FREE AND INFORMED CONSENT FORM

PARTICIPANT IDENTIFICATION DATA

NAME: .....
.....
IDENTITY DOCUMENT NO.: .....
GENDER: □ M □ F
DATE OF BIRTH: ...../...../.....
ADDRESS: .....
NUMBER: ..... APARTMENT: .....
NEIGHBORHOOD:
.....
CITY: .....
ZIP CODE: .....
PHONE: DDD (.....) .....
LEGAL REPRESENTATIVE
.....
RELATION (degree of kinship, guardian, curator, etc.):
.....
IDENTITY DOCUMENT: ..... GENDER: □ M □ F
DATE OF BIRTH: ...../...../....
ADDRESS: .....
NUMBER: ..... APARTMENT: .....
NEIGHBORHOOD:
..... CITY:
.....
ZIP CODE: ..... PHONE: DDD (.....)
.....

ABOUT THE RESEARCH

RESEARCH PROTOCOL: Phase I/IIa clinical trial to evaluate the safety and immunogenicity of StreptInCor, a synthetic vaccine against *Streptococcus pyogenes*, in healthy adult volunteers.

RESPONSIBLE RESEARCHER: Prof. Dr. Luiza Guilherme Guglielmi

REGIONAL COUNCIL REGISTRATION: 10,953 (CRF-SP)

POSITION/FUNCTION: Researcher II at the Immunology Laboratory of InCor/HCFMUSP.

EXECUTING RESEARCHER: Dr. Roney Orismar Sampaio

POSITION/FUNCTION: Assistant Physician at the Clinical Valve Disease Unit of InCor/HCFMUSP

REGIONAL MEDICAL COUNCIL REGISTRATION: 71,832

HCFMUSP UNITS: Immunology Laboratory and Clinical Valve Disease Unit – InCor/HCFMUSP

ASSESSMENT OF RESEARCH RISK:

MINIMAL RISK □

LOW RISK □X

MEDIUM RISK □

HIGHER RISK □

(probability that the individual may suffer some harm as a direct or delayed consequence of the study)

Study Duration: 60 weeks

The participant or responsible signs: _____

The researcher signs: _____

Justification and Objectives of the Research:

This information is provided to clarify your voluntary participation in this study. You are invited to participate in a research protocol aiming to develop a vaccine against a bacteria (infectious agent) called *streptococcus*. *Streptococcus* mainly affects the throat, causing infection (pain and fever), which in some cases can progress to more serious conditions, including damage to the heart, known as rheumatic heart disease.

The purpose of this research is to immunize individuals through vaccination with the investigational product, aiming to prevent throat infection and the possible progression of the disease to the heart.

To participate, you must be between 18 and 45 years old. You will be asked to sign two copies of this Free and Informed Consent Form (ICF) before any procedures are performed. One copy will be given to you.

If you agree to participate, a lottery will be held to determine whether you receive one of two treatments: the vaccine or a placebo, which is an inactive product (medication) with no expected effect on the body.

The study will involve three different doses (25 µg ,50 µg, 100 µg, 200 µg) of the StreptInCor vaccine, produced under Good Manufacturing Practices (GMP) and formulated with aluminum hydroxide as the adjuvant. The adjuvant alone will be used as the placebo.

Participant or responsible person signs: _____

The researcher signs: _____

Four groups, each consisting of twelve (12) healthy adult volunteers, will be randomly assigned to receive two doses of vaccine or placebo, spaced 28 days apart, plus a booster dose 6 months after the initial vaccination. In each group, for every three people receiving the active vaccine, one will receive the inactive treatment (aluminum hydroxide or placebo).

Depending on your random result, you will receive either the 25 μg, 50 μg, 100 μg, or 200 μg dose of the vaccine, and a total of 60 volunteers will participate in this study.

Participant or responsible person signs: _____

The researcher signs: _____

Description of Procedures, Purposes, and Non-Routine/Experimental Measures:

The duration of this study is 60 weeks (five years), and it will require you to attend scheduled visits with the study doctor. During participation, blood samples will be collected via venipuncture from your forearm. These samples will be used to monitor the behavior of the new vaccine in preventing *Streptococcus* infection.

You will have at least 14 visits to the research center over the course of the study. You will receive three doses of the vaccine under investigation. Blood samples will be collected during eight of these visits, designated as follows: (C1, initial screening visit), C3 (two weeks after the first dose), C4 (four weeks after the first dose), C5 (two weeks after the second dose), C6 (four weeks after the second dose), C10 (two weeks after the third dose), C11 (four weeks after the third dose), C12 (eight weeks after the third dose), and C14 (26 weeks after the third dose, which marks the end of the study at 54 weeks from the start).

Approximately 20 ml of blood (about one and a half spoonfuls) will be collected at each of these visits. For female volunteers of reproductive age, a pregnancy test (β-hCG) in urine will also be performed at visits C1 (screening), C2 (randomization), and C9. Pregnancy, breastfeeding, or plans to become pregnant are not allowed during the study period. If a volunteer becomes pregnant during the study, subsequent doses of the vaccine will be discontinued.

The participant or responsible signs: _____

The researcher signs: _____

These samples will be used to determine if there have been any changes in your tests caused by the vaccine, such as increased antibodies or protective cells against *Streptococcus*, or any damage to the body that could lead to study discontinuation.

