EFFICACY ASSESSMENT OF A PRODUCT THROUGH SELF-ASSESSMENTS COMPLETED BY STUDY SUBJECTS AND DENTAL CLINICAL EFFICACY ASSESSMENTS UNDER NORMAL USE CONDITIONS

FINAL REPORT

INVESTIGATIONAL PRODUCT TYPE: Toothbrush
INVESTIGATIONAL PRODUCT NAME: Perfect Smile Whitening Brush (Blue LED toothbrush)

INSTITUTE PRODUCT CODE: 094144-01
STUDY CODE: All-E-EP-ODON-094144-01-07-21
REPORT CODE: All-E-EP-ODON-094144-01-07-21-RFV01-Rev01

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EFFICACY ASSESSMENT OF A PRODUCT THROUGH SELF-ASSESSMENTS COMPLETED BY STUDY SUBJECTS AND DENTAL CLINICAL EFFICACY ASSESSMENTS UNDER NORMAL USE CONDITIONS

SUMMARY

Investigational Product Name	Perfect Smile Whitening Brush (Blue LED toothbrush)
Product Code of the Institute	094144-01
Study Code	All-E-EP-ODON-094144-01-07-21
Report Code	All-E-EP-ODON-094144-01-07-21-RFV01-Rev01
Sponsor	TH GENESIS
OBJECTIVE OF THE STUDY	To assess the efficacy of a toothbrush, under normal use conditions, through dental clinical assessment, microbiological collection for counting of total of microorganism presenting on the oral cavity (teeth, tongue and gums) and subjective self-perception of the study subject by Self-Assessments.
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 were also assessed by a dentist to verify the dental plaque through O'Leary's plaque index and to assess the parameters of teeth color (tint, value and chroma) through the Vitta scale before product use (T0) and after 7 (Day 7) and 14 (Day 14) days of product use. A microbiological collection was also performed on the oral cavity (teeth, tongue and gums) of the subjects by a trained technician after 7 days (Day 7) of product use. Self-assessment was performed, through questionnaire, after 14 days (Day 14) of product use.
INVESTIGATOR IN CHARGE	Gabrielli Brianezi
STUDY LENGTH	14 days.
APPLICATION SITE	Teeth, gums and tongue.
FREQUENCY OF APPLICATION	Two times daily.
INCLUDED STUDY POPULATION DESCRIPTION	50% male subjects and 50% female subjects, aged between 18 and 56 years old (mean age: 36 years); presenting O'Leary's plaque index at baseline of 3 or more and with yellowed/darkened teeth, stain in the teeth and bacterial plaque proved by the dental assessment.
NUMBER OF SUBJECTS	A total of 30 study subjects were included in the study and a total of 25 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 dental 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.

Dental Plaque Assessment

Percentage of Surface with Bacterial Plaque

The product promoted a reduction in the percentage of the surface with bacterial plaque after seven and fourteen days of use.

Number of Faces with Bacterial Plaque

The product promoted a reduction in the number of the faces with bacterial plaque after seven and fourteen days of use.

Expert Clinical Grading of Tooth Color

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

Microbiological Collection (TSA)

A reduction was observed in the logarithm of the microorganisms count after seven days of product use.

Self-Assessment Performed by the Study Subjects

Statement	% Positive answers
	Day 14
The toothbrush is easy to use.	**100.0%**
My teeth look visibly brighter.	**88.0%**
Toothbrush is suitable for my sensitive teeth.	**92.0%**
Teeth are 1-3 shades whiter after 7 days.	**76.0%**
Teeth are 1-3 shades whiter after 14 days	**56.0%**
Teeth are 4-6 shades whiter after 7 days.	36.0%
Teeth are 4-6 shades whiter after 14 days	32.0%
The appearance of my teeth is noticeably whiter.	**80.0%**
I can use this toothbrush with virtually no sensitivity.	**96.0%**
Teeth are significantly whiter.	**88.0%**
Teeth are significantly whiter and brighter.	**84.0%**
I can use this toothbrush without experiencing any pain.	**96.0%**
Visibly removes stains like red wine and coffee from my teeth.	**76.0%**
My teeth feel cleaner than brushing with a manual toothbrush.	**100.0%**

My teeth look cleaner than brushing with a manual toothbrush.	**100.0%**
My breath is fresher.	**96.0%**
I feel more confident smiling after using this toothbrush.	**88.0%**
I found the pressure sensor feature helped me become a better brusher.	**96.0%**
I can use this toothbrush to get to the harder to reach areas of my mouth than brushing with a manual toothbrush.	**80.0%**
My gums are healthier than brushing with a manual toothbrush.	**72.0%**
I am more comfortable showing my teeth in public after using this toothbrush.	**80.0%**

Bold/Shaded = “passing” claim, >50% of the panel responded favorably

Thus, the following claims can be supported:

- “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 and Self-Assessment;
- “Fast results” supported by Dental Plaque Assessment; Expert Clinical Grading of Tooth Color, Microbiological Collection and Self-Assessment;
- “Quick results” supported by Dental Plaque Assessment; Expert Clinical Grading of Tooth Color, Microbiological Collection and Self-Assessment;
- “Reduction of Plaque” supported by Dental Plaque Assessment;
- “In a clinical study proven to thoroughly Smile Whitening Brush statistically significantly remove plaque along the gum line” supported by Dental Plaque Assessment;
- “Reduction of Plaque on100% of consumers after 7 days” supported by Dental Plaque Assessment;
- “Up to 30% less plaque after 7 days” supported by Dental Plaque Assessment;
- “In a clinical study the Perfect Smile Whitening Brush statistically significantly reduced plaque, giving you healthier gums and whiter teeth.” supported by Dental Plaque Assessment;
- “The Perfect Smile Whitening Brush doesn't damage your gums” supported by Dental Clinical Assessment and Self-Assessment;
- “Teeth Whitening” supported by Expert Clinical Grading of Tooth Color and Self-Assessment;
- “Helps you break down plaque build-up” supported by Dental Plaque Assessment
- “Up to 3 shades whiter after 7 days”; supported by Self-Assessment.
- “100% of consumers stated that teeth feel cleaner than brushing with a manual toothbrush” supported by Self-Assessment;
- “100% of consumers stated that teeth look cleaner than brushing with a manual toothbrush”.
- “In a clinical study the Perfect Smile Whitening Brush was found to cleaner better than a manual toothbrush for 100% of consumers” supported by Self-Assessment;
- “The Perfect Smile Whitening Brush provides a superior clean vs. a regular manual toothbrush for 100% of consumers”; supported by Self-Assessment;
- “Anti-Microbial” supported by Microbiological Collection;
- “Anti-Bacterial” supported by Microbiological Collection;
- “Reduces microbes on the oral cavity” supported by Microbiological Collection;

- “Reduces bacteria on oral cavity” supported by Microbiological Collection;
- “Whitens teeth”. supported by Expert Clinical Grading of Tooth Color and Self-Assessment;
- “Whiter and Brighter in only 7 days” supported by Expert Clinical Grading of Tooth Color and Self-Assessment;
- “Visibly whiter teeth in only 7 days” supported by Expert Clinical Grading of Tooth Color and Self-Assessment.
- “Reduces stains like red wine and coffee” 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
09/28/2021

CONTENTS

1. ABBREVIATION LIST

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*
ICF	Informed Consent Form
ICH	International Conference on Harmonization
INC	Incorporated
LED	Light-emitting Diode
LTDA	Limited
No.	Number
NY	New York
SP	São Paulo State
St.	Street
TSA	Tryptic Soy Agar
Tx	Study Assessment Time-Point

2. INTRODUCTION

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

Industry awareness and consumer requirements caused cosmetic manufacturers to adopt a new procedure: before marketing a product, nowadays companies are concerned to conduct clinical tests on safety and efficacy, which are coordinated by dermatologists. This procedure provides cosmetic companies with greater safety, credibility, and reliability from their consumers. Dental research studies have been showing a considerable increase in Brazilian clinical research studies, both quantitative and qualitative, reflecting a marked presence of the industries in this research field (BUSATO, et al., 2001).

