CLINICAL STUDY, SINGLE-BLIND, CONTROLLED, OF POTENTIAL OF IRRITABILITY AND SKIN SENSITIZATION OF A PRODUCT FOR APPLICATION ON SKIN

FINAL REPORT

PRODUCT'S NAME: LUBRINAT

PRODUCT CODE: 051250-01
STUDY CODE: AII-S-RIPT-051250-01-01-15
REPORT CODE: AII-S-RIPT-051250-01-01-15-RFV01-Rev01

DATE OF REPORT: 03/03/2015

SPONSOR: MASTER INDÚSTRIA E COMERCIO DE PROD ODONTO E FARMAC LTDA

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A B S T R A C T

Product Name	LUBRINAT
Product code:	051250-01
Study Code:	AII-S-RIPT-051250-01-01-15
Report Code:	AII-S-RIPT-051250-01-01-15-RFV01-Rev01
PURPOSE OF THE STUDY	To prove the absence of potential primary irritation and accumulated and cutaneous sensitization of a product for application on the skin in maximized conditions, with application area and quantity controlled, accompanied by a dermatologist doctor.
METHODOLOGY	The product test and control were applied on disks of filter paper of the patch test and then applied to the back (scapular area) right or left side of research participants. The applications took place on Mondays, Wednesdays and Fridays during 3 consecutive weeks. Forty-eight hours (48h) after its application, the patch test was removed by trained technicians and, after about 30 minutes, the site was evaluated to check for possible clinical signs. After this period (induction) followed a period of, at least 10 days, when no patch was applied on the back of the participants (rest period). Then began the challenge period. A single application of patch test was carried out followed by readings after 48 h and 72 h. Research participants were evaluated by a dermatologist doctor at the beginning and the end of the study and monitored throughout the course thereof.
PRINCIPAL INVESTIGATOR	Dr. André Luiz Vergnanini
PERIOD OF TEST	6 Weeks
APPLICATION FREQUENCY	9 applications in the first 3 weeks (induction period). 1 application in the last week (challenge period).
TEST AREA	Back (scapular region).
NUMBER OF PARTICIPANTS	72 research participants
POPULATION DESCRIPTION	Female and male, aged between 18 to 70 years, phototype II to IV (Fitzpatrick
ETHICS	This study was conducted in accordance with the principles of the Declaration of Helsinki, the applicable regulatory requests, including CNS Resolution No. 466/12, and Good Clinical Practice (Document of the Americas and ICH E6: Good Clinical Practice).
RESULTS	During the study, no participant presented clinical signs related to skin product.
CONCLUSION	The product is not induced primary and accumulated irritation process or skin sensitization study group. The product is considered safe under the evaluated conditions.

QUALITY ASSURANCE

The study was performed in accordance to CNS Resolution No. 466/2012, in the spirit of the Good Clinical Practice and in accordance with the Allergisa Standard Operating Procedures.

Our quality Data are assured considering that our employees are trained and qualified according the research to be conducted, our equipment are maintained calibrated, and were used recognized and / or validated methods.

The Quality Assurance Area performs audit of the Management System; and is available to receive our customers for specific tutoring of their research.

Representative signature of Quality Assurance System means that the research was conducted as described above.

Quality Manager
Fatima Ap. Ortigoza de Lima
3/3/2015

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LIST OF ABBREVIATIONS

ICH E6:	Good Clinic. Practice
GCP/IC	Good Clinical Practice / International Conference on Harmonization.
ANVISA	Brazilian Health Surveillance Agency
CNS	Brazilian National Health Council
IC	Informed Consent
Visit xx	Participant visit - attendance at the institute for carrying out the research procedures

1- **INTRODUCTION**

In the last years, the cosmetic industry has grown considerably as well as its interest in developing effective and safe products. The creation of the Consumer Protection Code, the requirements of the Department of Health Surveillance from the Ministry of Health and the competition itself led to more cautious attitudes from the Industries regarding the action and benefits of their products, seeking to associate their affirmations to the scientific work.

The awareness of industry and consumer demands resulted in adoption of new procedures by the cosmetics manufacturers that lead them to better knowledge of their products, prior to the commercialization, carry out clinical tests of safety and efficacy, which are coordinated by specialist doctors. This procedure offers more safety, credibility and trust toward consumers.

