adherence to the Study

53 subjects completed the study.

A total of 30 subjects (002, 003, 007, 010, 011, 013, 018, 019, 023, 026, 027, 038, 039, 047, 054, 057, 059, 066, 067, 068, 070, 077, 079,083, 096, 097, 098, 099, 100 and 102) was absent due to personal reasons not related to the study.

Subjects 034 and 081 were removed from the study for presenting adverse event according to item 10.3.

A total of 05 subjects (051, 055, 056, 063 and 082) were removed from the study for being a protocol deviation, according to item 10.1.

10.3. Dermatological Clinical Assessment

Table 5: Adverse events during the study

Date	Subject Number	Adverse Event Description	Intensity	Site of the Event	Action Taken	Hypothesis or Rational + Diagnosis	Causal Nexus
07/28/2020	081	Pterygium	Not applicable	Left eye	Excluded from study	Considering the statement of the subject during anamnesis and the clinical assessment, the case was closed. It was a case of pterygium. Subject's data were not considered in the study.	Excluded
08/12/2020	034	Dermatosis	Intense	Superior dorsum and right and left retroauricular region	Excluded from study	Considering the statement of the subject during anamnesis, the clinical assessment and the localization of the clinical signs outside of and distant from the patch test application site, the case was closed. It was a case of dermatosis that occurred during the rest period, unrelated to test-product use. Subject's data were not considered in the study.	Excluded

During the study, no subjects presented any clinical sign in the Investigational product application site.

No subjects presented clinical signs in the control site.

Data obtained from the assessments of the site in contact with the product are recorded in Table 6.

Table 6. Assessment – Investigational product

	Induction Period									Rest Period	Challenge Period		
Subject Number	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
001	0	0	0	0	0	0	0	0	0	0	No procedure made	0	0	0
002	F/R	R	R	R	R	R	R	R	R	R		R	R	R
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	0	0	0	0	0		0	0	0
006	0	0	0	0	0	0	0	0	0	0		0	0	0
007	0	F/R	R	R	R	R	R	R	R	R		R	R	R
009	0	0	0	0	0	0	0	0	0	0		0	0	0
010	0	0	0	0	0	0	0	0	0	0		0	F/R	R
011	0	0	0	F	F/R	R	R	R	R	R		R	R	R
012	0	0	0	0	F	0	0	0	0	0		0	0	0
013	F/R	R	R	R	R	R	R	R	R	R		R	R	R
014	0	0	0	0	0	0	0	0	0	0		0	0	0
015	0	0	0	0	0	0	0	0	0	0		0	0	0
018	F/R	R	R	R	R	R	R	R	R	R		R	R	R
019	0	F/R	R	R	R	R	R	R	R	R		R	R	R
020	0	0	0	0	0	0	0	0	0	0		0	0	0
021	0	0	0	0	0	0	0	0	0	0		0	0	0
022	0	0	0	0	0	0	F	0	0	0		0	0	0
023	F/R	R	R	R	R	R	R	R	R	R		R	R	R
025	0	0	0	0	0	0	0	0	0	0		0	0	0
026	F/R	R	R	R	R	R	R	R	R	R		R	R	R
027	F/R	R	R	R	R	R	R	R	R	R		R	R	R
028	0	0	0	0	0	F	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
032	0	0	0	0	0	0	0	0	0	0		0	0	0
033	0	0	0	0	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
EA- = Adverse Event with Excluded Nexus
FS = Screening Failure checked after study start

