INFORMED CONSENT

Protocol title: Determination of the protective efficacy of the *Pv*CS/Montanide ISA-51 (*Pv*CS.2/M-51) vaccine formulation against controlled infection with *Plasmodium vivax* sporozoites

Written informed consent form for adults participating as volunteers in the study.

Study location:	Quibdó (Chocó)
Principal Investigator:	Sócrates Herrera Valencia, MD
Institution:	CENTRO DE ESTUDIOS CLÍNICOS ASOCLINIC LTDA – IPS
Description of the study population:	Adult individuals with and without previous malaria (naïve and semi-immune groups)
Name of study participant:	
Code assigned in the study:	

Study code: 2201-3

INTRODUCTION

The purpose of this document is to invite you to participate in a clinical health research study. Here you will find all the information you need to freely and responsibly decide whether or not you wish to participate.

Please read it carefully. If you prefer, this document can be read aloud to you. You may stop at any time to ask questions, which will be answered clearly by the study staff. You may also consult with family members, friends, or health professionals before making your decision.

Your participation is completely voluntary. If you decide not to participate, there will be no negative consequences for you or the care you receive from health services.

GENERAL STUDY INFORMATION

1. Why am I invited?

We have invited you because you are an adult who does not currently have malaria but lives in an endemic area and is therefore at risk of acquiring it. The study includes both people who have never had malaria (*naïve*) and those who have been previously exposed (*semi-immune*).

2. Purpose of the study

Malaria caused by *Plasmodium vivax* continues to be a major public health problem in Colombia and worldwide. Currently, there is no vaccine available against this parasite. This study seeks to evaluate a candidate vaccine (*Pv*CS.2 / M-51) to determine its safety, tolerability, and ability to induce protection against infection by this parasite.

The results will provide fundamental knowledge for the further development of this vaccine and new malaria prevention tools, which could benefit entire communities in endemic areas around the world.

3. Duration and procedures

Your participation will last approximately 8 to 11 months.

The main procedures will be:

- **Vaccination:** You will receive three doses of the vaccine in the upper arm muscle on days 0, 60, and 180 of the study.
- **Post-vaccination follow-up:** After each dose, you will remain under observation for 1 hour and then receive a follow-up call after 8 hours. There will then be follow-ups over the following weeks and months.
- **Blood draws:** Approximately 35 mL (less than half a small coffee cup) will be collected at various times during the study for immunological and safety analyses.
- **Controlled infectious challenge:** In month 7, you will be exposed in a controlled manner to the bite of 4 mosquitoes previously infected with *P. vivax* under laboratory conditions.
- **Clinical and laboratory monitoring:** You will be monitored frequently through clinical examinations and blood samples (thick smears) to detect or rule out the presence of the parasite.
- **Immediate treatment in case of infection:** if infection is confirmed, you will receive complete treatment according to current national protocols.
- **Long-term follow-up:** You will be evaluated for up to one year after the infectious challenge to ensure your safety and complete recovery.

In the case of women of childbearing age, periodic pregnancy tests and contraceptive methods will be required during the study, as pregnant or breastfeeding women are not allowed to participate.

4. Risks and discomforts

As with any clinical study, there are potential risks:

- **Blood collection:** may cause mild and temporary pain, bruising, or bleeding at the puncture site.
- **Vaccination:** fever, headache, arm pain, chills, fatigue. In some cases, more severe reactions, although rare.
- **Controlled infectious challenge:** risk of contracting *P. vivax* malaria. Although the risk is intentional, the infection will be detected early and treated immediately with safe medications available in Colombia.

- **Other rare risks:** anemia, vomiting, weakness, or severe allergic reactions such as anaphylaxis, which, although extremely rare, may require hospitalization.

You will have free medical care, immediate access to medications, and transportation to the hospital by ambulance, if necessary, at all times.

5. Benefits

- No direct benefits are expected for you.
- There may be indirect benefits, such as:
  - Early detection of infections or other abnormalities in laboratory tests.
  - Access to periodic medical evaluation throughout the study.
  - The opportunity to contribute to scientific progress and the development of a malaria vaccine that could benefit many people in the future.
- **Logistical support:** Although you will not be paid for your participation, the study will cover transportation costs, snacks, and compensation equivalent to one day's minimum wage for each study visit.

Protection for volunteers: All participants will be affiliated with the General Social Security System for Health (SGSS). In addition, the study will provide them with a prepaid medical plan and will have a civil liability policy to cover any eventuality related to their participation. Basic coverage of $500,000 USD and a deductible of $2,500 USD per event.

6. Risks and management of adverse events.

In the event of a serious adverse event (SAE), this will be immediately reported to the Research Ethics Committee and INVIMA, in accordance with current regulations. You will receive immediate medical attention and the necessary treatment at no cost. In addition, the study has a prepaid medical plan and a civil liability policy that will cover the expenses arising from any eventuality related to the research. Additionally, the study will assume any unforeseen additional costs that may arise in relation to the study.

7. Privacy and confidentiality

- All information will be handled confidentially.
- Your data will be encrypted and anonymized to prevent you from being identified in databases or publications.
- Blood samples may be stored for future studies for a period of up to 20 years for studies **related exclusively to malaria**, subject to your additional authorization. Upon expiration of this term or by prior decision, the samples will be disposed of using established biosafety standards.

8. Voluntary participation and right to withdraw

Your participation is entirely voluntary. You have the right to refuse to participate or withdraw at any time without consequences for your health, medical care, or social benefits.

9. Number of participants

In total, 60 volunteers are expected to participate in the vaccination and at least 5 others as parasite donors.

10. Access to the vaccine after the study

As this is a **Phase II** study, the vaccine is still under investigation and is not authorized for general use. For this reason, access to the vaccine cannot be guaranteed at the end of the study. If the results are favorable, the vaccine will need to be evaluated in subsequent phases and by regulatory authorities before it can be made available to the community.

11. Contact for questions or complaints

- **Principal Investigator:** Sócrates Herrera Valencia, MD
- **Study Coordinator:** Myriam Arévalo Ramírez, PhD
- **Chair of the Ethics Committee:** Ignacio Alberto Concha Eastman, MSc
- **Address:** Calle 21a - Cra 23, Zona Minera, La Virginia, Quibdó, Chocó
- **Telephone numbers:** (57) 317 517 0552 – (57) 317 517 0552 - 310 465 9004.
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- cei-asoclinic@inmuno.org /alberto.conchaeastman@gmail.com .

CONSENT FORM

I have read or had this document read to me. I have received clear and sufficient explanations about the study, the procedures, risks, benefits, and my right to withdraw at any time. All my questions have been answered.

I voluntarily consent to participate in this clinical study.

Additionally, I authorize or do not authorize my biological samples to be stored for future studies related solely to malaria and malaria vaccines:

☐ I authorize ☐ I do not authorize

Signatures

Participant

Name: _____ CC: _____

Signature: _____ Date: _____

Researcher or authorized representative

Witnesses (#3)

Nombre:_____Firma:_____Fecha:_____

Nombre:_____Firma:_____Fecha:_____

Nombre:_____Firma:_____Fecha:_____