Since the cosmetic product is freely available to the consumer, the same should be safe in normal or reasonably predicted use conditions (Guide to Safety Evaluation of cosmetic products from ANVISA). For this purpose, the raw materials used in the formula of the product must be raw materials with proven safety and whose use is established in the cosmetic industry. Furthermore, the final formula safety should be tested before its commercialization, as Guide to Safety Evaluation of cosmetic products from ANVISA

According to good Clinical Practices, is any unfavorable medical occurrence in a research subject administered a pharmaceutical product and which does not necessarily have a causal relationship with the treatment t (The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use -ICH).

To evaluate the irritation and sensitization potential of a product, a number of variables must be taken into consideration: components of the formula, concentration of ingredients, absorption, applied quantity, condition of the skin, mode and frequency of application and the cumulative effect (DOOMS- Goossens 1993).

The skin permeability varies according to the body region, wherein the folds and the face are areas of higher absorption. When applied on the skin, a product will have greater or lesser percutaneous absorption as a function of its concentration, type of vehicle used, the skin surface area and contact time with the skin (Zatz, 1993). Thus, some regions of the body are more susceptible to the occurrence of irritation than others..

Researches conducted with human beings are regulated according to laws very rigid, in order to protect and safeguard the individuals. These laws vary depending on the country. In Brazil, these studies are allowed, provided they follow the precepts of Declaration of Helsinki and CNS Resolution No. 466/12 (NATIONAL COUNCIL OF HEALTH, 2013).

The researches for evaluate cosmetic's safety aims to confirm the absence of risk associated with the use of the cosmetic product..

Compatibility researches conducted using patch test, seek to prove the absence of adverse events during the application of a cosmetic product for the first time on skin, thus proving that it is safe for use. Consist of repeated product application on skin evaluating the non-occurrence of irritation; or sensitization; (KLIGMAN & WOODING, 1967; FISHER, 1995). Also the absence of potential photo irritating or photo sensitization can be proven.

Yet the acceptability researches, evaluate safety; the product in actual conditions of use, thus allowing real knowledge of the product, at the same market conditions; thus they are performed with the finished product before its introduction to the market. (BARAN & Maibach, 1994).

It's possible to evaluate, through this research, besides the safety, the sensory characteristics of the product, detecting complaints and further comments related to its "performance".

Through the clinical tests the company is aware of possible considerations; and complaints that may arise during commercialization of the product, can develop strategies, as, par example, the specific training to the Customer Service (SAC), prior to launch the product (BARAN & Maibach, 1994).

2. OBJECTIVE

The objective of this study was to verify the absence of; the primary and accumulated irritating potential and skin sensitization; of a product for application on skin; to the skin in maximized conditions; maximized, with application area and quantity controlled and accompanied by a dermatologist doctor..

3. PRODUCT INVESTIGACIONAL

Product, information as declared by sponsor, are described in annex 3. A sample of the product has been catalogued and can be found in our archives, where will be maintained for a period of one month.

3.1. identification

Product name: LUBRINAT

Product Code: 051250-01

3.2 Application of the Product

The product-test was applied pure and was distributed on the filter paper disk of the patch test, properly identified., Sterile saline solution (NaCl 0.9%) was used as a control, it was properly identified and in another test filter paper disk.

3.3 Storage

The products supplied by the sponsor were initially stored in the Research Center sample room with temperature controlled and restricted access. The product release was controlled by the principal investigator or designated technicians responsible for it.

4. ETHICAL APPLICABLE CONSIDERATIONS

The study was conducted in compliance of the principles of Declaration of Helsinki, the applicable regulatory requirements including CNS Resolution No. 466/12, and in the spirit of the Good Clinical Practice (Document of the Americas and ICH E6: Good Clinical Practice).

Research participants were informed of the purpose of the study, its methodology and period, and the benefits possibly expected and restrictions related to the study and those who have confirmed their interest in participating signed an informed consent form (Appendix 1).

All the technical data of the research is found in the archives of Allergisa, where will be kept for a period of 5 years.

5. PERIOD OF STUDY

The total research time was 6 weeks.