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

Continuation Table 6. Assessment – Investigational product

	Induction Period									Rest Period	Challenge Period		
Subject Number	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
034	0	0	0	0	0	0	0	0	0	0	No procedure made	R	R	R
036	0	0	0	0	0	0	0	0	0	F		0	0	0
037	0	0	0	0	0	0	0	0	0	0		0	0	0
038	0	F/R	R	R	R	R	R	R	R	R		R	R	R
039	F/R	R	R	R	R	R	R	R	R	R		R	R	R
040	0	0	0	0	0	0	0	0	0	0		0	0	0
041	0	0	0	0	0	0	0	0	0	0		0	0	0
042	0	0	0	0	0	0	0	0	0	0		0	0	0
043	0	0	0	0	0	0	0	0	0	0		0	0	0
044	0	0	0	0	0	0	0	0	0	0		0	0	0
045	0	0	0	0	0	0	0	0	0	0		0	0	0
046	0	0	0	0	0	0	0	0	0	0		0	0	0
047	F/R	R	R	R	R	R	R	R	R	R		R	R	R
048	0	0	0	0	0	F	0	0	0	F		0	0	0
049	0	0	0	0	0	0	F	0	0	0		0	0	0
050	0	0	0	0	0	0	F	0	0	0		0	0	0
051	FS/R	R	R	R	R	R	R	R	R	R		R	R	R
052	0	0	0	0	0	0	0	0	0	0		0	0	0
053	0	0	0	0	0	0	0	0	0	0		0	0	0
054	F/R	R	R	R	R	R	R	R	R	R		R	R	R
055	FS/R	R	R	R	R	R	R	R	R	R		R	R	R
056	FS/R	R	R	R	R	R	R	R	R	R		R	R	R
057	F/R	R	R	R	R	R	R	R	R	R		R	R	R
058	0	0	0	0	0	0	F	0	0	0		0	0	0
059	0	0	0	0	0	0	F	F/R	R	R		R	R	R
061	0	0	0	0	0	0	0	0	0	0		0	0	0
062	0	0	0	0	0	0	0	0	0	0		0	0	0
063	FS/R	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
EA- = Adverse Event with Excluded Nexus
FS = Screening Failure checked after study start

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

Continuation Table 6. Assessment – Investigational product

		Induction Period									Rest Period	Challenge Period		
Subject Number	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
064	0	0	0	0	0	0	0	0	0	0	No procedure made	0	0	0
065	0	0	0	0	0	0	0	0	0	0		0	0	0
066	0	0	F/R	R	R	R	R	R	R	R		R	R	R
067	0	0	0	F	F/R	R	R	R	R	R		R	R	R
068	0	F/R	R	R	R	R	R	R	R	R		R	R	R
069	0	0	0	0	0	0	0	0	0	0		0	0	0
070	F/R	R	R	R	R	R	R	R	R	R		R	R	R
074	0	0	0	0	0	0	0	0	0	F		0	0	0
075	0	0	0	0	0	0	0	0	0	0		0	0	0
076	0	0	0	0	0	0	0	0	F	0		0	0	0
077	0	F/R	R	R	R	R	R	R	R	R		R	R	R
078	0	0	0	0	0	0	0	0	0	0		0	0	0
079	F/R	R	R	R	R	R	R	R	R	R		R	R	R
080	0	0	0	0	0	0	0	0	0	0		0	0	0
081	0	0	0	EA-/R	R	R	R	R	R	R		R	R	R
082	FS/R	R	R	R	R	R	R	R	R	R		R	R	R
083	F/R	R	R	R	R	R	R	R	R	R		R	R	R
084	0	0	0	0	F	0	0	0	0	0		0	0	0
085	0	0	0	0	0	0	0	0	0	0		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
090	0	0	0	0	0	0	0	0	0	0		0	0	0
091	0	0	0	0	0	0	0	0	0	0		0	0	0
092	0	0	0	0	0	0	0	0	0	0		0	0	0
093	0	0	0	0	0	0	0	0	0	0		0	0	0
094	0	0	0	0	0	0	0	0	0	0		0	0	0
095	0	0	0	0	0	0	0	0	0	0		0	0	0
096	0	0	0	0	0	F	0	0	0	0		F/R	R	R

Caption:
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F = Absence
R = Removed from the Study
DK = Darkening
DY = Dryness
F/R = Absence / Removed from the study
EA- = Adverse Event with Excluded Nexus
FS = Screening Failure checked after study start

