A 14-DAY CLINICAL STUDY TO EVALUATE THE EFFICACY AND TOLERANCE OF A TEETH BRIGHTENING SYSTEM

FINAL REPORT

INVESTIGATIONAL PRODUCT TYPE: Teeth Whitener
INVESTIGATIONAL PRODUCT NAME: Teeth Brightening System

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SPONSOR: TH GENESIS
122 Sheldon St.
El Segundo - California – United States
Telephone: 01 - 818-456-8918

STUDY CENTER: INTERNATIONAL RESEARCH SERVICES, INC.
222 Grace Church St.
Port Chester, NY 10573
Telephone: 914.937.6500
Fax: 914.937.8067
Investigator in Charge: Stephen R. Schwartz

STUDY SITE: ALLERGISA PESQUISA DERMATO-COSMÉTICA LTDA
452/466, Dr. Romeu Tórtima Avenue – Barão Geraldo
13084-791 – Campinas – SP - Brazil
Telephone: +55 (19) 3789-8600
Investigator in Charge: Gabrielli Brianezi

A 14-DAY CLINICAL STUDY TO EVALUATE THE EFFICACY AND TOLERANCE OF A TEETH BRIGHTENING SYSTEM

SUMMARY

Investigational Product Name	Teeth Brightening System
Product Code of the Institute	093405-01
Study Code	All-SE-ODON-EP-093405-01-06-21
Report Code	All-SE-ODON-EP-093405-01-06-21-RFV01-Rev01
Sponsor	TH GENESIS
OBJECTIVE OF THE STUDY	To evaluate the efficacy and tolerance of a teeth whitening system, through expert clinical grading of tooth color and consumer perception using subjective questionnaires.
METHODOLOGY	Subjects were instructed to use the product at home, according to the provided use directions, for 14 days. They were assessed by a dentist before product use for the verification of the inclusion and non-inclusion criteria. Subjects also underwent an expert clinical grading of the tooth color, through the Vita Classical Guide, performed by a dentist before product use (Baseline) and after 14 days of product use (Day 14). Self-assessments were performed, through questionnaires, after 7 days (Day 7) and 14 days (Day 14) of product use.
INVESTIGATOR IN CHARGE	Gabrielli Brianezi
STUDY LENGTH	14 ± 2 days.
APPLICATION SITE	Teeth.
FREQUENCY OF APPLICATION	Daily.
INCLUDED STUDY POPULATION DESCRIPTION	Male and female subjects, aged between 35 and 58 years old (mean age: 44 years); presenting yellowish teeth at baseline; 100% of the panel with self-perceived sensitive teeth; subjects with teeth that are free of excessive decay, calculus and extrinsic stains (if applicable, with all the restorations intact well-sealed); subjects with interest in using teeth whitening products and that are willing to discontinue the use of all teeth cleaning products.
NUMBER OF SUBJECTS	A total of 35 study subjects were included in the study and a total of 32 subjects completed the study.
ETHICS	This study was conducted in conformity with the Declaration of Helsinki principles and according to the demands of applicable regulations, including CNS Resolution No 466/12, and according to the Good Clinical Practices (Document of the Americas and ICH E6: Good Clinical Practice).

RESULTS / CONCLUSION

Dental Clinical Assessment

During the study, no subjects presented clinical signs related to product use.

During the study, no subjects stated discomfort sensations related to product use.

The product was considered safe under the study conditions.

Expert Clinical Grading of Tooth Color

The product promoted a reduction in the intensity of the color of the teeth after fourteen days of use.

Self-Assessment Performed by the Study Subjects

Statement	% Positive answers	
	Day 7	Day 14
The teeth whitening kit is convenient to use.	96.9%	96.9%
My teeth look visibly brighter.	96.9%	93.8%
Tooth whitening system is suitable for my sensitive teeth.	100.0%	100.0%
Teeth are 3 shades whiter.	84.4%	84.4%
Teeth are 6 shades whiter.	34.4%	43.8%
Teeth are 11 shades whiter.	34.4%	37.5%
The appearance of my teeth is noticeably whiter.	93.8%	96.9%
I can use this tooth whitening system with virtually no sensitivity.	96.9%	96.9%
Teeth are significantly whiter.	93.8%	93.8%
Teeth are significantly whiter and brighter.	90.6%	93.8%
I can use this tooth whitening system without experiencing any pain.	96.9%	96.9%
Prevents teeth from staining.	93.8%	96.9%

Thus, the following claims can be supported:

- “System provides 18.8% of brightening and whitening at 14 days”, supported by expert grading assessment,
- “System provides 3 shades of brightening and whitening at 7 and 14 days for 84.4% of consumers, supported by self-assessment,
- “System is well tolerated” supported by Dental Clinical Assessment;
- “Suitable for sensitive teeth” supported by Dental Clinical Assessment;
- ""Dentist Approved" supported by Dental Clinical Assessment;
- "Dentist Tested" supported by Dental Clinical Assessment;
- " Clinically Tested" supported by Dental Clinical Assessment;
- "Safe and Effective" supported by Dental Clinical Assessment;
- "Prevents teeth from staining" supported by self assessment;
- "Whiter and Brighter in only 7days", supported by self assessment;
- "Fast results", supported by self assessment;
- "Quick results", supported by self assessment;
- "Visibly whiter teeth in only 7 days", supported by self assessment;

- "3 shades whiter in only 7 days", supported by self assessment;
- "Noticeably whiter in only 7 days", supported by self assessment;
- "Significantly whiter in only 7 days", supported by self assessment;
- "84% of consumers saw whitening and brightening in only 7 days", supported by self assessment;
- "Whitening with virtually no sensitivity", supported by self assessment;
- "Whitening without experiencing any pain", supported by self assessment;
- "96% of consumers felt that this whitening kit is convenient to use", supported by self assessment.

QUALITY ASSURANCE

The study was conducted according to the CNS Resolution No. 466/12, the Good Clinical Practices and in conformity with the Standard Operating Procedures of the Institute.

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

The Quality Assurance Department is responsible by the Management System auditory; and it is completely available for any specific study monitory performed by the Sponsor.

The signature below indicates that the study was performed as above described and that the results were verified in comparison with the source documents.

Audited by: Cristiane Nunes Coelho Moreira
08/13/2021

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1. ABBREVIATION LIST

AIDS	Acquired Immunodeficiency Syndrome
ASTM	*American Society for Testing and Materials*
CI	Confidence Interval
CNS	Brazilian Health Council (Conselho Nacional de Saúde)
CRO	Regional Council of Odontology
Dr.	Doctor
E.g.	*Exempli gratia*
Etc.	*Et Cetera*
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
INC	Incorporated
LED	Light-emitting Diode
LTDA	Limited
ml	Milliliter
No.	Number
NY	New York
Sars-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SP	São Paulo State
St.	Street

2. INTRODUCTION

Over the last few years, the personal hygiene, household, cosmetic and perfume products industry has grown considerably, same as its concern in developing safe and effective products.