- **Medical Evaluation**: 01/09/2015.
- **Start of applications**: 01/12/2015;
- **Final**: 2/27/2015.

6. RESEARCH PARTICIPANTS

6.1 Recruitment of Research Participants

The recruitment of the research participants was conducted by the recruitment Section at the Research Center, which has a computerized record system updated. In this system are registered participants that have an interest in participating in this research, which were contacted to participate in the selection; and having all the necessary criteria, they were included in the study.

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6.2 Selection and Admission of Research Participants

During selection of the participants to this research, Allergisa made sure that they had no conditions that could interfere at the results of the study. The doctor is still responsible for the information present in the participant's Evaluation form, checking all the criteria of inclusion and exclusion for its admission to the research.

6.3 Description of the Population

For this study, 84 participants were recruited to the research (Annex 2). Among these, 12 (participants 003, 004, 005, 021, 023, 050, 057, 063, 066, 067, 070 and 072) did not meet the inclusion criteria or had some exclusion criteria.
The study was initiated with 72 participants, and 67 female and 05 male, aged between 18 and 70 years.

6.4 Inclusion Criteria

- Healthy participants;
- Skin intact in the test area;
- Concordance to adhere the procedures and requirements of the assay and attend to the Office at the day(s) and hour (s) set for evaluations;
- Capacity to consent written participation in the study (IC signed);;
- Aged between 18 and 70 years;
- Any sex;
- Phototype (Fitzpatrick): I to IV.

6.5 No Inclusion criteria:

- Skin spots on experimental area that interfere in the evaluation of potential skin reactions (pigmentation disorders, bad-vascular formations, scars, increasing Hairiness, Ephelides and nevus in large quantity, sunburn);
- Active dermatosis (local or widespread) that can interfere in the results of the study;
- Pregnant or lactating women;
- History of allergic reactions, irritation or intense discomfort sensation to topical products: cosmetics or medications;
- Participants with previous history of allergy to the material used in the study;
- History of atopy;
- History of diseases aggravated or triggered by ultraviolet radiation;
- People with immune deficiency;
- Intense sun exposure or tanning session up to 15 days before the initial evaluation;
- Prediction of intense sun exposure or tanning session, during the conduction of the study;
- Prediction of sea bathing, pool or sauna during the study;
- Participants who practice water sports;
- Dermographism;
- Use of the following topical medications or systemic immunosuppressant, anti-histamines, no steroidal anti-inflammatory, and steroids until 2 weeks before the selection;

- Treatment with acid vitamin A and / or its derivatives orally or topically even 01 month before the study;
- Aesthetic treatment and/or body dermatological until 03 weeks before screening;
- Vaccination forecast during the study or until 03 weeks prior to the study;
- Any condition not mentioned above which, in the opinion of the investigator, might compromise the evaluation of the study;
- History of lack of adherence or if you feel unwell in joining the study protocol;
- Professionals directly involved in the implementation of this Protocol and their families.

6.6 Interdiction and restriction

- Do not expose to sunlight excessively and do not undergo artificial tanning;
- Do not bathe in the sea, swimming pool or if expose to a sauna during the study;
- Do not wet the patch test;
- Do not use the following medicaments: non-steroidal anti-inflammatory continuous use*, antihistamines, immunosuppressant, acid vitamin A and derivatives If necessary for therapeutic use, the participant could be excluded from the research
- It was also forbidden during the study any aesthetic, cosmiatric or dermatological treatment at the body region.

7. METHODOLOGY

7.1 Study design.

Single-blind controlled clinical study.

7.2 Materials and Equipment

- Hypoallergenic adhesive Chart for patch test with filter paper discs of 1.0 cm^2 properly identified;
- Sterile saline solution 0.9% NaCl (0,9%);
- Gloves, masks and caps;
- Surgical pen;
- Swab;
- Distilled water;
- Beaker;
- Dropper flask;
- Transparent flask..

7.3 Study Area

The product was applied on the dorsum (scapular region) of the research participants.

*Sporadic use should be evaluated by the investigator regarding the exclusion of the study.

7.4 Population Size

This research was conducted with 72 participants approved for the purpose of obtaining at the end of the same, at least 50 responses.
This research served to indicate the Security Assessment Guide to cosmetic products of the national agency of sanitary surveillance-ANVISA.

