INFORMATION SHEET

CLINICAL AND INSTRUMENTAL EVALUATION OF BIO-REVITALIZING EFFECT ON FACE WITH FOLIAGE HYDROFIL MEDICAL DEVICE

N° subject:	_____
Center:	**Poliambulatorio di Medicina Estetica della Casa della Salute, Largo XII Ottobre 62**
City:	**Genova**
Principal Investigator:	**Dott.ssa Tiziana Lazzari**
Phone number:	**+ 39 010 8078631**

Dear Sir/Madam,

You have been invited to take part in a clinical investigation or "clinical study" on bio-revitalizing skin treatment with the already commercially available Foliage Hydrofil medical device. The Promoter of the clinical study is Phitogen Holding S.p.A., Via Valtellina, 19/21/23 - 63074 San Benedetto del Tronto (AP).

Before deciding whether or not to participate in the clinical investigation, it is important for you to understand why the research is being performed, the possible risks and benefits, and all that this participation entails. Therefore, please read the following information carefully and discuss it, if you wish, with the Physician in charge of the study, your primary care physician, or relatives, friends, or anyone you deem appropriate. In particular, if there is anything that is unclear or if you would like more information, please ask for clarification. Please take the time to decide whether or not you wish to take part in this study. We realize that you may have questions about it and hope that these pages can answer most of them.

READ CAREFULLY

1. What is this clinical investigation?

Skin aging is a completely normal and physiological process, which the skin undergoes from the age of 25-30 years. The natural causes of skin aging are time and genetic predisposition and, especially for women, hormonal changes, but also external, environmental (pollution), lifestyle (sun exposure, cigarette smoking, stress) and diet (diets low in fruits and vegetables) factors.
There are several remedies for skin aging, and in recent years treatments have been developed that involve minimally invasive techniques specifically designed to treat volume loss, wrinkles, and skin damage.

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Among the treatments available today is "bio-revitalization," which is a process that triggers the skin's natural collagen production and cellular rejuvenation through the injection of serums containing various substances, including hyaluronic acid. Hyaluronic acid is a natural molecule found in skin, joints, cartilage and other tissues, providing natural lubrication. This substance is hydrophilic, meaning it absorbs water. As we age, we have less naturally produced hyaluronic acid in our tissues, and skin dehydration becomes a telltale sign of aging. Because hyaluronic acid possesses great moisturizing power, it is widely used in bio-revitalization treatments. Its use results in supple, younger-looking skin with reduced wrinkles and improved elasticity.

Bio-revitalization procedures involve intradermal micro-injections of natural hyaluronic acid, performed at body areas with skin imperfections.

The areas that are most frequently treated are the face, neck and décolletage area and the back of the hands.

Hyaluronic acid is the main ingredient of the Foliage Hydrofil medical device, which is used in this clinical study.

The purpose of this study is to confirm the clinical performance and safety of the Foliage Hydrofil medical device in bio-revitalizing facial treatment.

2. What does this clinical investigation aim to demonstrate and what is the proposed treatment?

The objective of this clinical investigation is to evaluate and confirm the clinical performance and safety of Foliage Hydrofil in bio-revitalizing facial treatment.

For this purpose, No. 24 adults (males and females) who wish to undergo bio-revitalizing treatment will be enrolled and treated with three injection sessions with Foliage Hydrofil, 3 weeks apart. All subjects participating in this study will receive the same treatment.

3. Is my participation in this clinical investigation voluntary?

Yes, only you can decide whether or not to take part in this clinical investigation. If you decide to take part, you will be asked to sign and date the Informed Consent and Manifestation of Consent to the Processing of Personal Data. Also, again if you decide to participate, you will be free to discontinue your participation in the study at any time and without explanation. This decision will not alter the standard of care you will receive.

4. Is this medical device safe?

Foliage Hydrofil belongs to a class of so-called "minimally invasive" treatments used to maintain a youthful appearance. In addition, Foliage Hydrofil is a product that has already been on the market for some years.

The product will be injected through micro-injections into the dermis. The injections, even if done with micro-needles, could generate some risks and a certain level of discomfort. In order to avoid

risks, the physician will duly disinfect the injection sites before treatment. If necessary, anesthetic cream may also be used before the injections.

Following the administration of Foliage Hydrofil, you may experience soreness, redness, swelling, and minor bruising in the treated areas, all of which are generally mild and resolve in a short time. In such cases, the physician following you in the office will suggest the appropriate treatment to manage any of these side effects.

Other side effects, including serious (severe) ones, may, however, appear that we do not yet know about. Therefore, please notify the study physician immediately of any side effects that may occur.

Finally, there are no invasive tests or examinations in this study that may cause pain or discomfort.