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

Once the cosmetic product 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 cosmetic industry. In addition, the safety of the final formulation must be tested before it is marketed.

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

Tests conducted with humans are governed by very strict laws in order to protect and safeguard people. These laws vary from country to country. In Brazil, these studies are allowed, if they comply with the precepts of the Declaration of Helsinki and the CNS Resolution Nº 466/12 (NATIONAL HEALTH COUNCIL, 2013).

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

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

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

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

The benefits provided by a product must be consistent with the consumers' expectations generated by the claim.

In order to evaluate if a claim is appropriate, it is necessary to take into account the general consumers' impression concerning the presentation or the product advertisement. The *claims* must be

supported by solid, clear and relevant evidences. Such evidences may result from experimental studies (biochemical / instrumental methods, sensory evaluations, technical evaluations and evaluations without the participation of study subjects, *in vitro* testing in cell cultures, use of hair locks, etc.), and consumers evaluations (ASTM E 1958-06, 2006).

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

3. OBJECTIVE

The study objective was to evaluate the efficacy and tolerance of a teeth whitening system, through expert clinical grading of tooth color and consumer perception using subjective questionnaires.

4. STUDY DESIGN

Non-comparative clinical study.

5. TEST SITE

The subjects were instructed to apply the product on the teeth.

6. INVESTIGATIONAL PRODUCT

The investigational product was provided by the sponsor and was labeled with adequate codes and use directions. All products sent by the sponsor were initially stored in the sample room at the study center, with controlled temperature and restricted access. The products release was controlled by the principal investigator or by a previously designated technical staff. At the moment of receiving the product, the subjects were instructed on how to correctly store it, emphasizing the importance to keep it out of reach of children and/or animals.

Product information, as declared by the sponsor, is described in APPENDIX 5. One sample of the product was cataloged and can be found in the institute's archive, for a period of one month after the end of the study.

6.1. Identification

Table 1. Investigational Product Identification

Product Name	Product Type	Product Code
Teeth Brightening System	Teeth Whitener	093405-01

6.2. Use Directions

1. Rinse your mouth with water and dry your teeth. Rinse the mouthpiece with water.

Note: Dry teeth and mouthpiece thoroughly as water will dilute the whitening gel making it less effective.

2. Look in the mirror to record your whitening stage with the shade guide paper.

3. Twist whitening pen until the gel flows. Apply gel evenly on both upper and lower teeth. Use about 0.5 ml - 0.7 ml each time.

4. Place the mouthpiece in your mouth and bite down.

5. Press the power button for 1.5 seconds to start the treatment.

6. Start with the blue color for five seconds, then press the power button to turn red.

7. Press the power button twice after 5 seconds to turn red and blue.

8. The LED light will turn off automatically after 16 minutes.

9. Rinse the mouthpiece and your mouth with water.

10. Compare your teeth with the shade guide paper to again see how many stages you have improved.

Important: **Don't eat or drink anything except water for 30 minutes after treatment.**

Frequency: Daily.

Additional Notes

- Charging takes two hours to fully charge.
- Charging Status: Light Flashing
- Charged Fully: Lights should be off
- Press the power button for 1.5 seconds to turn on/off.

Warnings

1. Avoid applying the gel on the gum or lips. Rinse immediately with water if this happens. Any burning sensation should cease within 24 hours.

2. It is normal to feel slight sensitivity during treatment. Apply the desensitization gel after the whitening process. Stop treatment immediately if you experience severe pain.

3. Keep out of the reach of children.

4. Not suitable for ceramic or false teeth.

5. Not suitable for tooth discoloration caused by lesions or medication.

6. Not suitable for severe tetracycline and decayed teeth.

7. Not suitable for defective enamel, exerted dentin and damaged teeth.

8. Not suitable for children under 16 years old.

6.2.1. Product Use Compliance Check

The compliance of investigational product use by the subjects was verified through the verification of the completion of the daily-log of product use by the subjects.

7. STUDY PERIOD

The study lasted a total of 14 ± 2 days.

- **Start of the First Group:** 07/02/2021;
- **End of the Last Group:** 07/16/2021.

8. STUDY SUBJECTS

8.1. Study Subjects Recruitment

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

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

8.2. Selection and Admission of Study Subjects

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

8.3. Study Population

The sample size of the population to be recruited predicted by protocol was 35 subjects, with the objective of completing the study with 30 responses.

8.4. Inclusion Criteria

a) Females or Males in good general health, and between ages of 35 and 65 years old, inclusive at enrollment;
b) Subjects with yellowish teeth at baseline as determined by an expert grader using the Vita Classical guide (or similar);
c) Approximately 50% of the panel with self-perceived sensitive teeth;
d) Subjects with teeth that are free of excessive decay, calculus and extrinsic stains, if applicable all restorations are to be intact well sealed;

e) Subjects with interest in using teeth whitening products;
f) Able to read, understand and willing to sign an ICF, including HIPAA and state requirements, complete a brief personal/medical history;
g) Subjects are willing and able to follow all study directions, attend study visits as scheduled and must be willing to accept the restrictions of the study including but not limited to: discontinuing the use of all teeth cleaning products.

8.5. Non-Inclusion Criteria

a) Subjects with any gum tissue cuts or scratches;
b) Subjects with temporary tooth restorations (temporary fillings, crowns etc.);
c) Subjects with orthodontic appliances, full dental prosthesis and removable anterior teeth prosthesis;
d) Subjects with known allergies to flavoring, color additives, etc;
e) Subjects having an acute or chronic disease or medical condition, including dermatological problems, which could put her at risk in the opinion of the Principal Investigator or compromise study outcomes. Typical uncontrolled chronic or serious diseases and conditions which would prevent participation in any clinical trial are cancer, AIDS, diabetes, morbid obesity, renal impairment, mental illness, drug/alcohol addiction;
f) Subjects who are unreliable or unlikely to be available for the duration of the study;
g) History of allergic reactions, skin sensitization and/or known allergies to cosmetic ingredients, toiletries, sunscreens, etc;
h) Immunocompromised subjects;
i) Woman who started Hormone Replacement Therapy within the last three months preceding the screening visit;
j) Woman using oral contraception for less than three months before the screening visit or who has changed her contraceptive method within the three months before the Baseline visit or planning to modify her contraception treatment within the duration of the study;
k) Woman known to be pregnant, lactating or planning to become pregnant within six months. Subjects who be-come pregnant during the study must inform the Principal Investigator immediately;
l) Individuals unable to communicate or cooperate with the Principal Investigator due to language problems, poor mental development, or impaired cerebral function;
m) Employees of IRSI or other testing firms/ laboratories, cosmetic or raw goods manufacturers or suppliers employees of IRSI or other testing firms/ laboratories, cosmetic or raw goods manufacturers or suppliers.