7.5 Procedures

Research participants were initially evaluated by a dermatologist doctor for verification of the criteria for inclusion and exclusion.
The test method used was the patch test (KLIGMAN & WOODING, 1967), also called epicutaneous or contact test.
The product (0, 05 g/cm2) was distributed on a filter paper disk properly identified and sterile 0.9% saline solution, used as control, on another disk, also identified.
The contact test containing the test product and control has been set at, the scapular region, right or left side of the survey.

Induction Period: Applications were held three times a week for three consecutive weeks remaining in contact with the skin for 48 hours during the week and for 72 hours on weekends.
Rest period: This was followed by a rest period of at least 10 days after the induction period, when no patch was applied.
Challenge period: After the interval of rest, a patch with the test product and the control was applied on the back left or right of the participants in a Virgin area,. where it wasn't applied no patch previously.
The patch was removed by researchers after approximately 48 hours of contact with the
Skin

The evaluations were carried out (readings) approximately 30 minutes (48 h reading) and 24 hours { 72 hours reading) after the withdrawal of the patch test.
Participants were evaluated by a dermatologist doctor at the end of the research and accompanied throughout the course of the same.

7.5.1. Clinical Signs Rating (Readings)

If during the readings, a research participant presented clinical signs, the evaluation scale to be used would be the scale recommended by the International Group of Investigators of Contact Dermatitis- ICDRG-(FISHER, 1995).

Table 1: Scale of the International Group of Investigators of Contact Dermatitis- 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 (+++)

7.**6 –Procedure Schedule**

Table 2 – Study schedule

PHASES	Visit 1	Visit 2	Visit 3 to 10	Visit 11	visit 12	Visit 13	Visit 14
Informed consent form Signature	X	-	-	-	-	-	-
Clinical Dermatologist Evaluation	X	-	-	-	-	-	X
Application of Patch Test	-	X	X	-	X	-	-
Withdrawal of the Patch Test	-	-	X	X	-	X	-
Evaluations (Readings)	-	-	X	X	-	X	X

7.7 Criteria and procedures for withdrawal of Research participants

The exclusion of a research participant the by the investigator could occur due to the following reasons:

- Research participants not included: participants who signed the consent form, but they did not meet the criteria for inclusion and exclusion from the research,
- Research participants who presented, in the researcher's point of view any problem that would prevent the continuity of product applications, in any period of the study,
- Withdrawal of consent by research participant, regardless the reason,
- Lack of adherence from the research participant to the study. It would be considered a significant lack of adherence when the participant does not attend the center for evaluation
- Severe Adverse Event,
- Disease or concomitant treatment: any pathological process or treatment that occurred during the course of the study and that could interfere with the product of the study, as a drug interaction or mask the results.

Research participants withdrawn from the study by the investigator would be accompanied if they present any event possibly related to the study, even after his retirement. Participant withdrawn presenting adverse event would be accompanied till the full resolution of the case.

In case of withdrawal after the screening phase of the study, there would be no replacement of these participants.

8 - ADVERSE EVENTS

An adverse event is any untoward medical occurrence in a patient or clinical research participant you have used a product, but not necessarily a causal relationship with this treatment. An adverse event can therefore be any unexpected adverse signal (including abnormal laboratory results), symptoms, or temporarily diseases associated with the use of the product-test (modified of ICH, 1996).

According to good clinical practice (ICH, 1996), a serious adverse Event is any medical occurrence that results in:

- Death
- Life risk
- Hospitalization or prolongation of existing hospitalization;
- Disability/ Insignificant /Significant or persistent
- Birth defects/congenital

Any clinical sign, discomfort sensation, illness, or even worsening clinical significant of these conditions when compared with the condition verified in the initial visit is considered an adverse event. The lack of clinical or perceived efficacy of a cosmetic product or medication is not considered an adverse event.

Clinical signs and dermatological or systemic diseases occurred during the selection process of the research participants are not considered Adverse Events. This information is recorded in the medical evaluation form as a reason for non-inclusion and participants are not included in the research.