Teeth and other structures of the oral cavity may suffer direct lesion from chemical, physical, or mechanical agents with which they get in contact. Some of the diseases that attack the oral cavity more often and that are in evidence in the population in general are cavities, dental plaque, tartar, gingivitis, and bad breath. The oral cavity also allows to highlight some systemic diseases manifestations (NARVAI, 2003).

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).

Studies 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, provided that they comply with the precepts of the Declaration of Helsinki and the CNS Resolution nº 466/12 Resolution (NATIONAL HEALTH COUNCIL, 2013).

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 consider the general consumers' impression concerning the presentation or the product advertisement. The *claims* must be supported by solid, clear, and relevant evidence. Such evidence may result from experimental studies (biochemical / instrumental methods, sensory evaluations, technical evaluations, and evaluations without study subjects: *in vitro* testing in cell cultures, use of hair locks, etc.), and consumers' evaluations (ASTM E 1958-06, 2006).

By performing clinical trials, 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 assess the efficacy of a toothbrush, under normal use conditions, through dental clinical assessment, microbiological collection for counting of total of microorganism presenting on the oral cavity (teeth, tongue and gums) and subjective self-perception of the study subject by Self-Assessments.

4. STUDY DESIGN

Non-comparative clinical study.

5. TEST SITE

The subjects were instructed to apply the product on teeth, gums and tongue.

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
Perfect Smile Whitening Brush (Blue LED toothbrush)	Toothbrush	094144-01

6.2. Use Directions

Blue Light LED Toothbrush Usage Instructions

1. Insert the brush head into the main body head of the toothbrush according to the arrow direction.

2. Add a small amount of toothpaste onto the brush head and wet it using water.

3. After wetting the brush, choose the appropriate brushing mode(s), which best suits your brushing needs. Note: Please see the insert for additional details for each brushing mode.

4. Place the toothbrush into your mouth and start the toothbrush. Ensure that you move the toothbrush slowly and uniformly and allow the vibration to do most of the work!

5. While brushing your teeth and gums, the brush head should be at a 45 degree angle.

6. Brush two (2) times daily for a total of 2 minutes each time using the brushing mode(s) which best suit your brushing needs (see insert for brushing modes).

   a. Brush each section of your mouth for 30 seconds each using the guide. The brush has a 30 second interval pause which will remind you when to switch to the next area.

   b. Smart Brushing Guide (see the guide).

7. After brushing your teeth, rinse the brush head and brush directly with clean water.

Charging the Toothbrush

1. Be sure to turn the toothbrush off before charging. Charge by plugging the base into an outlet and place the handle on the charger. The charger indicator will turn RED, indicating that the handle is charging. After the battery is fully charged, the charge indicator light will turn GREEN.

2. The toothbrush must be fully charged for 12 hours prior to first use or if it has not be used for approximately 15 days.

3. To keep the battery fully charged, we recommend that you keep the toothbrush on the charger when not in use.

4. Note: It is normal for the toothbrush to be warm while charging.

Warnings

1. Never use the charger if the cord/plug is damaged.

2. Keep the cord away from heated surfaces.

3. This product is designed to clean your teeth, gums and tongue only. Discontinue use of this product and contact a physician/dentist if discomfort or pain occurs.

4. Keep out of the reach of children.

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 days.

- **Start of the First Group:** 07/27/2021;
- **End of the Last Group:** 08/09/2021.

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 30 subjects, with the objective of completing the study with 25 responses.

8.4. Inclusion Criteria

a) Healthy study subjects;
b) O'Leary's plaque index at baseline of 3 or more;
c) Intact oral cavity on the study area;
d) Agreement to adhere to the procedures and requirements of the study and to report to the institute on the day(s) and at the time(s) scheduled for the assessments;
e) Ability of giving consent for participation in the study;
f) Aged from 18 to 59 years old;
g) Study subjects 50% male and 50% female;
h) Subjects with yellowed/darkened teeth – proved by the dental assessment;
i) Subjects presenting stain in the teeth – proved by the dental assessment;
j) Subjects with bacterial plaque – proved by the dental assessment.

8.5. Non-Inclusion Criteria

a) Smokers;
b) Pregnancy or breastfeeding (only for female gender);
c) Changes out of the normality standard (assessed by the dentist) in the oral cavity, which might interfere with the study or put the subject´s health at risk;
d) Skin pathology on the area of product application;
e) Users of fixed orthodontic appliance, with total prostheses or partial removable;
f) Type 1 Diabetes Mellitus: insulin-dependent diabetes, presence of complications resulting from diabetes (retinopathy, nephropathy, neuropathy), presence of dermatosis related to diabetes (lipoidic necrobiosis, plantar ulcer, ring granuloma, opportunistic infections); antecedents of episodes of hypoglycemia, diabetic ketoacidosis and/or hyperosmolar coma;
g) Immune insufficiency;
h) Current use of the following topical or systemic medications: corticosteroids, immunosuppressant and anti-histaminic drugs;
i) History of reaction to the category of product tested;
j) Other diseases or medications that might directly interfere with the study or put the subject's health under risk.

8.6. Study Requirements

k) Do not apply any product of oral use to the test site, which might interfere with the study assessment;
l) Do not perform any dental treatments during the study;
m) Do not change the cosmetic habits, including body and oral hygiene.
n) Do not use mouth products with lightening action or for sensitive teeth during the study;
o) Reduce your intake of the following foods: coffee, black tea, chocolate, cola soft drinks, red wine or grape juice, açaí, tomato sauce, strong color isotonic drinks, candies and chewing gum with dyes.

9. METHODOLOGY

9.1. Materials and Equipment

- Gloves, masks and cap;
- Sterile cotton swab;
- Sterile saline solution;
- Vita Classical Guide.

9.2. General Procedures

At the initial visit (T0), a dental clinical assessment of the subjects was performed by a dentist for the verification of the inclusion and non-inclusion criteria, to verify the dental plaque through O'Leary's plaque index and to assess the parameters of teeth color (tint, value and chroma) through the Vitta Scale. A microbiological collection was also performed on the oral cavity (teeth, tongue and gums) of the subjects by a trained technician.

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.

After 7 (Day 7) and 14 days (Day 14) of product use, 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, to verify the dental plaque through O'Leary's plaque index and to assess the parameters of teeth color (tint, value and chroma) through the Vitta Scale. A new microbiological collection was performed on the oral cavity (teeth, tongue and gums) of the subjects by a trained technician only after 7 days of product use (Day 7).