9. METHODOLOGY

9.1. Materials and Equipment

- Vita Classical Guide.

9.2. General Procedures

A dental clinical assessment of the subjects was performed for the verification of the inclusion and non-inclusion criteria and to assess the tooth color of the subjects, through an expert clinical grading, using the Vita Classical Guide (Baseline).

A trained technician instructed the subjects on the correct way of using the product at home, following the use directions described in the daily-log of product use, during 14 days. The technician also instructed the subjects about the correct completion of the self-assessment questionnaires at home, after 7 (Day 7) and 14 (Day 14) days of product use, and informed the subjects that they should bring the completed questionnaires at the final visit of the study (Day 14).

After 14 days of product use (Day 14), a dental clinical assessment of the subjects was performed for the verification of possible adverse events and/or discomfort sensations, to confirm the correct product use and to assess the tooth color of the subjects, through an expert clinical grading, using the Vita Classical Guide.

9.3. Procedure Schedule

Table 2. Study Schedule

STAGES	Baseline	Day 7	Day 14
Informed Consent Form signature	X	-	-
Dental Clinical Assessment: verification of the inclusion/non-inclusion criteria	X	-	-
Dental Clinical Assessment: expert clinical grading of tooth color	X	-	X
Distribution of investigational product, daily-log of investigational product use and questionnaires	X	-	-
Self-assessment questionnaire by the study subjects at home	-	X	X
Return of investigational product, daily-log of investigational product use and questionnaires	-	-	X
Assessment of product compliance by the verification of the daily-log of investigational product use	-	-	X
Assessment of adverse events (if applicable)	-	-	X

9.4. Methods and Criteria of Assessment

9.4.1. Dental Clinical Assessment

The dental clinical assessment of the subjects was performed on the initial visit in order to verify the study inclusion and non-inclusion criteria and additionally at the final visit in order to check possible adverse events and/or discomfort sensations and to confirm the correct product use. At the initial and final visits the dentist also performed an expert clinical grading of the tooth color of the subjects using the Vita Classical Guide. Subjects were supervised by a dentist throughout the study and assessed in case there were any symptoms or clinical signs.

Subjects were instructed to contact the study coordinator at any time, in case they had any complaints. In these cases, they would be sent for evaluation and guidance by the dentist 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).

9.4.1.1. Dental Adverse Reactions

All reactions would be rated according to their intensity as: mild, moderate or intense. When necessary, product use would be interrupted.

9.4.1.2. Expert Clinical Grading of Tooth Color

What gives color to the teeth is dentin. It is porous (these pores are called dentinal tubules and it is inside these tubules where lie the pigment molecules). The enamel on the other hand is colorless, translucent (DOZIC, 2004).

The closer of the cervical area of the teeth (near the gums), the higher is the amount of dentin (the lower the amount of enamel), thus, this area of the teeth is darker. That is why in areas nearer to the gums (teeth cervical area) the tooth color is darker, and the closer to the tooth ends (incisal/occlusal areas), the lighter is the tooth (DOZIC, 2004).

The color has three dimensions: hue, chroma, and value.

The hue is the name of the color (blue, yellow, among others) and is divided into A, B, C, and D.

A: somewhat brown

B: somewhat yellow-orange

C: somewhat gray - green

D: somewhat gray-pink-red

Chroma is the hue saturation (if it is darker or lighter). E.g., navy blue, light blue, dark yellow, light yellow. It is divided into the following categories:

A1; A2; A3; A3,5; A4.

B1; B2; B3; B4.

C1; C2; C3; C4.

D2; D3; D4.

Finally, the value is the amount of white and black each hue has (JOINER, 2004).

The color evaluation was done by the comparative method of the Vita Classical Guide (APPENDIX 5) at the beginning of the study (Baseline) and after 14 days of product use (Day 14).

The evaluations were realized to Upper Incisors, Upper Canines, Upper Posterior Teeth, Lower Anterior Teeth, Lower Canines and Lower Incisors. The intensity of the evaluations within each group can vary from 1 to 4.

9.4.2. Self-Assessment Performed by the Study Subjects

The Self-Assessment was performed by following the “Standard Guide for Sensory Claim Substantiation” (ASTM E 1958-06, 2006), by using questionnaires. The ASTM (American Society for Testing and Materials) standards organization has been developed for over a century and represents one of the greatest voluntary organizations for standards development in the world, being a reliable source of technical standards of material, products, systems and services. Known by their high technical quality and relevance on market, ASTM standards have an important role in the infrastructure of the information guiding the study design, product manufacturing and commerce in global economy. The “Standard Guide for Sensory Claim Substantiation” is an ASTM standard that aims to disclose the good practices in sensory studies, approaching reasonable practices for executing sensory studies to validate product claims.

The study subject was instructed to assess the product through questionnaires (APPENDIX 4) after 7 days (Day 7) and 14 days (Day 14) of product use, at home.

So that the subjects knew the meaning of each assessed attribute, they were instructed by a trained technician on the first day of the study. The questionnaires of self-assessment were delivered to the subjects so that there were completed at home.

9.5. Criteria and Procedures for Study Subjects Withdrawal

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

- Study subjects not included: subjects who sign the ICF, but who do not meet the inclusion and non-inclusion criteria of the study;
- Subjects who present complications that affect their eligibility after the study consent;
- Subjects who present - at the Investigator's discretion - any problem that would prevent product applications from continuing, at any time during the study;

- Consent withdrawal by the study subject, regardless of the reason;
- Lack of adhesion of the study subject to the study. A significant lack of adhesion will be recorded if the subject does not visit the study center for assessments;
- Serious Adverse Event;
- Concurrent disorder or treatment: any pathological process or treatment that occurred during the study period and that might interfere with the study product, such as a medication interaction or masking of results.

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

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

10. ADVERSE EVENTS

An adverse event is any untoward medical occurrence in a patient or clinical investigation subject administered a product and that does not necessarily have a causal relationship with this treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the investigational product use (adapted from ICH, 2016).

According to the Good Clinical Practices (ICH, 2016), a Serious Adverse Event is any untoward medical occurrence that at any dose

- results in death;
- is life-threatening;
- requires inpatient hospitalization or prolongation of existing hospitalization;
- results in persistent or significant disability/incapacity;
- is a congenital anomaly/birth defect.