The adverse events cases that occurred due to the incorrect use of a cosmetic product or medication, for example, often inadequate or incorrect application, are considered adverse events that do not interfere in the evaluation of the product since the participant didn't follow, in this situation, the correct guidance for use as used in the labeling.

An Adverse Event form is filled for all cases, and these are reported to the sponsor through a communication of Events via email or in the Final report of the research.

After the appearance of an event with causal nexus doubtful, the investigation starts in order to determine whether such an event presents or not relation with research and product testing.

The procedures adopted during the investigation of the event are defined by the responsible physician based on the nature of the reaction, in the participant's medical history and the factors that can interfere with the occurrence of the event, such as medications or other concomitant diseases.
For completion of the final diagnosis, the relationship of an adverse event can be set using the following expressions:

- **Negative Nexus or Not Related** - There is no possibility of a positive causal nexus between the product and the observed adverse event.
- **Unlikely**- it is unlikely that there is a causal nexus between the product and the adverse event observed.
- **Possible** - There may be a positive causal nexus between the product and the adverse event observed, but there is no way to ensure that.
- **Probable** -it is likely that there is a causal nexus between the product and the adverse event observed, despite the relation not be fully proven.
- **Positive Nexus or Certainly Related** -according to the doctor in charge, there is evidence that allow completes the causal relationship as between the event and the application/use of the cosmetic product or medicine.

9- RESULTS

9.1- Adherence to Study

Completed the study 63 participants.
Dropped out of the study for personal reasons not related to the study 09 participants (participants 009, 013, 020, 036, 061, 062, 064, 074 and 080).

9.2- Clinic Dermatological Evaluation

During the study, none of the research participants presented clinical signs in the area of application of the product-test.
The data obtained from the evaluations of the contact region with the product are registered in Table 3
No participant presented clinical sign in the control application area.

Table 3: Patch Test Evaluations - PRODUCT-TEST

Participant Number	Application	Reading and Application	Reading and Application	Reading and Application	Reading and Application	Reading and Application	Reading and Application	Reading and Application	Reading and Application	Reading	Application	Reading	Reading
001	0	0	0	0	0	0	0	0	0	0	0	0	0
002	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	0	0	0	0	0	0	0	0	0	0	0	0
008	0	0	0	0	0	0	0	0	0	0	0	0	0
009	FR	R	R	R	R	R	R	R	R	R	R	R	R
010	0	0	0	0	F	0	0	0	0	0	0	0	0
011	0	0	0	0	0	0	0	0	0	0	0	0	0
012	0	0	0	0	0	0	0	0	0	0	0	0	0
013	0	0	0	0	0	0	F	FR	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
016	0	0	0	0	0	0	0	0	0	0	0	0	0
017	0	0	0	0	0	0	0	0	F	0	0	0	0
018	0	0	0	0	0	0	0	0	0	0	0	0	0
019	0	0	0	0	0	0	0	0	0	0	0	0	0
020	0	F	FR	R	R	R	R	R	R	R	R	R	R
022	0	0	0	0	0	0	0	0	0	0	0	0	0
024	0	0	0	0	0	0	F	0	0	0	0	0	0
025	0	0	0	0	0	0	0	0	F	0	0	0	0
026	0	0	0	0	0	0	0	0	0	0	0	0	0
027	0	0	0	0	0	0	0	0	0	0	0	0	0
028	0	0	0	0	F	0	0	0	0	0	0	0	0
029	0	0	0	0	0	0	F	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	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
034	0	0	0	0	0	0	0	0	0	F	0	0	0
035	0	0	0	0	0	0	0	0	0	0	0	0	0
036	FR	R	R	R	R	R	R	R	R	R	R	R	R
037	0	0	0	0	0	0	0	0	0	0	0	0	0
038	0	0	0	0	0	0	0	0	F	0	0	0	0
039	0	0	0	0	0	0	0	0	0	0	0	0	0
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

Legends: X- not applied/no reading
F= Missing R = Withdrawal from the Research
E = Darkening D-Dryness

0- Reaction Absent 3- Erythema + edema * papules
1- Mild Erythema 4- Erythema + edema * papules+ vesicles
2- Clear Erythema