After 14 days (Day 14) of product use the subjects answered the self-assessment questionnaire through telephone contact made by a trained technician.

9.3. Procedure Schedule

Table 2. Study Schedule

STAGES	T0	Day 7	Day 14
Informed Consent Form signature	X	-	-
Dental Clinical Assessment: verification of the inclusion/non-inclusion criteria	X	-	-
Dental Clinical Assessment: verification of the dental plaque performed through O'Leary's plaque index and assessment of the parameters of teeth color (tint, value and chroma) through the Vitta scale	X	X	X
Microbiological collection by trained technician *Note: the collection was done on the oral cavity of the subjects (considering teeth, tongue, and gums), with the aid of a sterile cotton swab damped in sterile saline solution.*	X	X	-
Distribution of investigational product and daily-log of investigational product use	X	-	-
Self-assessment questionnaire by the study subjects (through telephone contact).	-	-	X
Return of investigational product and daily-log of investigational product use	-	-	X
Assessment of product compliance by the verification of the daily-log of investigational product use	-	-	X
Assessment of adverse events (if applicable)	-	X	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 (T0) in order to verify the study inclusion and non-inclusion criteria and additionally after 7 days (Day 7) and 14 days (Day 14) of product use in order to check possible adverse events and/or discomfort sensations and to confirm the correct product use. At all visits of the study the dentist also verified the dental plaque through O'Leary's plaque index and assessed the parameters of teeth color (tint, value and chroma) through the Vitta Scale. 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 those cases, they would be sent for evaluation and guidance by the dentist in charge, who would assess 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 Plaque Assessment

The assessment of the dental plaque was performed through the O'Leary plaque index, which consists of the note of the plaque found on the tooth crown after being dyed. The percentage index was obtained the following way: the number of remaining teeth is taken (those not dyed) and it is multiplied by 4 (four), to represent the number of surfaces, vestibular, lingual, mesial, and destial (V-L-M-D, respectively), obtaining the total number of surfaces. Then, the dyed faces were counted by the plaque marker recorded in an especially aimed graph (BUTLER, MOREJON, LOW,1996).

By the end, the plaque index is calculated by using a simple rule of three (proportion): the total number of dental surfaces was 100 (one hundred), as the number of faces with plaque was x. The mathematical expression was:

Subject No. of teeth X 4 – 100

Subject No. surfaces with plaque – x

From this expression, the operation is performed, in which x indicates the percentage of plaque assessed. This percentage was assessed before the product use (T0) and after 7 (Day 7) and 14 (Day 14) days of product use.

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., dark 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 assessment was done by the comparative method of the Vita Classical Guide (APPENDIX 4) before the product use (T0) and after 7 (Day 7) and 14 (Day 14) days of product use.

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.

9.4.1.3. Dental Adverse Reactions

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

9.4.2. Microbiological Collection (TSA)

The samples collected were properly diluted, and the plating was done by pour plate technique. The medium used for growth of the microorganisms was the Tryptic Soy Agar (TSA). The reduction provided by the product was obtained through the comparison of the counting obtained on final with the initial counting.

Following classical microbiology, it was performed a total count of microorganisms, without differentiation of genus and species.

9.4.3. 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 questionnaire (table 3) after 14 days (Day 14) of product use. Subjects answered the self-assessment questionnaire through telephone contact made by a trained technician.

Table 3. Self-Assessment questionnaire: time of evaluation, statement and scale.

Time of evaluation	Statement	Scale
T14	1) The toothbrush is easy to use.	1 – Strongly disagree 2 – Disagree 3 - Neither agree, nor disagree 4 – Agree 5 – Strongly Agree
	2) My teeth look visibly brighter.	
	3) Toothbrush is suitable for my sensitive teeth.	
	4) Teeth are 1-3 shades whiter after 7 days.	
	5) Teeth are 1-3 shades whiter after 14 days.	
	6) Teeth are 4-6 shades whiter after 7 days.	
	7) Teeth are 4-6 shades whiter after 14 days.	
	8) The appearance of my teeth is noticeably whiter.	
	9) I can use this toothbrush with virtually no sensitivity.	
	10) Teeth are significantly whiter.	
	11) Teeth are significantly whiter and brighter.	
	12) I can use this toothbrush without experiencing any pain.	
	13) Visibly removes stains like red wine and coffee from my teeth.	
	14) My teeth feel cleaner than brushing with a manual toothbrush.	
	15) My teeth look cleaner than brushing with a manual toothbrush.	
	16) My breath is fresher.	
	17) I feel more confident smiling after using this toothbrush.	
	18) I found the pressure sensor feature helped me become a better brusher.	
	19) I can use this toothbrush to get to the harder to reach areas of my mouth than brushing with a manual toothbrush.	
	20) My gums are healthier than brushing with a manual toothbrush.	
	21) I am more comfortable showing my teeth in public after using this toothbrush.	

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 4. Detailed statistical analysis

Data Type	Statistical Method	Data Reported	Sample size
Expert clinical grading of tooth color	Descriptive Statistics Wilcoxon signed-rank test	Mean, standard error, confidence interval, standard deviation, median, minimum and maximum Percent improvement on the mean Percent of subjects with reduction p-value (compared to T0)	25
Microbiological collection Dental plaque assessment	Descriptive Statistics Student t test	Mean, standard error, confidence interval, standard deviation, median, minimum and maximum Percent improvement on the mean Percent of subjects with reduction p-value (compared to T0)	
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

It was not possible to get in contact with subject 005 to perform the self-assessment questionnaire through telephone. Therefore, the subject data were not considered in the study.

Subject 007 was instructed on the correct way of using the product at home but used the product only one time on T0 and on days 2, 4 and 6, and on the others days realized the correct use (two times daily), verified through the daily-log of product use completed by the subject. However, this did not interfere with the product efficacy so the subject data were considered in the study.

13.2. Study Population Description and Study Adherence

A total of 30 subjects were included in the study, among them, 25 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 5. 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]**
33	03	00	30	15	15	18	56	36	04	01	25
Subjects									018, 020, 030 and 032	005	

[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 005 was removed from the study for characterizing as protocol deviation as described in item 13.1.

The study achieved its objective to obtain, at its end, a minimum of 25 answers.

Table 6. Frequency and percentage of the population included and Adherence to the study by quotas.

Quotas	
Population Included	**Finishing Population**
15 (50%) male	13 male
15 (50%) female	12 female

13.3. Dental Clinical Assessment

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

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

13.4. Dental Plaque Assessment

13.4.1. Percentage of Surface with Bacterial Plaque

The product promoted a significant reduction in the percentage of the surface with bacterial plaque, after 7 and 14 days of use in relation to time T0 (before product use).

Table 7. Descriptive Statistics and results of comparison

Statistics	T0	Day 7	Day 14	Δ(Day 7 - T0)	Δ(Day 14 - T0)
Mean	**80.2**	**56.3**	**65.0**	**-23.9**	**-15.2**
Standard error	**4.1**	**3.3**	**2.8**	**2.8**	**2.6**
95% CI	[71.8; 88.6]	[49.5; 63.1]	[59.2; 70.8]	[-29.7; -18.1]	[-20.6; -9.8]
Δ(%) improvement on the mean				**29.8**	**19.0**
% of subjects with reduction				**100.0**	**92.0**
P-value				**<0.001***	**<0.001***

*Significant at 5% (Student's t test).

