PROTOCOL TITLE: EN18-0688-01 A DOUBLE-BLIND, RANDOMIZED CLINICAL STUDY TO EVALUATE THE EFFICACY SUPERIORITY IN THE TREATMENT OF ACNE FROM THE COMBINATION OF ORAL PROBIOTICS TO THE TOPICAL USE OF THE FIXED COMBINATION OF BENZOYL PEROXIDE AND ADAPALENE VERSUS PLACEBO AND FIXED COMBINATION.

PARTICIPANT'S INITIALS: _____
(04 first letters of the 1st name; 1st letter of last name)

Participant No.: _____
(Screening)

You are being invited to participate in a research intended to evaluate the effect of an oral acne treatment product in combination with another topical product for 180 days. To perform this study, 400 participants of both genders, aged between 12 and 35 years, who have mild or moderate acne on the face will be invited.
You may receive the following treatment options from your doctor:
Investigational product (oral use) in combination with a topical product (applied to the skin) or a **Placebo product for oral use (no pharmacological action) in combination with a topical product (applied to the skin).** The treatment definition will be done through randomization, where you and the professionals involved in the research will not know which of the products will be given to you.
After you agree to participate in this study, the Informed Consent Form must be read and properly understood. Only then, with your agreement, you will sign it and, later, be evaluated by a doctor.

Visit 01 (D0)
After agreeing to participate in the study, you will receive a copy of this Informed Consent Form, if you are a women, you will be instructed to carry out a pregnancy test before starting the study procedures, if the negative result is confirmed, you will undergo a medical evaluation to check if you are able to participate in the research according to the study criteria and later be evaluated on your skin conditions. Men will be referred directly for clinical evaluation after study consent.
After medical evaluation, you will be sent to the instrumental measurement room, where photos of your face will be taken (front and sides) with the Visia equipment (Canfield), then you will answer a subjective questionnaire about your skin and receive treatment products and sunscreen with instructions for use and next study visits. In addition, you will also receive a diary to fill in according to the use of the products received.

Visit 02 (D30), Visit 03 (D60)
After 30, 60 days of treatment, you will return to the Research Site to carry out new clinical and subjective assessments and photographic record of your face, under the same conditions of visit 01 (D0). You must bring treatment products, sunscreen and the completed usage diary. The research assistant will check the products and the diary, confirming the correct use, within the expected frequency of use, new products will be dispensed with a new diary to be filled out.

Visit 04 (D90)
After 90 days of treatment, you will return to the Research Site to carry out further clinical and subjective assessments. You must bring treatment products, sunscreen and the completed usage diary. The research assistant will check the products and the diary, confirming the correct use, within the expected frequency of use, you will receive only one of the treatment products (oral use) and sunscreen to continue the study and the use diary to be filled out.

Visit 05 (D120), Visit 06 (D150)
After 120 and 150 days of treatment, you will return to the Research Site to carry out further clinical and subjective assessments. You must bring the treatment product, sunscreen and the completed use diary.
The research assistant will check the product and the diary, confirming the correct use, within the expected frequency of use, new products will be dispensed with a new diary to be filled out.

Visit 07 (D180)
After 180 days of treatment, you will return to the Research Site to carry out new clinical and subjective assessments and photographic records of your face, under the same conditions as for visit 01 (D0). You must bring treatment products, sunscreen and the completed use diary. The research assistant will check the products and the diary, confirm correct use, within the expected frequency of use, and the study will be terminated and you will be dismissed.

If important information about the study emerges, you will be notified in advance and you may withdraw your participation from the study at any time, communicating your withdrawal to the Institute, without this having any negative consequences for you.

All substances that make up the products are known and considered safe for this study purpose.

The products used in this study may rarely cause some adverse reactions, such as: itching, peeling, redness, dryness, burning, among others.

In addition to the aforementioned effects, the administration of any drug can cause unpredictable reactions. However, in studies with the drugs, the emergence of adverse events with the initial dose administered has not been observed.

Any adverse event that you experience will be duly monitored by the research site team. And if, for reasons arising from this study, you need medical assistance, hospitalization, clinical examinations, and other treatments, all expenses arising from these procedures will be paid by the sponsoring company, if it is proven that it was due to the study product.

If, due to any reason arising from this study, you need medical assistance or clarification, please contact the researcher physician in charge Dr. Sérgio Schalka or his medical team at MEDCIN: Rua Atílio Delanina, 178. Vila Campesina. Phone: (0XX11) 3654-3849 from 8:00 am to 6:00 pm. Outside these hours, call the 24-hour hotline (0xx11) 9867-2768. If you have any questions, doubts, clarifications or complaints about the ethical aspects of this research, such as, for example, if the study is safe or if it will cause any harm, you can contact: Research Ethics Committee of Universidade São Francisco, Av. São Francisco de Assis, 218 – Jardim São José, telephone 011-24548981.

All your information will be treated confidentially, that is, it will not be disclosed, and only people directly linked to this study (Monitor, Auditor, Research Ethics Committee, Regulatory Authorities and Medcin) will have access to your information. If the study results are published, your identity will remain confidential, that is, your name and age will not be disclosed.

_____	_____	_____
Participant's Initials/Signature	Research Assistant's Initials/Signature	Investigating Physician's/Co-Investigator's Initials/Signatur

You will not receive any personal benefit from taking part of this study; however treatment with the products may benefit you by improving the condition of your skin in relation to the signs and symptoms of acne.

You will also be helping a product to be placed on the market safely, reducing the chance that other people will have some kind of unknown reaction using the product. For your voluntary act, you will receive reimbursement for your expenses (transportation and food) through a voucher for use in an accredited network.

Instructions during use:
Instructions for use:
TABLETS: Take 01 green tablet and 01 white tablet a day.

GEL: Apply to acne-affected areas once a day at night on clean, dry skin. A thin layer of gel should be applied with the fingertips, avoiding contact with the eyes, nostrils and lips.

SUNSCREEN SPF50: Apply before each sun exposure. Daily use. Reapply whenever necessary.
- Keep the products tightly closed;
- Keep the products out of the reach of children;
- If any intercurrence occurs, talk to the Medcin's medical team;

During the study period it is important to:
- Communicate to the doctor any use of drug or any other cosmetic product;
- Avoid changing hygiene products. Ex.: Moisturizers, soaps, makeup, etc.;
- Do not perform any type of dermatological procedure (peeling, laser or applications and fillers);
- You must attend on the agreed date;
- The products should only be used during the study period, only in the weeks specified in the instructions for use.

The investigating physician is committed to comply with items IV3 of Res. 466/12, regarding the guidelines and regulatory standards for research involving human beings.

After being clarified by the investigator and having understood what was explained to me, I

_____
(participant's full name)

declare that I agree to participate in this research protocol, and that I am receiving a copy of the Informed Consent Form and the instructions for use of the study product, and I also declare that I am aware that this study was approved by the Ethics Committee and that my expenses with transportation and food will be reimbursed.

_____ _____
Participant's Name Digital (if required)

_____ _____/_____/___
Participant's Signature Date

_____ _____ _____/_____/____
Research Assistant's Name Signature Date

_____ _____/_____/____
Stamp and Initials of the Investigating Physician/Co-investigator Date

NOTE: A copy of this consent form was given to the participant for instructions during the study period.