Table 3 Continuation -: Patch Test Evaluations - PRODUCT-TEST

Participant Number	Application	Reading and Application	Reading and Application	Reading and Application	Reading and Application	Reading and Application	Reading and Application	Reading and Application	Reading and Application	Reading	Application	Reading	Reading
042	0	0	0	0	0	0	0	0	0	0	0	0	0
043	0	0	0	0	0	F	0	0	0	0	0	0	0
044	0	0	0	0	0	F	0	0	0	0	0	0	0
045	0	0	0	0	0	0	0	0	F	0	0	0	0
046	0	0	0	0	0	0	0	0	0	0	0	0	0
047	0	0	0	0	0	0	0	0	0	0	0	0	0
048	0	0	0	0	0	0	0	0	0	0	0	0	0
049	0	0	0	0	0	0	0	F	0	0	0	0	0
051	0	0	0	0	0	0	0	0	F	0	0	0	0
052	0	0	0	0	0	0	0	0	F	0	0	0	0
053	0	0	0	0	0	0	0	0	0	0	0	0	0
054	0	0	0	0	0	0	0	0	0	0	0	0	0
055	0	0	0	0	0	0	0	0	0	0	0	0	0
056	0	0	0	0	0	0	0	0	F	0	0	0	0
058	0	0	0	0	0	0	0	0	0	F	0	0	0
059	0	0	0	0	0	0	0	0	0	0	0	0	0
060	0	0	0	0	0	F	0	0	0	0	0	0	0
061	0	0	0	0	F	0	0	0	0	FR	R	R	R
062	0	0	0	0	0	F	FR	R	R	R	R	R	R
064	FR	R	R	R	R	R	R	R	R	R	R	R	R
065	0	0	0	0	F	0	0	0	0	0	0	0	0
068	0	0	0	0	0	0	0	0	0	0	0	0	0
069	0	0	0	0	0	0	0	0	0	0	0	0	0
071	0	0	0	0	0	0	0	0	0	0	0	0	0
073	0	0	0	0	0	0	0	0	0	0	0	0	0
074	FR	R	R	R	R	R	R	R	R	R	R	R	R
075	0	0	0	0	0	0	0	0	0	0	0	0	0
076	0	0	0	0	0	0	0	0	0	0	0	0	0
077	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	0	0	0	0	0	0	0	0
080	0	0	F	FR	R	R	R	R	R	R	R	R	R
081	0	0	0	0	0	0	0	0	0	0	0	0	0
082	0	0	0	0	0	0	0	0	0	0	0	0	0
083	0	0	0	0	0	0	0	0	0	0	0	0	0
084	0	0	0	0	0	0	0	0	0	0	0	0	0

Legends: X- not applied/no reading
F= Missing R = Withdrawal from the Research
E = Darkening D-Dryness

0- Reaction Absent 3- Erythema + edema * papules
1- Mild Erythema 4- Erythema + edema * papules+ vesicles
2- Clear Erythema

1O. CONCLUSION

According to the methodology used to evaluate the potential of primary and accumulated irritability and skin sensitization of LUBRINAT product sent by the company MASTER INDÚSTRIA E COMERCIO DE PROD ODONTO E FARMAC LTDA , it could be concluded that:

• During the study, no participant had cutaneous clinical signs related to the product.
• The product did not induce process of irritation and skin sensitization in the study group.
• The product was considered safe in the evaluated conditions.