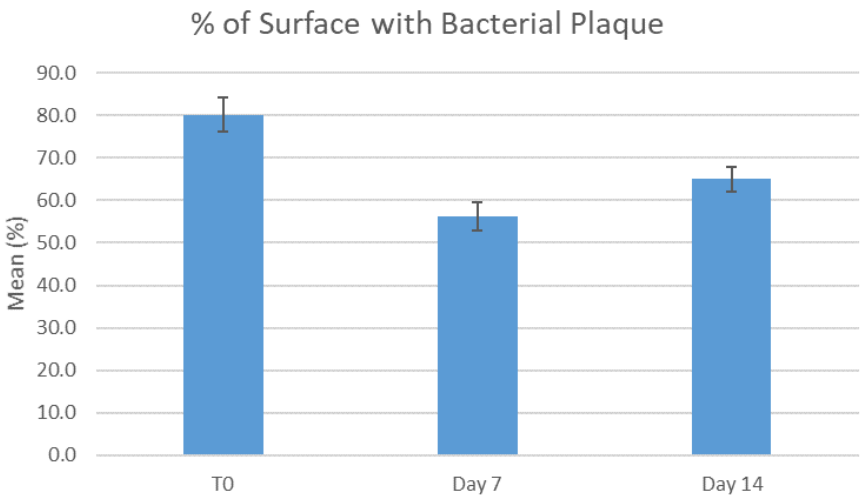

Figure 1 Mean ± standard error of the percentage of surface with plaque by time

13.4.2. Number of Faces with Bacterial Plaque

The product promoted a significant reduction in the number of the faces with bacterial plaque, after 7 and 14 days of use in relation to time T0 (before product use).

Table 8. Descriptive Statistics and results of comparison

Statistics	T0	Day 7	Day 14	Δ(Day 7 - T0)	Δ(Day 14 - T0)
Mean	**90**	**63**	**73**	**-27**	**-17**
Standard error	**5**	**4**	**3**	**3**	**3**
95% CI	[80; 100]	[55; 71]	[67; 79]	[-34; -20]	[-23; -11]
Δ(%) improvement on the mean				**30.0**	**18.9**
% of subjects with reduction				**100.0**	**88.0**
P-value				**<0.001***	**<0.001***

*Significant at 5% (Student's t test).

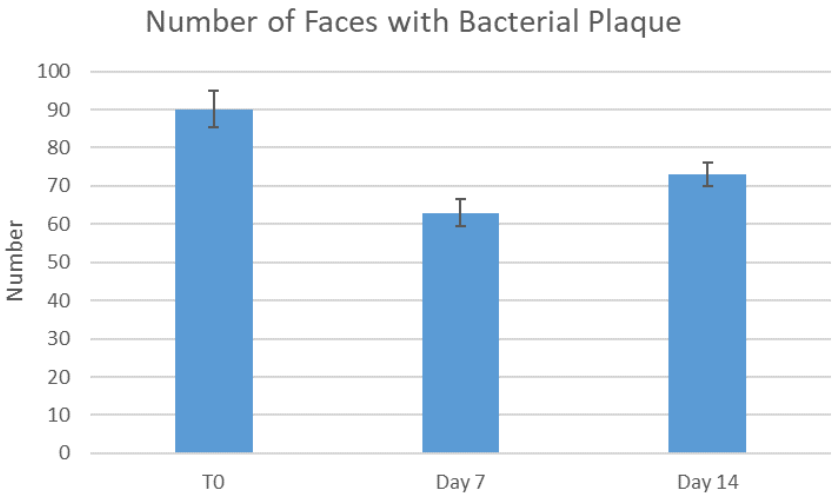

Figure 2 Mean ± standard error of the percentage of number of faces by time

13.5. Expert Clinical Grading of Tooth Color

Four groups of colors can be assigned to subject for the assessment of teeth whitening, as follows:

A: Reddish - Brown

B: Reddish - Yellow

C: Shades of gray

D: Reddish - Gray

Note that the majority of subjects have a tone A followed by a tone B. None of the participants had a tone C or D.

Table 9. Frequency and Percentage

Tone	n	%
A: Reddish - Brown	18	72.0%
B: Reddish - Yellow	7	28.0%
C: Shades of gray	0	0.0%
D: Reddish - Gray	0	0.0%

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. The following table illustrates the results for the average of all evaluated teeth.

The product promoted a significant reduction in the intensity of the color of the teeth, after 7 and 14 days of use in relation to time T0 (before product use).

Table 10. Descriptive Statistics and results of comparison

Statistics	T0	Day 7	Day 14	Δ(Day 7 - T0)	Δ(Day 14 - T0)
Mean	**3.0**	**2.9**	**2.9**	**-0.1**	**-0.1**
Standard error	**0.1**	**0.1**	**0.1**	**0.0**	**0.0**
95% CI	[2.8; 3.2]	[2.7; 3.1]	[2.7; 3.1]	[-0.2; 0]	[-0.2; 0]
Δ(%) improvement on the mean				**3.3**	**3.3**
% of subjects with reduction				**44.0**	**44.0**
P-value				**0.002***	**0.002***

*Significant at 5% (Wilcoxon signed-rank test).

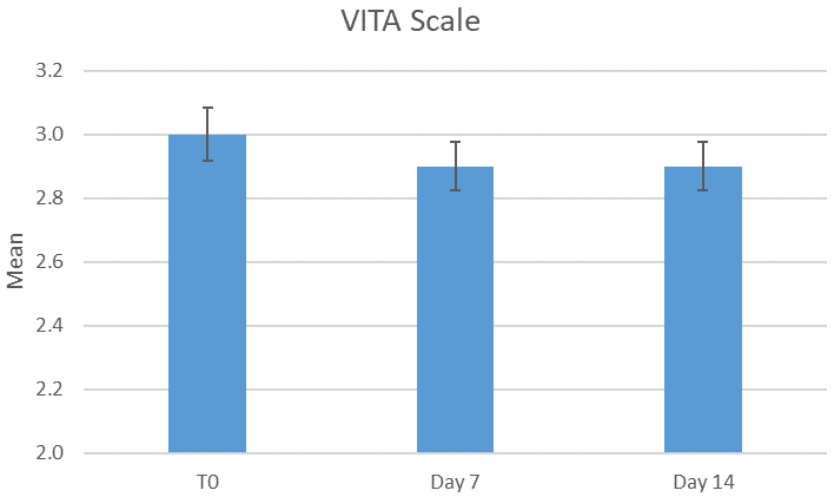

Figure 3 Mean ± standard error for intensity of color by time-point

13.6. Microbiological Collection (TSA)

A significant reduction was observed in the logarithm of the microorganisms count at the time-point Day 7 in relation to the time-point T0.