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

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

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

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

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

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

- Very likely: Only cases in which the clinical condition is considered to be evocative are classified as a very likely nexus, the following conditions occurring together: (i) the temporality of the facts is compatible with an adverse reaction to cosmetics and (ii) there is a laboratory test that confirm the relationship with the investigational product (e.g.: positive patch test for the investigational product).
- Likely: The cases in which the clinical condition is considered to be evocative are classified as likely causal nexus, occurring with the following conditions together: (i) the temporality of the facts is compatible with an adverse reaction to cosmetics and (ii) there is no laboratory test to confirm the relationship with the investigational product (e.g. diagnosis of contact dermatitis, without patch test, cosmetic acne - there are no laboratory tests to confirm the relationship with the product).
- Not clearly attributable: Cases in which the clinical scenario is not considered to be evocative or the chronology is not clearly compatible or unknown, are classified as nexus not clearly attributable.
- Unlikely: The following two cases are associated with an unlikely nexus: the clinical scenario is not considered to be evocative; the chronology is not clearly compatible or unknown, and the result of the investigation with the investigational product is negative (patch test or re-exposure).
- Excluded: The cases in which the diagnosis corresponds to a dermatosis of well-known cause and / or known to be caused by the use of products are classified as excluded nexus (e.g. vitiligo, tineas, pityriasis rosea, pityriasis versicolor, psoriasis, folliculitis, solar melanosis, ephelides, among others), when there is no correlation between the subject's complaint and the use of a 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 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 product use).

11. APPLICABLE ETHICAL REMARKS

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

Before the study started, the subjects were informed about the study objective, its methodology and length, and about the possibly expected benefits and the constraints related to the study. Subjects

who agreed to take part in the study signed an Informed Consent Form (ICF) (APPENDIX 1), elaborated according to the Declaration of Helsinki and CNS Resolution No 466/12. The process of obtaining the ICF confirmed the voluntary nature of subjects' participation in the study.

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

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

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

12. STATISTICAL ANALYSIS

The description of the treatment applied to the data is presented on the table below.

Table 3. Detailed statistical analysis

Data Type	Statistical Method	Data Reported	Sample size
Expert clinical grading of tooth color	Descriptive Statistics Student t test (for Vita scale)	Frequency (n, %) per response Mean, standard error, standard deviation, confidence interval, median, minimum and maximum Percent improvement on the mean Percent of subjects with reduction p-value (compared to baseline)	32
Self-Assessment	Descriptive Statistics	Frequency (n, %) per response Positive response percent	

The confidence level used on the comparative analysis was 95%.

Software: MINITAB 14 and XLSTAT 2021.

The raw data can be found in APPENDIX 3.

13. RESULTS

13.1. Protocol Deviations

For this study 35 subjects with self-perceived sensitive teeth were included, which did not interfere in the study results because even with a population of 100% of subjects with self-perceived sensitive teeth, no subjects presented adverse event related to product use.

13.2. Study Population Description and Study Adherence

A total of 35 subjects were included in the study, among them, 32 finished the study. The summarized description of the population and adherence to the study is available in the following table. The detailed description of the study group can be found in APPENDIX 2.

Table 4. Population Included and Adherence to the Study

Population Included									Adherence		
Recruited[1]	**Not Included[2]**	**Withdrawn[3]**	**Included[4]**	**Gender (F)**	**Gender (M)**	**Minimum Age (years)**	**Maximum Age (years)**	**Mean Age (years)**	**Absences[5]**	**Removed[6]**	**Finished the Study[7]**
36	01	00	35	29	06	35	58	44	02	01	32
Subjects									027 and 032	023	

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

Subject 023 was removed from the study due to presenting adverse event as described in item 13.4.

The study achieved its objective to obtain, at its end, a minimum of 30 answers.

13.3. Dental Clinical Assessment

During the study, no subjects presented clinical signs related to the investigational product use.

During the study, no subjects stated discomfort sensations related to the investigational product use.

13.4. Adverse Event

During the study, 01 subject presented adverse event. The adverse event is summarized in the table below.

Table 5. Adverse event

Date	Subject Number	Study Day	Adverse Event Description	Intensity	Site of the Event	Frequency	Action Taken	Hypothesis or Rational + Diagnosis	Causal Nexus	Data considered in the study
07/26/2021	023	Day 8	Fever	Mild	Systemic	Continuous	Not applicable - Final Date of the Study	Considering subject' statement, the case was closed. It was a case of Sars-CoV-2, confirmed by exam. The subject was followed-up, presenting complete remission of the scenario on 07/17/2021. As the subject did not come to the final visit of the study, subject's data were not considered in the study.	Excluded	No
			Headache							
			Malaise							
			Coryza							
			Body pain							

13.5. Expert Clinical Grading of Tooth Color

The vast majority of subjects have a tone A followed by a tone B. None of the participants had a tone D and only 1 had a tone C.

Table 6. Frequency and Percentage

Tone	n	%
A: Reddish - Brown	28	87.5%
B: Reddish - Yellow	3	9.4%
C: Shades of gray	1	3.1%
D: Reddish - Gray	0	0.0%

The product promoted a significant reduction in the intensity of the color of the teeth, after fourteen days of using the product in relation to Baseline (before product use), indicating teeth brightening and whitening.

Table 7. Descriptive Statistics and results of comparison

Statistics	Baseline	Day 14	Δ(Day 14 - Baseline)
Mean	3.2	2.6	-0.6
Standard error	0.1	0.1	0.1
95% CI	[3.1; 3.3]	[2.4; 2.8]	[-0.7; -0.5]
Δ(%) improvement on the mean			**18.8**
% of subjects with reduction			**100.0**
P-value			**<0.001***

* Significant at 5% (Student t test).

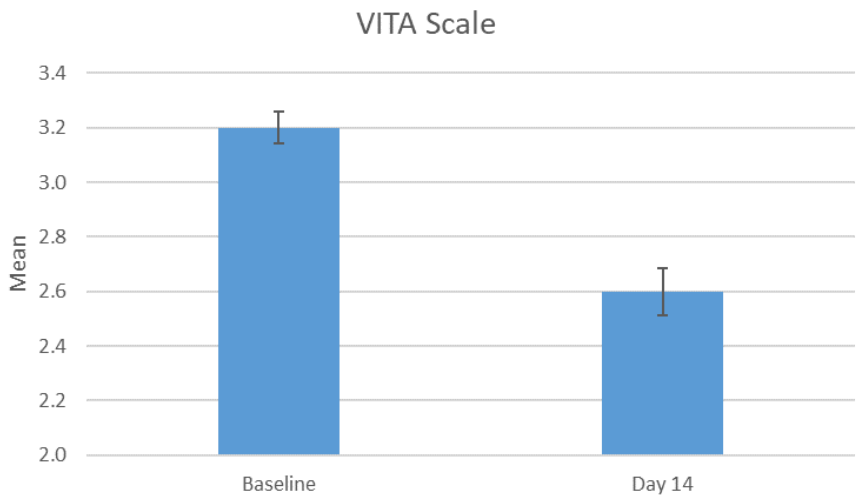

Figure 1 Mean ± standard error for intensity of color by time-point

13.6. Self-Assessment Performed by the Study Subjects

The table and figure below present the positive answers (sum of the categories "Agree" and "Completely agree") for assessments performed by the subjects (subjective perception) after 7 days (Day 7) and 14 days (Day 14) of product use.