Study Coordinator
Vivian Pessdto-- 03/03/2015

Principal Investigator

Dr. André Luiz Vergnanini
Dermatologist (CRM 45125)
03/03/2015

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ANNEX 1 INFORMED CONSENT

- You are invited to participate in a research. We ask you to understand in detail all the steps and if you agree, sign this consent form;
- The objective of the study is to evaluate the potential of irritability and skin sensitization of cosmetic products (soaps, shampoos, deodorants, talc, oil bath, moisturizers, lotions, perfumes, colognes, sunscreen and others), health products (bandages, adhesive plasters) and / or topical medication (ointments, gels for use on skin);
- Irritability and skin sensitization are irritation and allergic reactions that can possibly occur on the skin after application of these products;
- The research will be conducted with up to 72 people participating in the research;
- Your participation in the study will be 1 week for the research of Primary Irritability (3 returns lasting 2 hours each), and 6 weeks for the research Irritability / Sensitization (RIPT) (up to 19 returns lasting 2 hours each),
- In total you must appear at the Institute 19 times.
- You will be examined by a dermatologist doctor at the beginning and end of the study, and monitored throughout all the research;
- For the research of Primary Irritability, will be applied the "patch test" (tape) containing the evaluating products on dorsum (back) right and / or left, once. The patch test is removed after about 48 hours of skin contact and you must attend to the evaluations of possible reactions on your skin (reading);
- For the research of Irritability Accumulated / Sensitization (RIPT) the "patch test" will be applied (tape) containing the evaluating product reviews on the dorsum (back) right and / or left, for three consecutive weeks. You must appear Mondays, Wednesdays and Fridays for application / reading. After this period of "induction", you will be at rest for at least 10 days and will return to apply the "contact test" again that will be removed after about 48 hours and you must attend to perform the readings;
- Do not wet the "patch test" throughout the application period;
- In general, these products used topically have a good risk / benefit ratio, however, can cause sensitization and local irritation, especially with prolonged use. In the event of any type of reaction, you will be assessed and monitored by a dermatologist;
- You may be dispensed after signing the informed consent and informed by a dermatologist if you have any of the exclusion criteria and also if the vacancies are prefilled;
- Your agree to not engage in any other research in the course of this study;
- If female, you claim not to be pregnant or breastfeeding and is committed not to become pregnant during the study period;
- Your consent does not relieve the organizers of the research center of its responsibilities;
- You are aware that, on certain occasions, a representative of the sponsoring company may be present to observe the study;
- You agree that, in the context of this study, your data will be collected and may be subject to electronic processing. In the event of any changes in your registration data (phone, address etc ...), ask the organizers of the study to update ;
- All raw materials used in products are approved for topical use and are not toxic. However, like any product, they may cause unexpected reactions as "redness", "Swelling", "itching" and "burning" in product application sites;
- As a benefit of this research, you will be examined before the start of the study by a specialist doctor and, if a problem is observed in the evaluated region, will be alerted and oriented. In addition, your participation in the research will contribute to the launch of products for topical use that do not cause irritability and skin sensitization in the study group;
- All questions arising during and after the research will be clarified;
- Your participation in the research is completely voluntary;

- You may withdraw from the study at any time if so desired, however, it shall notify the institute of withdrawal;
- You may be withdrawn from the study if you do not fulfill your responsibilities, according to the study protocol, and the criteria of the investigator;
- Your voluntary collaboration will be of great importance for research, so please attend at the times and dates indicated throughout the course of the research;
- If there is any change in your habits, we ask you to notify us to better interpret the results;
- Do not use any type of product (ex.: deodorant or antiperspirant, talc, oil, bath, creams, lotions, perfumes, colognes and topical medications) in areas near the test. If you use any of these products or make use of any medication, inform us;
- In the case of moderate itching, persistent or severe and even other signs of irritation, immediately report, appearing to the test application site or by phone 19-3517- 6800 (office hours) or 19-99778-0204 (08h - 22h);
- We ensure that any adverse reactions (reactions, skin irritation or discomfort sensations in the skin) will be accompanied by a dermatologist doctor and / or expert responsible for the project to its completion and, if necessary, will be provided the appropriate medication;
- Any compensation is assured;
- We ensure that any new relevant information (important information) that may interfere with your consent will be given;
- All information obtained about the participants will be kept confidential (secret), and by signing this term, you give freedom to the sponsor and regulatory authorities (regulatory agencies of research) to conduct analysis of documents and research data;
- CONTACT: In case of doubt or problem, you can contact by phone 19-3517-6800 or at the address. Doutor Romeu Tórtima, 452/466 - Barão Geraldo - Campinas - SP;
- A copy of this term will remain in Allergisa file and the other will be given to the research participant.

I agree to participate in the study "Clinical study, single-blind, controlled of potential of irritability and skin sensitization of a product for application on the skin" and I declare that I have been informed about all of the above.