Table 11. Results observed, descriptive statistics and result of the comparison between T0 and Day 7

Statistics	T0	Day 7	Δ(Day 7 - T0)
Mean	**6.60**	**6.40**	**-0.20**
Standard error	**0.07**	**0.08**	**0.07**
95% CI	[6.5; 6.7]	[6.2; 6.6]	[-0.3; -0.1]
Δ(%) improvement on the mean			**3.0**
% of subjects with reduction			**68.0**
P-value			**0.002**

*Significant at 5% (Student's t test).

13.6.1. Comparison of the decimal reductions

Reduction of 1 log (90%)

The decimal reduction on Day 7 was significantly inferior to 1 log (p-value = 0.002).

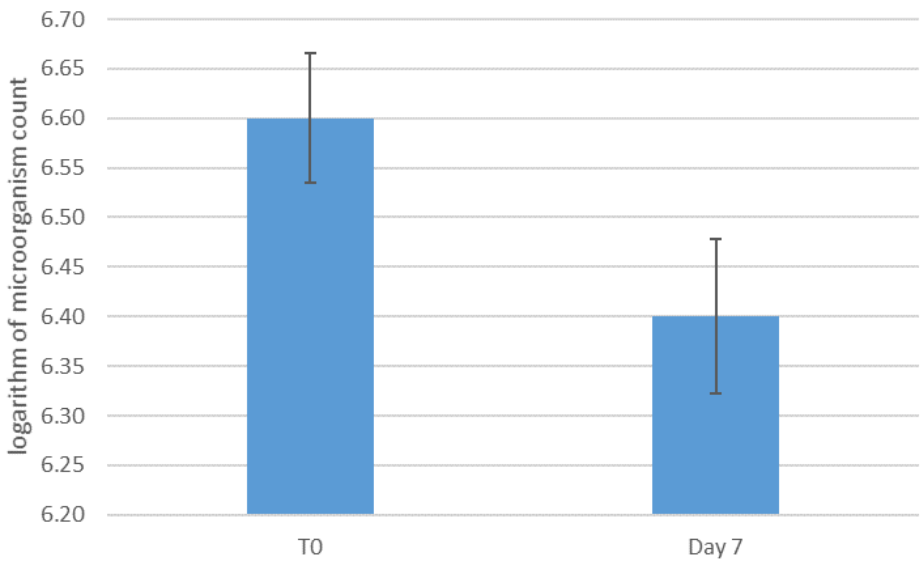

Figure 4 95% confidence interval for the log of the microorganisms count by time-point

13.7. Self-Assessment Performed by the Study Subjects

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

Table 12. Percentage and frequency () of positive answers by statement

Statement	% Positive answers
	Day 14
The toothbrush is easy to use.	100.0% (25)
My teeth look visibly brighter.	88.0% (22)
Toothbrush is suitable for my sensitive teeth.	92.0% (23)
Teeth are 1-3 shades whiter after 7 days.	76.0% (19)
Teeth are 1-3 shades whiter after 14 days	56.0% (14)
Teeth are 4-6 shades whiter after 7 days.	36.0% (9)
Teeth are 4-6 shades whiter after 14 days	32.0% (8)
The appearance of my teeth is noticeably whiter.	80.0% (20)
I can use this toothbrush with virtually no sensitivity.	96.0% (24)
Teeth are significantly whiter.	88.0% (22)
Teeth are significantly whiter and brighter.	84.0% (21)
I can use this toothbrush without experiencing any pain.	96.0% (24)
Visibly removes stains like red wine and coffee from my teeth.	76.0% (19)
My teeth feel cleaner than brushing with a manual toothbrush.	100.0% (25)
My teeth look cleaner than brushing with a manual toothbrush.	100.0% (25)
My breath is fresher.	96.0% (24)
I feel more confident smiling after using this toothbrush.	88.0% (22)
I found the pressure sensor feature helped me become a better brusher.	96.0% (24)
I can use this toothbrush to get to the harder to reach areas of my mouth than brushing with a manual toothbrush.	80.0% (20)
My gums are healthier than brushing with a manual toothbrush.	72.0% (18)
I am more comfortable showing my teeth in public after using this toothbrush.	80.0% (20)