Table 8. Percentage and frequency () of positive answers per question

Statement	% Positive answers	
	Day 7	Day 14
The teeth whitening kit is convenient to use.	96.9% (31)	96.9% (31)
My teeth look visibly brighter.	96.9% (31)	93.8% (30)
Tooth whitening system is suitable for my sensitive teeth.	100.0% (32)	100.0% (32)
Teeth are 3 shades whiter.	84.4% (27)	84.4% (27)
Teeth are 6 shades whiter.	34.4% (11)	43.8% (14)
Teeth are 11 shades whiter.	34.4% (11)	37.5% (12)
The appearance of my teeth is noticeably whiter.	93.8% (30)	96.9% (31)
I can use this tooth whitening system with virtually no sensitivity.	96.9% (31)	96.9% (31)
Teeth are significantly whiter.	93.8% (30)	93.8% (30)
Teeth are significantly whiter and brighter.	90.6% (29)	93.8% (30)
I can use this tooth whitening system without experiencing any pain.	96.9% (31)	96.9% (31)
Prevents teeth from staining.	93.8% (30)	96.9% (31)

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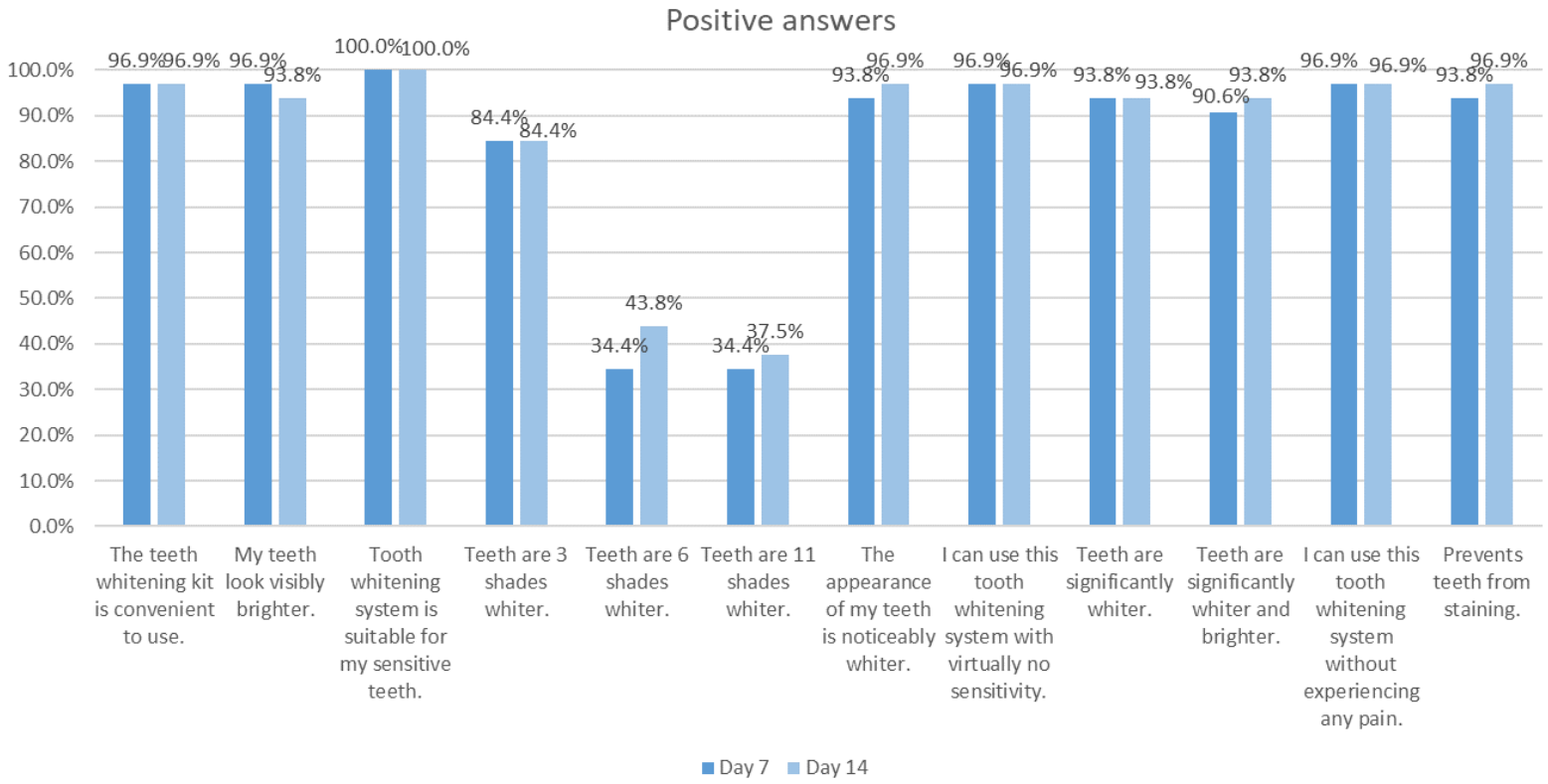

Figure 2 Percentage of positive answers per question

14. CONCLUSION

According to the methodology used to assess the safety and efficacy of the product **Teeth Brightening System**, submitted by the company **TH GENESIS**, it could be concluded that:

Dental Clinical Assessment

- During the study, no subjects presented clinical signs related to product use.
- During the study, no subjects stated discomfort sensations related to product use.
- The product was considered safe under the study conditions.

Expert Clinical Grading of Tooth Color

The product promoted a reduction in the intensity of the color of the teeth after fourteen days of use, indicating teeth brightening and whitening.

Self-Assessment Performed by the Study Subjects

Statement	% Positive answers	
	Day 7	Day 14
The teeth whitening kit is convenient to use.	96.9%	96.9%
My teeth look visibly brighter.	96.9%	93.8%
Tooth whitening system is suitable for my sensitive teeth.	100.0%	100.0%
Teeth are 3 shades whiter.	84.4%	84.4%
Teeth are 6 shades whiter.	34.4%	43.8%
Teeth are 11 shades whiter.	34.4%	37.5%
The appearance of my teeth is noticeably whiter.	93.8%	96.9%
I can use this tooth whitening system with virtually no sensitivity.	96.9%	96.9%
Teeth are significantly whiter.	93.8%	93.8%
Teeth are significantly whiter and brighter.	90.6%	93.8%
I can use this tooth whitening system without experiencing any pain.	96.9%	96.9%
Prevents teeth from staining.	93.8%	96.9%

For positive answers the sum of the categories *"Agree"* and *"Completely agree"* was considered.