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

Continuation Table 6. Assessment – Investigational product

		Induction Period									Rest Period No procedure made	Challenge Period		
Subject Number	**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**
097	F/R	R	R	R	R	R	R	R	R	R		R	R	R
098	F/R	R	R	R	R	R	R	R	R	R		R	R	R
099	0	0	F/R	R	R	R	R	R	R	R		R	R	R
100	F/R	R	R	R	R	R	R	R	R	R		R	R	R
101	0	0	0	0	F	0	0	0	0	0		0	0	0
102	F/R	R	R	R	R	R	R	R	R	R		R	R	R

Caption:
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F = Absence
R = Removed from the Study
DK = Darkening
DY = Dryness
F/R = Absence / Removed from the study
EA- = Adverse Event with Excluded Nexus
FS = Screening Failure checked after study start

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

Table 7 describes the positive answers observed during the Induction and Challenge periods.

Table 7. Positive answers observed during the study

Number of subjects who completed the study	Positive responses during the Induction Period	Positive responses during the Challenge Period
53	0	0
	Description of the signs:	**Number of sensitization confirmed responses**
	-	0

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

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

11. CONCLUSION

According to the methodology used to assess the absence of the skin primary and cumulative irritation potential and skin sensitization of the product **DC-7-0940.**, submitted by the company **Stratpharma AG**, it could be concluded that:

- The product did not induce process of skin primary and cumulative irritation in the study group.
- The product did not induce process of skin sensitization in the study group.
- The product is considered safe in the study conditions.

The claim *"Dermatologically tested"* can be supported.

Vivian Pessoto Rosa
Investigator in Charge
09/11/2020

Dr. André Luiz Vergnanini
Dermatologist (CRM 45125)
09/11/2020

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APPENDIX 1. INFORMED CONSENT FORM

Due to the study sharing among different sponsors, the ICF is regarding all studies the subject was clarified and included.

ALLERGISA

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

NAME OF THE INVESTIGATOR IN CHARGE: Vivian Pessoto Rosa

STUDY SITE: Allergisa Pesquisa Dermato-Cosmética Ltda.

You were invited to participate in this study through telephone call (because of the need for social isolation), and you are now being asked to confirm your written consent.

Even if you have given consent to the participation through telephone contact, you can withdraw your consent after reading this document, therefore, it is important that you read the information being presented carefully and if you decide to continue your participation, you will be asked to sign two original copies of this Informed Consent Form and a copy 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.

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, multipurpose products among others) and/or raw materials (examples: individual ingredients that compose a cosmetic product).

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 have to present good health, as attested by the expert physician via initial teleconsultation and meet other requirements called inclusion and non-inclusion criteria, that will be assessed and discussed by the expert.

What is a teleconsultation?

The teleconsultation is a remote appointment done by a physician through a telephone call or video conference. In addition to the telephone call, for this study in specific, the submission of a photograph of your back, the site of application of the products, was requested. The photograph or the video image provided was done with the aid of a person present in your house at the moment of the teleconsultation with complete your previous complete authorization and consent. During the teleconsultation, you were 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

Subject's Initials: _____

Initials of the person in charge for applying the ICF:_____

Allergisa Pesquisa Dermato-Cosmética Ltda. *IRRITATION - SENSITIZATION*

F-SOP_15.01_ CT Rev.20 10/14/2019

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present during the call.

On the last day of the study, the clinical assessment will also be done on-site, following the same confidentiality and privacy required.

How many people will join this study?

The study will be conducted with up to 150 subjects.

Where will the study be conducted?

Your first contact with the team at the Institute was through a teleconsultation performed as explained above. The performance of the products application and the returns will be done on-site, at one of the units of ALLERGISA pesquisa dermato-cosmética Ltda., Headquarters located at 452, Dr. Romeu Tórtima Avenue – Barão Geraldo – Campinas – SP, with all precautions for your safety.

What will I have to do?