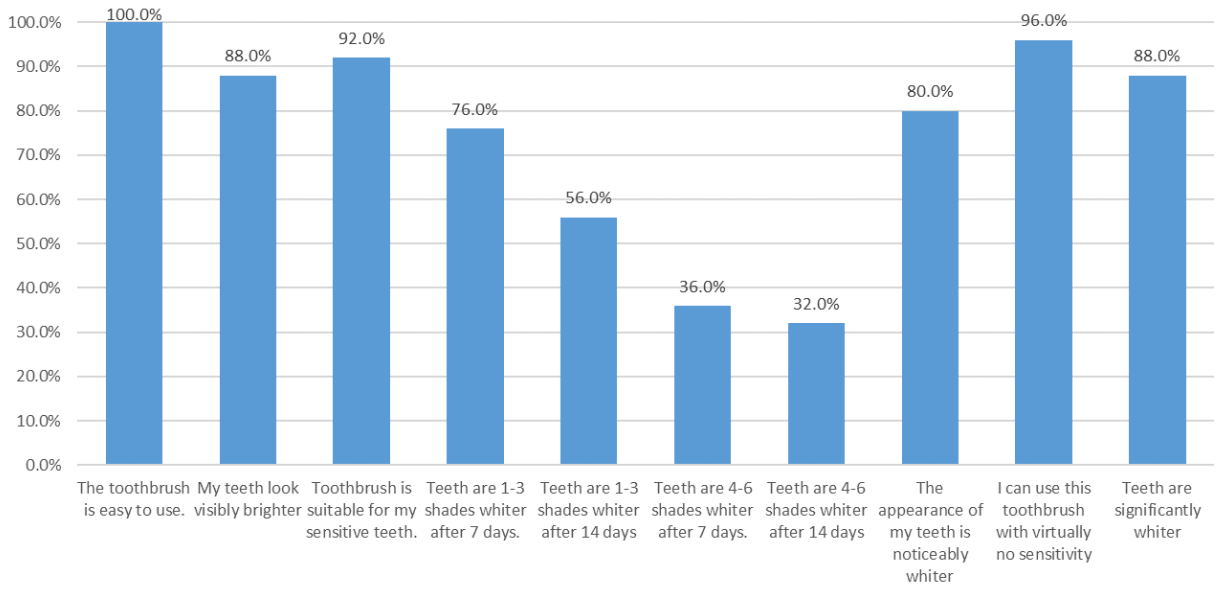

Figure 1. Percentage of positive answers by question

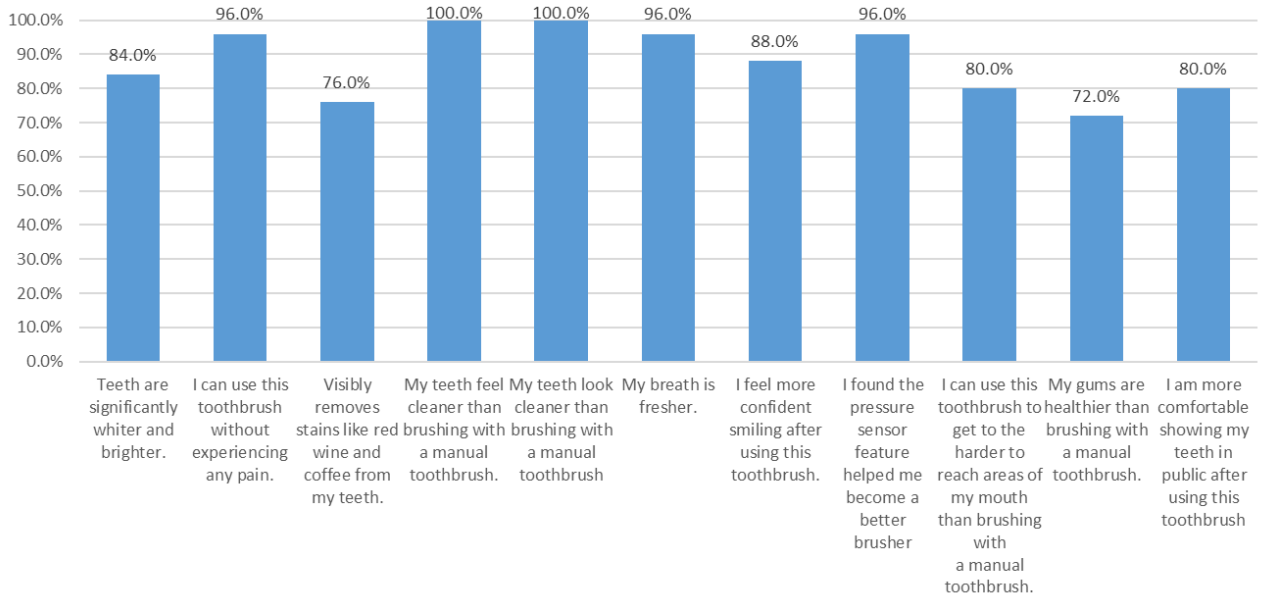

Figure 2. Percentage of positive answers by question

14. CONCLUSION

According to the methodology used to assess the safety and efficacy of the product **Perfect Smile Whitening Brush (Blue LED toothbrush)**, submitted by the company **TH GENESIS**, it could be concluded that:

14.1. Dental Clinical Assessment

During the study, no subjects presented dental clinical signs and/or stated discomfort sensations related to product use. Thus, the investigational product can be considered as safe under the study conditions.

14.2. Dental Plaque Assessment

14.2.1. Percentage of Surface with Bacterial Plaque

The product promoted a reduction in the percentage of the surface with bacterial plaque after seven and fourteen days of use.

14.2.2. Number of Faces with Bacterial Plaque

The product promoted a reduction in the number of the faces with bacterial plaque after seven and fourteen days of use.

14.3. Expert Clinical Grading of Tooth Color

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

14.4. Microbiological Collection (TSA)

A reduction was observed in the logarithm of the microorganisms count after seven days of product use.

14.5. Self-Assessment Performed by the Study Subjects

Statement	% Positive answers
	Day 14
The toothbrush is easy to use.	**100.0%**
My teeth look visibly brighter.	**88.0%**
Toothbrush is suitable for my sensitive teeth.	**92.0%**
Teeth are 1-3 shades whiter after 7 days.	**76.0%**
Teeth are 1-3 shades whiter after 14 days	**56.0%**
Teeth are 4-6 shades whiter after 7 days.	36.0%
Teeth are 4-6 shades whiter after 14 days	32.0%
The appearance of my teeth is noticeably whiter.	**80.0%**
I can use this toothbrush with virtually no sensitivity.	**96.0%**
Teeth are significantly whiter.	**88.0%**
Teeth are significantly whiter and brighter.	**84.0%**
I can use this toothbrush without experiencing any pain.	**96.0%**
Visibly removes stains like red wine and coffee from my teeth.	**76.0%**
My teeth feel cleaner than brushing with a manual toothbrush.	**100.0%**
My teeth look cleaner than brushing with a manual toothbrush.	**100.0%**
My breath is fresher.	**96.0%**
I feel more confident smiling after using this toothbrush.	**88.0%**
I found the pressure sensor feature helped me become a better brusher.	**96.0%**
I can use this toothbrush to get to the harder to reach areas of my mouth than brushing with a manual toothbrush.	**80.0%**
My gums are healthier than brushing with a manual toothbrush.	**72.0%**
I am more comfortable showing my teeth in public after using this toothbrush.	**80.0%**

Bold/Shaded = “passing” claim, >50% of the panel responded favorably

Thus, the following claims can be supported:

- “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 and Self-Assessment;
- “Fast results” supported by Dental Plaque Assessment; Expert Clinical Grading of Tooth Color, Microbiological Collection and Self-Assessment;
- “Quick results” supported by Dental Plaque Assessment; Expert Clinical Grading of Tooth Color, Microbiological Collection and Self-Assessment;
- “Reduction of Plaque” supported by Dental Plaque Assessment;
- “In a clinical study proven to thoroughly Smile Whitening Brush statistically significantly remove plaque along the gum line” supported by Dental Plaque Assessment;
- “Reduction of Plaque on100% of consumers after 7 days” supported by Dental Plaque Assessment;
- “Up to 30% less plaque after 7 days” supported by Dental Plaque Assessment;

- “In a clinical study the Perfect Smile Whitening Brush statistically significantly reduced plaque, giving you healthier gums and whiter teeth.” supported by Dental Plaque Assessment;
- “The Perfect Smile Whitening Brush doesn't damage your gums” supported by Dental Clinical Assessment and Self-Assessment;
- “Teeth Whitening” supported by Expert Clinical Grading of Tooth Color and Self-Assessment;
- “Helps you break down plaque build-up” supported by Dental Plaque Assessment
- “Up to 3 shades whiter after 7 days”; supported by Self-Assessment.
- “100% of consumers stated that teeth feel cleaner than brushing with a manual toothbrush” supported by Self-Assessment;
- “100% of consumers stated that teeth look cleaner than brushing with a manual toothbrush”.
- “In a clinical study the Perfect Smile Whitening Brush was found to cleaner better than a manual toothbrush for 100% of consumers” supported by Self-Assessment;
- “The Perfect Smile Whitening Brush provides a superior clean vs. a regular manual toothbrush for 100% of consumers”; supported by Self-Assessment;
- “Anti-Microbial” supported by Microbiological Collection;
- “Anti-Bacterial” supported by Microbiological Collection;
- “Reduces microbes on the oral cavity” supported by Microbiological Collection;
- “Reduces bacteria on oral cavity” supported by Microbiological Collection;
- “Whitens teeth”. supported by Expert Clinical Grading of Tooth Color and Self-Assessment;
- “Whiter and Brighter in only 7 days” supported by Expert Clinical Grading of Tooth Color and Self-Assessment;
- “Visibly whiter teeth in only 7 days” supported by Expert Clinical Grading of Tooth Color and Self-Assessment.
- “Reduces stains like red wine and coffee” supported by Self-Assessment.

Gabrielli Brianezi
Investigator in Charge
09/28/2021

José Marcos M. Vendramini
Statistician in Charge
09/28/2021

Lilian Pessoto Rosa
Dentist (CRO 76471)
09/28/2021

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APPENDIX 1 INFORMED CONSENT FORM

Sub No.: _____

INFORMED CONSENT FORM

STUDY PROJECT TITLE: EFFICACY ASSESSMENT OF A PRODUCT THROUGH SELF-ASSESSMENTS COMPLETED BY STUDY SUBJECTS, AND DENTAL CLINICAL EFFICACY ASSESSMENTS, UNDER NORMAL USE CONDITIONS

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 attentively 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 the study is to verify the efficacy after the use of a **TOOTHBRUSH (*094144-01*),** by confirming its efficacy in reducing dental plaque, when used under normal use conditions, followed-up by a dentist, and to assess the product efficacy based on your perception, through a questionnaire.