Thus, the following claims can be supported:

- “System provides 18.8% of brightening and whitening at 14 days”, supported by expert grading assessment,
- “System provides 3 shades of brightening and whitening at 7 and 14 days for 84.4% of consumers, supported by self-assessment,

- “System is well tolerated” supported by Dental Clinical Assessment;
- “Suitable for sensitive teeth” supported by Dental Clinical Assessment;
- “"Dentist Approved" supported by Dental Clinical Assessment;
- "Dentist Tested" supported by Dental Clinical Assessment;
- " Clinically Tested" supported by Dental Clinical Assessment;
- "Safe and Effective" supported by Dental Clinical Assessment;
- "Prevents teeth from staining" supported by self assessment;
- "Whiter and Brighter in only 7days", supported by self assessment;
- "Fast results", supported by self assessment;
- "Quick results", supported by self assessment;
- "Visibly whiter teeth in only 7 days", supported by self assessment;
- "3 shades whiter in only 7 days", supported by self assessment;
- "Noticeably whiter in only 7 days", supported by self assessment;
- "Significantly whiter in only 7 days", supported by self assessment;
- "84% of consumers saw whitening and brightening in only 7 days", supported by self assessment;
- "Whitening with virtually no sensitivity", supported by self assessment;
- "Whitening without experiencing any pain", supported by self assessment;
- "96% of consumers felt that this whitening kit is convenient to use", supported by self assessment.

Gabrielli Brianezi
Investigator in Charge
08/13/2021

José Marcos M. Vendramini
Statistician in Charge
08/13/2021

Lilian Pessoto Rosa
Dentist (CRO 76471)
08/13/2021

15. REFERENCES

ASTM, 2006 E 1958-06 - Standard Guide for Sensory Claim Substantiation.

BARAN, R. & MAIBACH, H.I., (ed.). Cosmetic Dermatology, Baltimore, Willians & Wilkins, 1994.

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

DOZIC, A. et al.. Relation in color of three regions of vital human incisors. Dent. Mater., v.20, n.9, p.832-838, 2004.

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

JOINER, A. Tooth colour: a review of the literature. J. Dent., v.32, n.1, p.03-12, 2004.

NATIONAL HEALTH COUNCIL. Resolution No. 466/12 of the Ministry of Health. Federal Official Journal, 06/13/2013.

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

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

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

SAMPAIO, S.A.P. & RIVITTI, E.A. DERMATOLOGIA BÁSICA, 2A EDIÇÃO, SÃO PAULO, ARTES MÉDICAS, 2000.

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

ZATZ, J.L. Aumento da penetração cutânea. Cosmetics & Toiletries, 7: 52-58, 1995.

APPENDIX 1 INFORMED CONSENT FORM

Sub No.: _____

INFORMED CONSENT FORM

VER_01 – 06/28/2021 page 1 of 8

STUDY PROJECT TITLE: EFFICACY AND ACCEPTANCE ASSESSMENT OF A TEETH WHITENING PRODUCT AFTER 14 DAYS OF USE

NAME OF THE INVESTIGATOR IN CHARGE: Gabrielli Brianezi

STUDY CENTER: Allergisa Pesquisa Dermato-Cosmética Ltda.

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

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

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

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

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

What are the objectives of this study?

The objective of this study is to verify the acceptance and efficacy of a **TEETH WHITENER (*093405-01*),** by confirming the efficacy in teeth brightening and whitening and absence of adverse reactions and mouth discomfort sensations, when applied under normal use conditions on subjects who have sensitive teeth, or not, supervised by a dentist, and to assess product efficacy based on your perception, through a questionnaire.

Can I join the study?

For participating in the study, firstly you have to present good health and meet other requirements called inclusion and non-inclusion criteria, that will be assessed and discussed by the dentist.

You can still be dismissed by the dentist, after signing the informed consent form, if you present any of the non-inclusion criteria of the study, also in case the total amount of subjects is already reached.

How many people will join this study?

The study will be conducted with up to 35 subjects.

Where will the study be conducted?

The study will be conducted at one of the facilities of ALLERGISA pesquisa dermato-cosmética ltda, head office located at 452/466 Dr. Romeu Tórtima Avenue – Barão Geraldo – Campinas – SP, with all the necessary precautions for your safety.

What will I have to do?

Your participation in the study will last 14 days. During this period, there will be 02 visits.

You can also call at any time, to clarify any questions, or to inform any discomfort sensations you might present during the study. If the discomfort creates a need for on-site assistance, a visit will be scheduled, during which all the care recommended by experts will be taken to ensure your safety.

At the beginning of the study, you will undergo a dental assessment, and you will be supervised all along the study duration. During the dental assessment, the dentist will keep a minimum distancing of 1 meter, and will wear gloves, facial masks and acrylic face shield. After each subject, the table and chair used for the attention service will be sanitized.

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 should use the product according to the use directions described in your daily-log on the 1st day of the study.

What are the study procedures?

The following procedures will be performed during the study:

- Before the beginning of the study, a technician will clean the counter and the chairs of the room using 70% Gel Alcohol hand sanitizer.
- Before entering or leaving the test room, the technician will put the hand sanitizer on your hands, so that you can sanitize them.
- You will be instructed to sit and get comfortable in the chair of the test room, respecting a minimum distance of 1 meter from other subjects.
- You will be instructed to avoid talking to other subjects to minimize the risk of contamination inside the test room.
- Upon arriving at the Institute, you will receive a mask of mandatory use during the whole time of permanence in the test room.
- You will be instructed to avoid touching your face and mask.
- You will be questioned if your mask is wet; if so, you will get another one for use.
- If you feel the need to go to the toilet, you must wash your hands with water and soap and, then, sanitize them again with the gel alcohol hand sanitizer provided.
- You will be informed about the study objective, its methodology and duration, and about the possibly expected benefits and the constraints related to the study and, if you agree, you will sign this Informed Consent Form.
- You will undergo a dental assessment at the beginning, at the end of the study and you will be supervised throughout the study.
- The assessments will occur individually (one subject at a time).
- You will receive the test product, a daily-log, and the questionnaires of the study. You will be instructed to use the product according to the use instructions described in the daily-log, under normal use conditions, for 14 days and to complete the questionnaire after the last product application at home. Still at the initial visit, a technician will instruct you on the correct completion of the questionnaires at home and will inform that you should bring the questionnaires completed on the final visit of the study.
- You should return, at the end of the study, the daily-log and test product.

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IMPORTANT!!!