5. What health benefits can I expect from participating in this clinical investigation?

By participating in this clinical investigation, we hope that you will experience skin improvement in the treated areas, with a rejuvenating effect.

Your participation in this study may also help us to improve our knowledge of the Foliage Hydrofil product and bio-revitalization techniques.

We also specify that for your participation in this clinical investigation you will not receive any compensation or reimbursement of expenses

6. Am I the only subject in this clinical investigation?

No, a total of about 24 adult subjects (males and females) who wish to receive bio-revitalization treatment at the facial level will be included.

7. Are there alternative treatments to the one proposed in this study?

There are several treatments to improve the appearance of the skin. The Physician following you in the study will explain the possible treatments as an alternative to this one we are proposing. You are free to decide not to participate in the proposed study, and refusal to participate will in no way compromise the treatment of your condition by the Physician following you in the study who will inform you about alternative treatments to their potential benefits and risks. Should you decide not to participate in the study, your attending Physician will inform you of the treatments that he/she considers most suitable for you and their potential risks and benefits.

8. How long will the study last and what should I do?

The study will last approximately 14 weeks (3 ½ months) which will include 4 visits, with the first three visits in which the treatment will be carried out, 3 weeks apart, and a final visit only at approximately 2 months after the last treatment.

First, after you have received all the necessary instructions for correct and complete information, if you agree to participate in the study, you will be asked to sign the Information and Manifestation of

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Consent to the Processing of Personal Data and the Informed Consent of which you will also receive a copy signed by the Physician following you in the study.

STUDY PROCEDURES

The following table outlines the main activities that will be carried out during the 4 visits.

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Procedure	**Procedure details**	**Visit 1** **1° treatment**	**Visit 2** **2° treatment**	**Visit 3** **3° treatment**	**Visit 4** **Final visit**
		DAY 1	**DAY 21 (±4)**	**DAY 42 (±4)**	**DAY 98 (±7)**
Informed consento	Your attending Physician in the Practice will explain the investigation to you in detail. At the end of the information procedure, you will be asked to sign and date the Consent Statement	√			
Collection of Data and Demographic Information	You will be asked to provide your demographic information (e.g., your date of birth)	√			
Assessment of Medical and Surgical History	You will be asked to report your previous and current illnesses and/or surgeries and/or any recent medical procedures	√			
Control of Suitability for Investigation	The Study Physician will ascertain your eligibility to participate in the Clinical Study	√			
Physical Examination	The Study Physician will assess your general health by performing a complete physical examination.	√	√	√	√
Pregnancy Test	If you are a woman of childbearing age, a urine pregnancy test will be performed.	√			
Treatment	The Study Physician will perform the micro-injections, in the agreed areas.	√	√	√	

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Photographs and corneometer analysis of treated areas.	The physician attending you in the office will take photographs of the areas to be treated/treated and perform a skin examination with a special instrument to assess the degree of hydration of the skin (a probe will be passed over the affected areas).	√	√	√	√
Assessment of skin characteristics (texture, color, tone, etc.)	The Physician following you in the practice will assess your skin characteristics in the areas to be treated/treated, prior to the injections.	√	√	√	√
Assessment of cosmetic improvement PAIS - GAIS	The Physician following you in the office will ask you to fill out a simple questionnaire (PAIS) for the evaluation of the aesthetic improvement you perceive and in turn will fill out one (GAIS) quite similar, giving their opinion.		√	√	√
Overall satisfaction questionnaire	The attending physician in the study will ask you to fill out a simple questionnaire assessing your satisfaction with the study product.				√
Assessment of Adverse Events and Concomitant Therapies	You should report any adverse events that have occurred to your Study Physician and you should report to the Study Physician any changes in the therapies you are taking.	√	√	√	√

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It is important that you adhere to the cadence of visits scheduled by the study.

We remind you that:

- **- throughout the duration of the study You shall not perform tissue augmentation treatments with non-permanent fillers nor botulinum toxin treatments, aesthetic surgical treatments, laser treatments, mesotherapy or any form of peeling of the face, neck or décolletage. In addition, she will not have to use injectable revitalizing preparations, retinoic acid products and permanent filler treatments. Finally, she should not expose herself to the sun or tanning booths or UV sources (if sun exposure cannot be avoided, always use sunscreen with SPF 50+ filter to protect the treated areas). You will also need to avoid exposure of the treated area to intense cold.**
- **- it is very important that you do not take any medication without informing the Physician following you in the office, especially if it is chemotherapy, cortisone or immunosuppressive drugs, thrombolytics or anticoagulants or antiplatelet drugs.**
- **- In the vicinity of treatment, it is advisable that you avoid taking drugs that affect blood flui¬dity such as aspirin, F.A.N.S., Vitamin E;**
- **- pregnant or breastfeeding women cannot participate in the study, therefore, we urge you to adopt proven effective contraceptive methods (e.g., oral contraceptives, condom, mechanical methods) or maintain complete abstinence, for the duration of the study, choosing what you feel best suits your personal, ethical or religious beliefs. If You should initiate a pregnancy during this study, You should immediately notify the Physician following You in the study who will indicate the best treatment for Your medical condition and the safety of the unborn child.**