Dental plaque is a colorless and sticky film formed on the teeth surface. With the reduction of dental plaque, it is possible to prevent cavities from forming.

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 30 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.

ALLERGISA

ALLERGISA

INFORMED CONSENT FORM

What will I have to do?

Your participation in the study will last 14 days. During this period, there will be 03 visits to the Institute.

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. In this dental assessment, the dentist will be wearing gloves, facial mask, 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 come on 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, during the return visit, at the end of the study, and you will be supervised throughout the study.
- The assessments will occur individually (one subject at a time).
- A microbiological collection will be done for the total counting of microorganisms in your oral cavity (teeth, tongue, and gums) with the aid of a swab. This procedure will be conducted before test product use and during the study return visit after 7 days of test product use. This procedure is painless.

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Sub No.: _____

INFORMED CONSENT FORM

• You will receive the test product, a daily-log, and the questionnaires of the study. You will be instructed to use the product in accordance with the instructions for use described in your daily-log under normal use conditions for 7 days, and to complete the questionnaires 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.

• After 7 days of product use, you will return the daily-log and the test product.

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 70% alcohol, 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 Test-product, daily-log, and questionnaire delivery	T0	01 hour
Answer to questionnaires	At Home	-
Dental Assessment Test product and daily-log return	T7	01 hour
Dental Assessment Return of 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 us 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 the dentist through a telephone call or video conference. During the teleconsultation, you will be ensured of the confidentiality of the dental attention, that is, that it was done in a place where only the dentist 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, concerning 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.
- Do not apply any product of oral use to the test site, which might interfere with the study assessment.
- Do not change the cosmetic habits, including body and oral hygiene.
- Do not use mouth products with lightening action or for sensitive teeth during the study.
- Reduce the ingestion of the following foods: coffee, black tea, chocolate, cola sodas, red wine or grape juice, acai, tomato sauce, isotonic drinks with strong colors, candy, and gums with pigments.

• 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 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 or biological material) 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 a proven reduction of the dental plaque for prevention of cavities and with proven self-perceived efficacy of the product. 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 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 dentist 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.

ALLERGISA

ALLERGISA

Sub No.: _____

INFORMED CONSENT FORM

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, 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.

INFORMED CONSENT FORM

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 ASSESSMENT OF A PRODUCT THROUGH SELF-ASSESSMENTS COMPLETED BY STUDY SUBJECTS, AND DENTAL CLINICAL EFFICACY ASSESSMENTS, UNDER NORMAL USE CONDITIONS

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

I am aware that the 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
001	33	M	I
002	34	F	I
003	40	F	I
004	53	F	I
005	41	F	I
006	40	F	I
007	34	M	I
008	38	F	I
009	40	F	I
010	53	F	NI
011	31	M	NI
012	20	F	I
013	53	F	NI
014	33	M	I
015	28	F	I
016	38	F	I
017	42	F	I
018	27	F	I
019	53	F	I
020	23	F	I
021	38	F	I
022	53	M	I
023	19	M	I
024	46	M	I
025	24	M	I
026	52	M	I
027	35	M	I
028	56	M	I
029	25	M	I
030	18	M	I
031	34	M	I
032	33	M	I
033	42	M	I

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

Percentage of Surface with Bacterial Plaque

Table 13. Raw data and descriptive statistics – % of Surface with Bacterial Plaque

Subject	T0	Day 7	Day 14	Δ(Day 7 - T0)	Δ(Day 14 - T0)
001	37.5	25.0	33.3	-12.5	-4.2
002	100.0	81.0	80.4	-19.0	-19.6
003	78.0	75.0	75.0	-3.0	-3.0
004	92.9	83.9	86.6	-8.9	-6.3
006	79.2	67.7	72.9	-11.5	-6.3
007	100.0	92.9	96.4	-7.1	-3.6
008	80.6	61.1	66.7	-19.4	-13.9
009	75.0	60.7	69.6	-14.3	-5.4
012	100.0	57.5	61.7	-42.5	-38.3
014	75.0	51.7	60.3	-23.3	-14.7
015	100.0	61.7	79.2	-38.3	-20.8
016	71.0	54.0	60.5	-16.9	-10.5
017	75.0	59.8	67.0	-15.2	-8.0
019	79.2	54.2	63.3	-25.0	-15.8
021	100.0	56.5	63.7	-43.5	-36.3
022	100.0	58.3	61.7	-41.7	-38.3
023	75.0	50.0	53.6	-25.0	-21.4
024	77.2	50.0	67.4	-27.2	-9.8
025	100.0	51.7	72.4	-48.3	-27.6
026	100.0	58.3	68.8	-41.7	-31.3
027	45.7	31.9	45.7	-13.8	0.0
028	100.0	60.6	71.2	-39.4	-28.8
029	39.3	32.1	51.8	-7.1	12.5
031	79.8	40.4	59.6	-39.4	-20.2
033	43.8	31.3	37.5	-12.5	-6.3
Mean	**80.2**	**56.3**	**65.0**	**-23.9**	**-15.2**
Standard error	**4.1**	**3.3**	**2.8**	**2.8**	**2.6**
95% CI	[71.8; 88.6]	[49.5; 63.1]	[59.2; 70.8]	[-29.7; -18.1]	[-20.6; -9.8]
Standard deviation	**20.3**	**16.4**	**14.0**	**13.9**	**13.0**
Median	79.2	57.5	66.7	-19.4	-13.9
Minimum	37.5	25.0	33.3	-48.3	-38.3
Maximum	100.0	92.9	96.4	-3.0	12.5

Number of Faces with Bacterial Plaque

Table 14. Raw data and descriptive statistics – Number of faces with bacterial plaque

Subject	T0	Day 7	Day 14	Δ(Day 7 - T0)	Δ(Day 14 - T0)
001	45	30	40	-15	-5
002	116	94	90	-22	-26
003	78	75	78	-3	0
004	104	94	97	-10	-7
006	76	65	70	-11	-6
007	112	104	108	-8	-4
008	87	66	72	-21	-15
009	84	68	78	-16	-6
012	120	69	74	-51	-46
014	87	60	70	-27	-17
015	120	74	95	-46	-25
016	88	67	75	-21	-13
017	84	67	75	-17	-9
019	95	65	76	-30	-19
021	124	70	79	-54	-45
022	120	70	74	-50	-46
023	84	56	60	-28	-24
024	71	46	62	-25	-9
025	116	60	84	-56	-32
026	96	56	66	-40	-30
027	53	37	53	-16	0
028	104	63	74	-41	-30
029	44	36	58	-8	14
031	83	42	62	-41	-21
033	56	40	48	-16	-8
Mean	**90**	**63**	**73**	**-27**	**-17**
Standard error	**5**	**4**	**3**	**3**	**3**
95% CI	[80; 100]	[55; 71]	[67; 79]	[-34; -20]	[-23; -11]
Standard deviation	**24**	**18**	**15**	**16**	**15**
Median	87	65	74	-22	-15
Minimum	44	30	40	-56	-46
Maximum	124	104	108	-3	14