Your participation in the study will last 06 weeks. During this period, about 13 on-site visits will be made. In addition to the teleconsultation previously performed, you will be supervised during the whole conduction of the study by a physician and the attention through teleconsultation or on-site will be performed always when necessary.

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:

You have given a prior consent by telephone, when you were informed of the purpose of the study, its methodology and duration, of the expected risks and benefits and restrictions linked to the study.

After this contact, a physician got in contact with you again through a teleconsultation and verified all the inclusion and non-inclusion criteria of the study with you and all the important information on your current health condition.

The scheduling of the first on-site visit at the Institute was done (Today). You will sign this Informed Consent, if you still agree to participate in the study, before performing the products applications. 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

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Date: _____/_____/_____ Group: _____

will also attend the Institute to apply the products and perform the readings after the applications and on the last day of the study; also, an on-site clinical assessment will be performed with the expert physician.

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
Consent by telephone	Recruitment	15 minutes
Dermatological Clinical Assessment done through a teleconsultation	Teleconsultation	10 minutes
Signature of the Informed Consent Form 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. 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.

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

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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.

During the teleconsultation, the physician present in the attention room will keep your confidentiality and privacy of the information exchanged, and the system used for the calls and video conferences is safe for use, ensuring complete safety for you 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.

The teleconsultation will be performed with a tool that presents data safety, ensuring confidentiality of the medical attention.

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:

- 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 ask you to wear the masks provided for your commute and permanence at the Institute, always wash the hands and use gel alcohol sanitizer provided.

Arrive only at the time scheduled to avoid crowds.

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

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We also ask you to communicate the Institute about any type of medication or external/skin use or oral, 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 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

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the visits, it is important to follow the safety measures of hands hygienization 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, coughing, 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, lost 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?

Nobody who is pregnant or breastfeeding will be able to join the study. Therefore, 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.

As the study products have no information about any possible dangerous effects to the baby, if you get pregnant and find out during the study, inform immediately to the investigator in charge or team. He/she will assure that you get advising about what to do during pregnancy and you will be supervised during the pregnancy until the birth.

If you get pregnant, you cannot continue in the study.

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, privately.

Can I be removed from the study?

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

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

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Date: _____/_____/_____ Group: _____

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: 19-3517-6800 (working hours) or 19-99778-0204 (from 5 pm to 10 pm). In case of any doubts or problems, you can contact the investigator in charge (Vivian Pessoto Rosa) 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.

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 739, Dr. Romeu Tórtima Avenue – Cidade Universitária – Campinas-SP – Postal Code: 13084-791 by the telephones (19) 3517-6830 and (19) 99822-9083. 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.

Subject's Initials: _____

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

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Important information!

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

IF YOU FEEL ANY FLU SYMPTOMS SUCH AS FEVER, COUGH, SHORTNESS OF BREATH, LOSS OF SENSE OF SMELL OR TASTE AMONG OTHER INDISPOSITIONS THAT COULD BE RELATED TO THE CONTAMINATION BY CORONA VIRUS, PLEASE CONTACT THE INSTITUTE IMMEDIATELY FOR INSTRUCTIONS.

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

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 No.	INITIALS (NAME)	AGE (YEARS)	GENDER	PHOTOTYPE	STATUS
001	SDDM	39	F	II	I
002	JADPS	47	F	IV	I
003	SDS	43	F	III	I
004	APFDS	29	F	IV	I
005	EDSB	41	F	III	I
006	JDJS	21	F	IV	I
007	JLNP	33	M	II	I
008	ACRC	26	F	III	NI
009	FB	38	F	III	I
010	IM	54	F	III	I
011	IMC	22	F	IV	I
012	AFDSF	24	F	IV	I
013	MLMDS	44	F	III	I
014	LBV	42	F	III	I
015	IB	46	F	III	I
016	RODCS	44	F	III	NI
017	CSDODS	43	F	III	NI
018	GAFDL	32	F	III	I
019	LCDC	39	F	III	I
020	VPDC	24	F	III	I
021	NDCS	57	F	II	I
022	CRDA	36	F	IV	I
023	SSDJ	30	F	II	I
024	NAP	48	F	II	NI
025	TPDQ	27	F	III	I
026	SRDS	33	F	IV	I
027	KCDSM	41	F	IV	I
028	CADSO	52	F	IV	I
029	SFDLS	50	F	III	I
030	MADOF	56	F	III	I
031	SDSH	59	F	IV	NI
032	CADS	52	M	IV	I
033	JRDSP	46	F	IV	I
034	RHS	19	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 (Not applicable)
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 non-inclusion criteria and/or not present some of the inclusion criteria)
FS = Screening Failure checked after study start
DE = Withdrawal after ICF and before initial clinical assessment