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

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

Procedures Summary:

PROCEDURES	VISIT	TIME SPENT AT THE INSTITUTE
Signature of the Informed Consent Form Dental Assessment Receipt of the test product, daily-log of product use and self-assessment questionnaires;	T0	01 hour
Questionnaire after 7 weeks of test product application.	At Home	-
Questionnaire completion after last test product application	At Home	-
Dental Assessment Return of the test product, daily-log of product use, and questionnaires	T14	01 hour

You will be given the product to tested to use at home, as well as the Daily-log of Product Use at Home, which will have to be filled out with the frequency of the test product use and with any complaint - in case you find necessary - related to the product. By signing this informed consent form, you guarantee the truthfulness of the information provided and at the end of the study you should return the product and the daily-log duly completed.

All the material received was duly sanitized, but you must, after receiving the product, sanitize it again with the alcohol provided for more safety.

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 oral cavity (mouth).

If you present an adverse reaction with clinical sign in your oral cavity (mouth) (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 the information. Your identity will always be kept confidential.

Your identity will be kept confidential during the photographic records performance.

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

What is a teleconsultation?

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

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

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

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

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

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

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

What are my responsibilities in this study?

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

- Wearing a mask during the whole study procedure and commute to the Institute.
- Respecting the social distancing.
- Performing frequent cleaning of the hands with soap and/or gel alcohol hand sanitizer.
- Attending only at the times scheduled to avoid crowds.
- Allowing temperature measures performed by the technical team on all visits to the Institute, if necessary.
- You cannot perform any dental treatment during the study. If the treatment is necessary, immediately inform the study center.
- We ask you to communicate the study center about any type of medication or external/skin use or oral rout tablets and liquids (solutions and syrups) or injections, such as cortisone, anti-allergic or any other.

You must bring your daily-log and the bottle of the product every time you attend the institute so that we can check the use.

The products must be used exclusively by yourself.

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 any mouth products and topical medication on the areas near to the product application area. If you use any of these products or if you 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 wish of giving up.

What benefits will I have to join the study?

Studies in this cosmetic area aim to prove the safety and efficacy of those products. By joining this study, you will be contributing that this product is used by the population with much lower risk of reactions on the oral cavity (mouth), and confirmed teeth brightening and whitening, and product efficacy. You will also undergo free dental assessments and instructions on how to use the product, in order to assure better results.

Is there any risk related to the study participation?

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 sensation” on the product application sites.

The risks presented are already known, and if they occur, they will be as minimized as possible. You will be clinically supervised by the study site, until your health clinical conditions are reestablished, regardless of the time that it might take.

Any health problems you might have during the study should be informed to the investigator or study team immediately. All immediate or late assistance will be provided.

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

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

During the study conduction, a test for diagnosis of COVID-19 (disease caused by the new coronavirus) may be performed, as one more measure of safety taken by the Institute during this period. This test will be done with a manual device, through a small hole in your finger, to collect a small blood sample. The advantage of this test is to

obtain a quick and practically painless result. In case of suspect or confirmation by COVID-19, follow the recommendations that the Institute will provide based on the health organs. All immediate or late assistance will be provided and, for cases of possible infections by Covid-19, all the instructions to perform a quarantine or seek hospital attention will be given according to the recommendations of the health organs. The subject will be supervised until his/her health is reestablished.

What if I am pregnant or breastfeeding?

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

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

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

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

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

How can I know about the study results?

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

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

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

Can I be removed from the study?

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

It is duty of the investigator, at any moment, to remove you from the study, if you present any reaction to the product 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 interferes with 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 immediately, because he/she will know how to give you instructions about the best conduct for your case.

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

If you do not feel well or in case of any irritation signs on your oral cavity (mouth), immediately communicate,

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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 (Gabrielli Brianezi) or medical team through 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.

We ask you to call the Institute at any moment if you feel symptoms such as cough, fever, coryza, sore throat or shortness of breath, or if you would like to cancel your participation in the study, through the telephones 19-3517-6800 (business hours) or 19-99778-0204 (from 5 p.m. to 10 p.m.). Subjects who present these symptoms will not be allowed to participate in the study and if you arrive at the Institute with the symptoms, you will not be allowed inside and will be instructed to go home.

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Important information!

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

Please, keep this document for your information.

Signatures Page – EFFICACY AND ACCEPTANCE ASSESSMENT OF A TEETH WHITENING PRODUCT AFTER 14 DAYS OF USE

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 photos taken for the investigation procedure, in case of any reaction, are part of the procedure of this study and I agree with those images capturing.

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

01	Initials of the study subject	Date (MM/DD/YYYY)
	Signature of the Study Subject *(as in the ID or Driver's License)*	
02	Signature of the person in charge of explaining the ICF	Date (MM/DD/YYYY)

APPENDIX 2 STUDY GROUP

SUBJECT	AGE (YEARS)	GENDER	STATUS	SELF-PERCEIVED SENSITIVE TEETH
001	41	M	I	Yes
002	50	F	I	Yes
003	45	M	I	Yes
004	51	F	I	Yes
005	56	F	I	Yes
006	51	M	I	Yes
007	43	F	I	Yes
008	53	F	I	Yes
009	36	F	I	Yes
010	51	F	I	Yes
011	36	F	I	Yes
012	40	F	I	Yes
013	44	F	I	Yes
014	46	F	I	Yes
015	36	F	I	Yes
016	36	F	I	Yes
017	38	F	I	Yes
018	52	F	I	Yes
019	37	M	I	Yes
020	38	F	I	Yes
021	43	F	I	Yes
022	48	F	I	Yes
023	37	F	I	Yes
024	46	F	NI	-
025	44	F	I	Yes
026	43	F	I	Yes
027	35	M	I	Yes
028	39	F	I	Yes
029	49	F	I	Yes
030	44	F	I	Yes
031	43	F	I	Yes
032	43	F	I	Yes
033	35	F	I	Yes
034	50	M	I	Yes
035	58	F	I	Yes
036	51	F	I	Yes

Caption:

F= Female;

M = Male;

I = Included;

NI = Not Included (presented any non-inclusion criteria and/or did not present some of the inclusion criteria).