_____ _____

- Signature of participant research (equal to ID card) Date:

_____ _____

- Signature of Responsible for applying the IC Date:

ANNEX 2 - STUDY GROUP

Participant Number	name Initials	Age (Years)	Sex	Phototype	Status
001	PAN	61	F	IV	I
002	MIPS	37	F	III	I
003	AJS	49	F	III	NI
004	CSG	19	F	V	NI
005	CGC	23	F	V	NI
006	ALAGM	36	F	II	I
007	MLL	65	F	II	I
008	IMAB	49	F	II	I
009	EAG	35	F	III	I
010	MMC	62	F	III	I
011	LLNB	56	F	III	I
012	JSPS	43	F	IV	I
013	SS	52	F	III	I
014	MJGA	43	F	III	I
015	MPP	67	F	III	I
016	MASG	64	F	III	I
017	MHGBO	47	F	Ii	I
018	MLL	61	F	III	I
019	MAM	67	F	III	I
020	EAM	34	F	III	I
021	NFIS	55	F	II	NI
022	FP	35	F	II	I
023	ALFA	38	F	IV	NI
024	VM	42	F	III	I
025	SVLS	39	F	IV	I
026	NCSS	23	F	IV	I
027	JCJM	22	F	IV	I
028	BPP	70	F	II	I
029	RJAM	48	F	IV	I

F= Female; M= Male
Participants selection failure / dropouts did not have their classified phototypes - N / A or NC
Phototype according to Fitzpatrick scale:
I- skin suffers sunburn easily, never tans
II- The skin suffers sunburn easily, tans lightly
III- The skin suffers sunburn moderately, tans gradually
IV - The skin suffers sunburn lightly, tans easily
V - The skin rarely suffer sunburns, tans intensely
VI - The skin never suffer sunburn and is highly pigmented
I = Included; NI = Not included (has some of the exclusion criteria and / or doesn't have some of the inclusion criteria) SF = Selection failure, Q = quitter, PD = Protocol Deviation

ANNEX 2 - STUDY GROUP - CONTINUATION

Participant Number	Name Inicials	Age (Years)	Sex	Phototype	Status
030	SRMS	49	F	III	I
031	VFMS	32	F	III	I
032	MSB	32	F	IV	I
033	SAF	39	F	II	I
034	REG	21	F	III	I
035	MJPB	52	F	II	I
036	MBPD	51	F	III	I
037	SCA	37	F	III	I
038	FGDC	49	F	III	I
039	RCL	53	F	IV	I
040	ERBS	59	F	III	I
041	JMC	56	F	III	I
042	RJF	56	F	IV	I
043	EA	31	F	II	I
044	ESS	27	M	IV	I
045	VBSS	34	F	II	I
046	EAM	46	F	II	I
047	LCR	26	F	III	I
048	MJLS	55	F	IV	I
049	DR	60	F	III	I
050	SSA	33	M	IV	**NI**
051	AAC	31	F	IV	I
052	LACP	18	F	IV	I
053	MAP	62	F	II	I
054	KTP	37	F	III	I
055	JCOR	23	F	IV	I
056	MHNJF	51	F	IV	I
057	TCSS	19	F	IV	**NI**
058	ACM	53	F	IV	I

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ANNEX 2 - STUDY GROUP - CONTINUATION

Participant Number	Name Inicials	Age (Years)	Gender	Phototype	Status
059	**ARBS**	47	F	IV	I
060	**MANC**	67	F	III	I
061	KMTB	24	F	II	I
062	JAB	54	M	III	I
063	**NTB**	53	F	III	NI
064	ACR	39	F	III	I
065	**CR**	40	F	III	I
066	**MLK**	64	F	III	NI
067	MLM	47	F	IV	NI
068	RPC	35	F	III	I
069	**MSAR**	55	F	IV	I
070	MPBF	39	F	IV	NI
071	MJFP	58	F	II	I
072	AS	50	**M**	IV	NI
073	**NAM**	63	F	IV	I
074	NLS	57	F	II	I
075	TCSC	18	F	III	I
076	VCSC	28	**M**	IV	I
077	TJPL	48	F	III	I
078	VRR	61	F	II	I
079	ASS	67	**M**	III	I
080	DOS	35	F	III	I
081	JASS	18	M	III	I
082	ESC	52	F	IV	I
083	CRS	41	F	IV	I
084	MHS	44	F	III	I

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