Study Group: Continuation

SUBJECT No.	INITIALS (NAME)	AGE (YEARS)	GENDER	PHOTOTYPE	STATUS
035	RMV	21	M	III	NI
036	PGDC	19	F	IV	I
037	DFDO	36	F	IV	I
038	MDLSA	38	F	IV	I
039	TSD	24	F	III	I
040	AFR	21	F	IV	I
041	TC	29	F	III	I
042	KFDS	36	F	IV	I
043	VPDA	30	F	IV	I
044	VPDAS	28	F	IV	I
045	GCR	23	F	IV	I
046	LMPDA	45	F	III	I
047	CVDS	27	M	IV	I
048	FPDS	20	F	IV	I
049	GADS	21	F	IV	I
050	VADCDS	40	F	IV	I
051	CCRO	46	F	IV	FS
052	MSS	51	F	III	I
053	DFCM	23	F	III	I
054	YDSDF	21	F	III	I
055	MARDS	55	F	III	FS
056	MADS	48	F	IV	FS
057	JCAR	38	M	III	I
058	GVFR	18	F	III	I
059	FRM	45	F	IV	I
060	AMMM	23	F	IV	NI
061	MDSL	21	F	IV	I
062	DSDS	28	F	IV	I
063	FJDP	21	F	IV	FS
064	FRMDS	37	F	IV	I
065	GAL	54	F	III	I
066	EKBN	26	F	IV	I
067	PMDSB	28	F	III	I
068	NNDS	58	F	IV	I

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Study Group: Continuation

SUBJECT No.	INITIALS (NAME)	AGE (YEARS)	GENDER	PHOTOTYPE	STATUS
069	ALDOF	19	F	II	I
070	SAPDO	57	F	III	I
071	VLM	52	F	IV	NI
072	JL	35	M	III	NI
073	MJDMO	51	F	IV	NI
074	JHDS	26	F	IV	I
075	SDFDSA	40	F	IV	I
076	ALDS	34	M	IV	I
077	FDSB	33	F	II	I
078	RVDS	52	F	III	I
079	EJDS	35	F	IV	I
080	ARDSFDA	25	F	III	I
081	MGDS	41	F	IV	I
082	HMDC	49	F	IV	FS
083	RDDSA	48	F	IV	I
084	TCPDC	40	F	IV	I
085	ACDSF	50	F	III	I
086	ARF	47	M	IV	I
087	ARDS	47	F	IV	I
088	IOO	57	F	II	NI
089	MSMDS	55	F	IV	NI
090	LRDB	48	F	IV	I
091	ARS	39	F	IV	I
092	AFS	30	F	IV	I
093	CDCA	37	F	III	I
094	EAFV	35	F	IV	I
095	CGDO	18	M	II	I
096	TAL	25	M	III	I
097	AVBDT	40	F	III	I
098	JCDS	26	M	IV	I
099	RDCMES	42	F	II	I
100	PHLC	24	M	IV	I
101	SDSCDS	49	F	IV	I
102	JAA	23	F	IV	I

Caption:
F = Female; M = Male
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APPENDIX 3. PRODUCT INFORMATION

“FORMULA NOT RECEIVED”