Samples may also be used in experimental procedures and could be stored frozen and used in future research with the same objectives, upon your authorization.

Additional exams such as an electrocardiogram (ECG) will be performed during four visits (C1, screening; C7; C12; and C14, study end), along with echocardiograms (at the same visits where ECGs are performed). These exams evaluate heart rhythm and structure. Both are minimally risky and unlikely to cause harm.

The participant or responsible signs: _____

The researcher signs: _____

Description of Expected Discomforts and Risks:

Possible discomfort includes a needle prick during blood collection or vaccination. A bruise (hematoma) at the puncture site may occur. The vaccine might cause reactions such as redness, pain, fever, muscle pain, sleepiness, irritability, sweating, joint pain, or other unexpected reactions.

Electrodes used during ECG and echocardiogram may rarely cause contact allergy, resulting in redness or itching, which usually resolves quickly. If you experience any of these symptoms or other unforeseen issues, contact the study doctor immediately.

If clinical signs of harm related or unrelated to the vaccine are detected at any exam, you will be informed immediately, and necessary measures will be taken, including study discontinuation if needed. You will be monitored for adverse events, which include any disease or side effect that might occur during the study, whether or not related to the vaccine.

The participant or responsible signs: _____

The researcher signs: _____

4. Benefits for the Participant:

There are no direct benefits to you from participating. However, the knowledge gained may help develop a vaccine against bacteria that cause rheumatic fever, improving prevention in healthy people and treatment for patients. All exams performed may be made available upon your request.

5. Alternative Procedures that Might Be Advantageous:

There are no alternative procedures that might be advantageous compared to participation in this study.

6. Guarantee of Access to Care:

At any stage, you will have access to the research team for clarification. The lead investigator is Dr. Roney O. Sampaio (email: Roney.sampaio@hc.fm.usp.br telephone: (11) 2661-5056). In case of emergency, you may go to the Cardiology Emergency Department of the Heart Institute or contact the above professionals directly, or call (11) 2661-5405.

The responsible researcher is Dr. Luiza Guilherme Guglielmi (address: Av. Dr. Enéas Carvalho Aguiar, 44, InCor, 9th floor, Building II; phones: (11) 2661-5911, (11) 2661-5901; email: **luizagui@usp.br**).

If you have any ethical concerns regarding the research, you can contact the Research Ethics Committee (CEP) — Rua Ovídio Pires de Campos, 225 – 5th floor. Phone: 3069-6442, extensions 16, 17, 18, or 20. Fax: 3069-6442, extension 26 — email: **cappesq.adm@hc.fm.usp.br**.

The participant or responsible signs: _____

The researcher signs: _____

Compensation and Withdrawal Guarantee:

You are free at any time to withdraw from the study and to revoke this consent form without affecting your continued treatment at the institution. The institution, the researcher, and the sponsor guarantee treatment for any medical issues related to your participation through specific insurance.

After the study ends, you will be followed for an additional 12 months (or more if deemed necessary) by the Valvular Heart Disease outpatient clinic at the Heart Institute (HCFMUSP) to ensure safety regarding possible delayed adverse effects related to the study medication.

Participant or Responsible Signature: _____

Researcher Signature: _____

Confidentiality:

Your data confidentiality, according to Brazilian regulations, will be maintained during and after the study. All information obtained—including medical records, personal data, and research data—are confidential and will only be used for this research. Your personal identity, such as your name, address, and other data, will be kept secret in the research center.

To ensure privacy, you will be identified via a code and initials, and only the research team can link the code to your full name. This information will be stored securely and kept confidential for five years after the study concludes. The results will be published for academic and scientific purposes without revealing the identity of participants.

If you are followed by a personal doctor and wish so, the study doctor can inform them of your participation.

The participant or responsible signs: _____

The researcher signs: _____

Right to Information:

You have the right to be kept updated on the partial results of the research or on results from similar studies that are known to the researchers.

10. Expenses and Compensation:

You will incur no personal expenses during any phase of the study, including exams and visits. Any additional costs will be covered by the research budget. There is no financial compensation for participation, except for transportation and snacks during scheduled visits.

11. Commitment to Use Data and Material Only for the Current and Future Research:

The biological material collected will not be patented or used commercially. It may only be stored for future research with the same objective, with your consent.

12. Biorepository:

Stored material may be used in future research upon your explicit consent, as indicated below:

- (.....) YES. I want to be consulted and give permission for each future research that uses my stored material.
- (.....) NO. I waive future consent, and I am informed that the Research Project Analysis Committee (CAPPesq) will review and decide on the use of my donated material.
- **The participant or responsible signs: _____**
  The researcher signs: _____

The storage duration of the samples will be authorized by the CAPPesq. The participant will be informed if samples are lost, destroyed, or if the biorepository is closed. For international use of stored material, the responsible researcher will comply with national and international regulations, including resolution 441 of the National Health Council (May 12, 2011).

I declare that I have been sufficiently informed regarding the information I read or was read to me, describing the study "Phase I/IIa clinical trial to evaluate the safety and immunogenicity of StreptInCor, a synthetic vaccine against *Streptococcus pyogenes*, in healthy adult volunteers."

I have discussed with Dr. Roney Orismar Sampaio and Prof. Dr. Luiza Guilherme Guglielmi from the research team about my decision to participate in this study. The purpose, procedures, discomfort

Participant or responsible signature:

_____

Researcher signature:

_____