APPENDIX 3 RAW DATA

Expert Clinical Grading of Tooth Color

Table 9. Raw data and descriptive statistics – Vita Scale

Subject	Baseline	Day 14	Δ(Day 14 - Baseline)	Color
001	3.3	3.0	-0.3	A
002	3.5	2.5	-1.0	B
003	3.3	3.2	-0.1	A
004	3.2	3.0	-0.2	A
005	3.5	2.5	-1.0	B
006	3.3	3.0	-0.3	A
007	3.0	2.3	-0.7	A
008	3.7	3.2	-0.5	A
009	3.3	2.5	-0.8	A
010	3.3	3.1	-0.2	A
011	3.0	2.7	-0.3	A
012	2.3	1.5	-0.8	C
013	3.5	3.0	-0.5	A
014	3.0	2.8	-0.2	A
015	3.2	2.3	-0.9	A
016	3.5	3.0	-0.5	A
017	3.3	2.8	-0.5	A
018	3.3	3.0	-0.3	A
019	3.5	3.0	-0.5	A
020	3.7	2.7	-1.0	A
021	3.2	3.0	-0.2	A
022	2.3	1.3	-1.0	A
025	3.2	2.0	-1.2	A
026	3.0	2.3	-0.7	A
028	3.2	2.3	-0.9	A
029	3.3	2.0	-1.3	A
030	3.3	2.3	-1.0	A
031	3.0	2.0	-1.0	B
033	3.8	3.3	-0.5	A
034	3.3	2.5	-0.8	A
035	3.4	2.3	-1.1	A
036	3.2	2.3	-0.9	A
Mean	**3.2**	**2.6**	**-0.6**	**-**
Standard error	**0.1**	**0.1**	**0.1**	**-**
95% CI	[3.1; 3.3]	[2.4; 2.8]	[-0.7; -0.5]	-
Standard deviation	**0.3**	**0.5**	**0.3**	**-**
Median	3.3	2.6	-0.7	-
Minimum	2.3	1.3	-1.3	-
Maximum	3.8	3.3	-0.1	-

Self-Assessment Performed by the Study Subjects

Table 10. Percentage and frequency () by question – Day 7

Statement	Completely agree	Agree	Disagree	Completely disagree
The teeth whitening kit is convenient to use.	40.6% (13)	56.3% (18)	3.1% (1)	0% (0)
My teeth look visibly brighter.	18.8% (6)	78.1% (25)	3.1% (1)	0% (0)
Tooth whitening system is suitable for my sensitive teeth.	15.6% (5)	84.4% (27)	0% (0)	0% (0)
Teeth are 3 shades whiter.	12.5% (4)	71.9% (23)	15.6% (5)	0% (0)
Teeth are 6 shades whiter.	3.1% (1)	31.3% (10)	53.1% (17)	12.5% (4)
Teeth are 11 shades whiter.	3.1% (1)	31.3% (10)	46.9% (15)	18.8% (6)
The appearance of my teeth is noticeably whiter.	15.6% (5)	78.1% (25)	6.3% (2)	0% (0)
I can use this tooth whitening system with virtually no sensitivity.	31.3% (10)	65.6% (21)	3.1% (1)	0% (0)
Teeth are significantly whiter.	18.8% (6)	75.0% (24)	6.3% (2)	0% (0)
Teeth are significantly whiter and brighter.	18.8% (6)	71.9% (23)	9.4% (3)	0% (0)
I can use this tooth whitening system without experiencing any pain.	46.9% (15)	50.0% (16)	3.1% (1)	0% (0)
Prevents teeth from staining.	18.8% (6)	75.0% (24)	6.3% (2)	0% (0)

Table 11. Percentage and frequency () by question – Day 14

Statement	Completely agree	Agree	Disagree	Completely disagree
The teeth whitening kit is convenient to use.	34.4% (11)	62.5% (20)	3.1% (1)	0% (0)
My teeth look visibly brighter.	18.8% (6)	75.0% (24)	6.3% (2)	0% (0)
Tooth whitening system is suitable for my sensitive teeth.	21.9% (7)	78.1% (25)	0% (0)	0% (0)
Teeth are 3 shades whiter.	12.5% (4)	71.9% (23)	15.6% (5)	0% (0)
Teeth are 6 shades whiter.	0% (0)	43.8% (14)	53.1% (17)	3.1% (1)
Teeth are 11 shades whiter.	0% (0)	37.5% (12)	53.1% (17)	9.4% (3)
The appearance of my teeth is noticeably whiter.	15.6% (5)	81.3% (26)	3.1% (1)	0% (0)
I can use this tooth whitening system with virtually no sensitivity.	31.3% (10)	65.6% (21)	3.1% (1)	0% (0)
Teeth are significantly whiter.	18.8% (6)	75.0% (24)	6.3% (2)	0% (0)
Teeth are significantly whiter and brighter.	15.6% (5)	78.1% (25)	6.3% (2)	0% (0)
I can use this tooth whitening system without experiencing any pain.	50.0% (16)	46.9% (15)	3.1% (1)	0% (0)
Prevents teeth from staining.	21.9% (7)	75.0% (24)	3.1% (1)	0% (0)

APPENDIX 4 QUESTIONNAIRE

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Ver_01-07/01/2021

Self-Assesment Questionnaire - TX

1) The teeth whitening kit is convenient to use.

1	2	3	4
☐	☐	☐	☐
Completely disagree	Disagree	Agree	Completely agree

2) My teeth look visibly brighter.

1	2	3	4
☐	☐	☐	☐
Completely disagree	Disagree	Agree	Completely agree

3) Tooth whitening system is suitable for my sensitive teeth.

1	2	3	4
☐	☐	☐	☐
Completely disagree	Disagree	Agree	Completely agree

4) Teeth are 3 shades whiter.

1	2	3	4
☐	☐	☐	☐
Completely disagree	Disagree	Agree	Completely agree

5) Teeth are 6 shades whiter.

1	2	3	4
☐	☐	☐	☐
Completely disagree	Disagree	Agree	Completely agree

6) Teeth are 11 shades whiter.

1	2	3	4
☐	☐	☐	☐
Completely disagree	Disagree	Agree	Completely agree

Allergisa Pesquisa Dermato Cosmética Ltda. JUN_PAINEL_14_06-21

F.C. 0052 O.N. 0001 PAGE 002 / 002

Ver_01-07/01/2021

Self-Assesment Questionnaire - TX

7) The appearance of my teeth is noticeably whiter.

1	2	3	4
☐	☐	☐	☐
Completely disagree	Disagree	Agree	Completely agree

8) I can use this tooth whitening system with virtually no sensitivity.

1	2	3	4
☐	☐	☐	☐
Completely disagree	Disagree	Agree	Completely agree

9) Teeth are significantly whiter.

1	2	3	4
☐	☐	☐	☐
Completely disagree	Disagree	Agree	Completely agree

10) Teeth are significantly whiter and brighter.

1	2	3	4
☐	☐	☐	☐
Completely disagree	Disagree	Agree	Completely agree

11) I can use this tooth whitening system without experiencing any pain.

1	2	3	4
☐	☐	☐	☐
Completely disagree	Disagree	Agree	Completely agree

12) Prevents teeth from staining.

1	2	3	4
☐	☐	☐	☐
Completely disagree	Disagree	Agree	Completely agree

Responsible for the conference:_____

Allergisa Pesquisa Dermato Cosmética Ltda. *JUN_PAINEL_14_06-21*

APPENDIX 5 EXPERT CLINICAL GRADING OF TOOTH COLOR - VITA CLASSICAL GUIDE

Figure 1. The Vita Classical Guide used for grading tooth color

APPENDIX 6 INVESTIGATIONAL PRODUCT INFORMATION

“FORMULA NOT SUBMITTED”