Expert Clinical Grading of Tooth Color

Table 15. Raw data and descriptive statistics – Vita Scale

Subject	T0	Day 7	Day 14	Δ(Day 7 - T0)	Δ(Day 14 - T0)	Color
001	3.2	3.2	3.2	0.0	0.0	A
002	3.3	3.2	3.2	-0.1	-0.1	A
003	3.2	3.2	3.2	0.0	0.0	A
004	4.0	3.7	3.7	-0.3	-0.3	B
006	3.2	3.0	3.0	-0.2	-0.2	A
007	3.0	3.0	3.0	0.0	0.0	B
008	3.2	3.1	3.1	-0.1	-0.1	A
009	3.5	3.0	3.0	-0.5	-0.5	A
012	3.0	3.0	3.0	0.0	0.0	A
014	3.2	3.0	3.0	-0.2	-0.2	A
015	3.0	3.0	3.0	0.0	0.0	A
016	3.0	3.0	3.0	0.0	0.0	A
017	3.0	2.7	2.7	-0.3	-0.3	B
019	3.2	3.0	3.0	-0.2	-0.2	A
021	3.0	3.0	3.0	0.0	0.0	A
022	3.2	3.0	3.0	-0.2	-0.2	A
023	3.0	3.0	3.0	0.0	0.0	A
024	3.2	3.2	3.2	0.0	0.0	A
025	3.2	3.2	3.2	0.0	0.0	A
026	3.3	3.0	3.0	-0.3	-0.3	A
027	2.3	2.0	2.0	-0.3	-0.3	B
028	3.0	3.0	3.0	0.0	0.0	B
029	2.0	2.0	2.0	0.0	0.0	B
031	3.0	3.0	3.0	0.0	0.0	B
033	2.0	2.0	2.0	0.0	0.0	A
Mean	**3.0**	**2.9**	**2.9**	**-0.1**	**-0.1**	**-**
Standard error	**0.1**	**0.1**	**0.1**	**0.0**	**0.0**	**-**
95% CI	[2.8; 3.2]	[2.7; 3.1]	[2.7; 3.1]	[-0.2; 0]	[-0.2; 0]	-
Standard deviation	**0.4**	**0.4**	**0.4**	**0.1**	**0.1**	**-**
Median	3.2	3.0	3.0	0.0	0.0	-
Minimum	2.0	2.0	2.0	-0.5	-0.5	-
Maximum	4.0	3.7	3.7	0.0	0.0	-

Microbiological Collection (TSA)

Table 16. Results observed, descriptive statistics, and result of the comparison between T0 and T7

Subject	T0	Day 7	Δ(T7 - T0)
001	7,00	6,17	-0,83
002	7,00	7,00	0,00
003	7,00	6,49	-0,51
004	6,49	6,54	0,05
006	6,59	6,56	-0,03
007	7,00	6,31	-0,69
008	6,51	5,92	-0,59
009	6,61	6,50	-0,11
012	6,37	5,85	-0,52
014	6,49	6,21	-0,28
015	6,73	6,70	-0,03
016	7,00	7,00	0,00
017	6,35	6,37	0,02
019	6,34	6,44	0,10
021	6,62	6,17	-0,45
022	6,67	6,71	0,04
023	7,00	6,78	-0,22
024	7,00	6,57	-0,43
025	6,03	5,30	-0,73
026	6,63	6,61	-0,02
027	6,65	6,54	-0,11
028	6,74	6,14	-0,60
029	5,75	6,05	0,30
031	6,41	7,00	0,59
033	7,00	6,53	-0,47
Mean	**6,60**	**6,40**	**-0,20**
Standard error	**0,07**	**0,08**	**0,07**
95% CI	[6.5; 6.7]	[6.2; 6.6]	[-0.3; -0.1]
Standard deviation	**0,33**	**0,39**	**0,35**
Median	6,63	6,50	-0,11
Minimum	5,75	5,30	-0,83
Maximum	7,00	7,00	0,59

Self-Assessment Performed by the Study Subjects

Table 17. Percentage and frequency () by statement – Day 14

Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
The toothbrush is easy to use.	4% (1)	96% (24)	0% (0)	0% (0)	0% (0)
My teeth look visibly brighter	4% (1)	84% (21)	4% (1)	8% (2)	0% (0)
Toothbrush is suitable for my sensitive teeth.	0% (0)	92% (23)	8% (2)	0% (0)	0% (0)
Teeth are 1-3 shades whiter after 7 days.	0% (0)	76% (19)	20% (5)	4% (1)	0% (0)
Teeth are 1-3 shades whiter after 14 days	8% (2)	48% (12)	32% (8)	12% (3)	0% (0)
Teeth are 4-6 shades whiter after 7 days.	4% (1)	32% (8)	32% (8)	32% (8)	0% (0)
Teeth are 4-6 shades whiter after 14 days	0% (0)	32% (8)	40% (10)	28% (7)	0% (0)
The appearance of my teeth is noticeably whiter	0% (0)	80% (20)	16% (4)	4% (1)	0% (0)
I can use this toothbrush with virtually no sensitivity	0% (0)	96% (24)	4% (1)	0% (0)	0% (0)
Teeth are significantly whiter	0% (0)	88% (22)	8% (2)	4% (1)	0% (0)
Teeth are significantly whiter and brighter.	0% (0)	84% (21)	16% (4)	0% (0)	0% (0)
I can use this toothbrush without experiencing any pain.	0% (0)	96% (24)	4% (1)	0% (0)	0% (0)
Visibly removes stains like red wine and coffee from my teeth.	4% (1)	72% (18)	16% (4)	8% (2)	0% (0)
My teeth feel cleaner than brushing with a manual toothbrush.	8% (2)	92% (23)	0% (0)	0% (0)	0% (0)
My teeth look cleaner than brushing with a manual toothbrush	4% (1)	96% (24)	0% (0)	0% (0)	0% (0)
My breath is fresher.	4% (1)	92% (23)	4% (1)	0% (0)	0% (0)
I feel more confident smiling after using this toothbrush.	4% (1)	84% (21)	12% (3)	0% (0)	0% (0)
I found the pressure sensor feature helped me become a better brusher	8% (2)	88% (22)	4% (1)	0% (0)	0% (0)
I can use this toothbrush to get to the harder to reach areas of my mouth than brushing with a manual toothbrush.	4% (1)	76% (19)	20% (5)	0% (0)	0% (0)
My gums are healthier than brushing with a manual toothbrush.	0% (0)	72% (18)	24% (6)	4% (1)	0% (0)
I am more comfortable showing my teeth in public after using this toothbrush	0% (0)	80% (20)	20% (5)	0% (0)	0% (0)

APPENDIX 4 EXPERT CLINICAL GRADING OF TOOTH COLOR - VITA CLASSICAL GUIDE

Figure 3. The Vita Classical Guide used for grading tooth color

APPENDIX 5 INVESTIGATIONAL PRODUCT INFORMATION

“FORMULA NOT SUBMITTED”