9. Can I change my mind after I agree to participate?

Yes, your participation is completely voluntary. You may decide to withdraw from the clinical investigation at any time, without explanation and without affecting any of your rights to receive the most appropriate treatment. We kindly ask you, should you make this decision, to notify the Physician following you in the study.

10. Are there circumstances under which my participation in the clinical investigation could be interrupted?

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Yes, your participation may be terminated for the following reasons:
- Safety reasons (pregnancy, adverse events that could potentially endanger your life, hypersensitivity reactions associated with the study treatment, occurrence of serious illness, use of concomitant medications or treatments not allowed by the study);
- Non-adherence to what the study envisages and requires;

In these cases, the Physician following you in the study, however, will ask you to report to the clinical center to make a final overall visit.

11. Will anyone know that I am participating in the clinical investigation?

Yes, the Physician in charge of the study and some of his collaborators (physicians, nurses).
All clinical aspects of this study have been reviewed and approved by the Independent Ethics Referral Committee of this clinical center.

Other information

We do not expect you to have any health problems related to the study. However, should you suffer any physical problems or have any health repercussions as a result of the study, you will be covered by an insurance policy taken out by the Investigation Promoter, with the insurance company Chubb European Group SE, policy no. ITLSCQ58614) which provides coverage for the entire duration of the study, providing compensation for any damages suffered by the subjects while using the experimental product.
This compensation will also cover any expenses that may be necessary for subsequent treatment and care until your health condition is restored.
The insurance policy operates for damages that have occurred no later than 24 months after the completion of the study to the subjects participating in this study and whose claim has been filed no later than 36 months after the date of the conclusion of the study. However, this limitation does not affect the right of the injured subject to obtain compensation from the party responsible for the damage, if any.
The insurance policy also operates up to the maximum amount of €5,000,000.00 with a sub-limit of €1,000,000.00 per individual enrolled subject.

In order for you to enjoy your insurance rights, you will have to warn the Physician following you in the study of any signs or symptoms you observe during treatment.
In the event of harm caused by this study, please contact the relevant clinical center and you will be directed where to obtain necessary medical treatment. If further medical treatment is required, the center staff will direct you where to obtain it. Please be advised that the possibility of compensation provided for any harm reported by persons participating in this study does not extend to any harm to the embryo or fetus.

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Other information regarding the experimental treatment may become known during the study. The Trial Promoter will make known such information to the Physician following you in the study who will inform you if it may influence your decision to continue participating in the study.
In addition, if you are interested and request it, at the end of the study, you will be informed of the results of the study in general and those concerning you in particular.

You will not incur any expenses for either medical examinations or examinations under the study.

In case you agree to participate in the study and deem it advisable to inform your attending physician (general practitioner), you will be given a letter that you may deliver to your physician, containing, in addition to basic information about the study, the name and telephone contact information of the Physician who is attending you in the study who is available to provide your physician with further clarification.
Should you have, or should you have in the future, any other questions about the study, side effects, your rights, or anything else, you can ask the physician, Dr. Tiziana Lazzari (Physician following you in the study) at phone number + 39 010 8078631.

Should you have any questions regarding your rights as a subject involved in a clinical trial, you may call the Regional Ethics Committee at: 010/555 4214.

The protocol of the study proposed to you, this Information Sheet, the Information and Manifestation of Consent to the Processing of Personal Data, and the Informed Consent are in accordance with the Standards of Good Clinical Practice of the European Union, the relevant Italian legislation, and the current revision of the Declaration of Helsinki, and have been approved by the Ethics Committee responsible for this facility to which you may report any facts you deem appropriate to point out, regarding the study, by addressing correspondence to the Chairman of the Ethics Committee itself.

If you have no further questions and wish to participate in the clinical study, please sign the Information and Manifestation of Consent to the Processing of Personal Data and the Informed Consent.

You will be given a copy of this Information Sheet, the signed and dated Information and Expression of Consent to the Processing of Personal Data and Informed Consent form.

Please be advised that, anyone wishing to receive information about this study may contact the Investigation Promoter, at the following numbers:

- telephone number: 0735762020

- e-mail: farmacovigilanza@phitogenspa.it

Thank you for your cooperation.