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Title : A randomized, double-blind, placebo-controlled Phase 1 trial to evaluate the safety, tolerability, immunogenicity, and efficacy of Sanaria® PfSPZ-LARC2 Vaccine, a late-arresting, replication-competent, genetically attenuated Plasmodium falciparum vaccine by controlled human malaria infection in malaria-naïve healthy adults.

Document Date: 6/26/25

INFORMATION ABOUT A UNIVERSITY OF WASHINGTON RESEARCH STUDY

A randomized, double-blind, placebo-controlled Phase 1 trial to evaluate the safety, tolerability, immunogenicity, and efficacy of Sanaria® PfSPZ-LARC2 Vaccine, a late-arresting, replication-competent, genetically attenuated *Plasmodium falciparum* vaccine by controlled human malaria infection in malaria-naïve healthy adults

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What is this study about and what will you be asked to do?

We are doing this study to test an investigational malaria vaccine called PfSPZ-LARC2 Vaccine. Investigational means the vaccine is not yet approved by the United States Food and Drug Administration (US-FDA). In this study, we want to learn what effects, good or bad, the PfSPZ-LARC2 Vaccine has on people. We want to understand the safety of the vaccine and its side effects. We also want to look at the body's immune response against malaria. Finally, we want to look at whether the vaccine can prevent malaria. You are being asked to participate because you are an adult between 18 and 45 years of age and in good health.

If you decide to be in this study, we will ask you to attend up to 38 visits over about a year, depending on the group you are assigned to. The study involves you first being screened for the study and if you are eligible, you will receive 3 injections with either the investigational malaria vaccine or a placebo. An injection will be given by inserting a small needle into a vein in your arm. The insertion of the needle is similar to when you have your blood drawn.

In this study, the placebo is saline (salt water). At the first visit, you will be randomly (by chance, like flipping a coin) assigned to either receive the PfSPZ-LARC2 Vaccine or the placebo. Neither you nor the study staff will know what you are receiving. This type of study is called a double-blind study. By keeping both the staff and you blinded to what you receive, it will help us better understand how well the vaccine is working.

Three to 4 months after your last injection, you will be injected with malaria. This process is known as controlled human malaria infection (CHMI) or also called a challenge study. After CHMI, we can learn if the vaccine provided protection from malaria infection. It is possible that you may get malaria from the CHMI, for example, if you received the placebo or the vaccine does not work. You will be treated for malaria, whether or not you show signs or symptoms of malaria.

While you are in the study, you will be seen at the research clinic with a study clinician, we will collect information about your medical history and you will have physical exams, tests and/or procedures including injections, blood draws, and physical examinations.

Reasons you might say "yes" to being in the study.	Reasons you might say "no" to being in the study.
• You may indirectly benefit by learning more about your health status through your medical history, your physical exams, and lab tests. • You will receive financial compensation for your participation. • You are helping to advance medical science and our understanding of how to prevent people from getting malaria.	• You will be injected with an infectious malaria parasite during this study. The PfSPZ-LARC2 Vaccine may not be effective against malaria, or you may be assigned to the placebo, and you may get malaria as part of the CHMI. • You will be treated for malaria whether or not you show signs or symptoms of malaria. You could have side effects from this treatment. • The injections may cause you to feel unwell and so could the treatment for malaria. • The version of the PfSPZ-LARC2 Vaccine used in this study has not been given to humans, and the risks are not well known right now. If you receive the vaccine, it is possible that it could be more harmful to you than we anticipate. • You will have to come into the clinic frequently and avoid travel at certain times during the study. If treatment is not started or taken correctly, a serious malaria infection may cause kidney, liver or brain injury (seizures, coma), and lead to death. If you do not have enough time and flexibility in your schedule for frequent clinic visits, you might not want to be in this study.

Do I have options outside of this study?

You do not have to be in the study. You are free to say "yes" or "no", or to drop out after joining. If you say "no," you would have no penalty or loss of benefits. Whatever you decide, your regular medical care would not

change. You may want to consider other options outside of the research. You should discuss possible options with your regular doctor, and they may include not participating in this research study. The research team will discuss these options with you and provide information about the risks and benefits of participating in this study. Enrollment in this study may prevent you from joining other research studies.

What can you do if you want more information?

Read more about this study. The next pages of this form give you more information about the study including procedures, risks, benefits, confidentiality information, use of specimens, and research-related injuries.

Talk to the study team. We are here to help you understand the study. Please ask us any questions you have, even about things that are not in this document. It is our responsibility to give you the information you need to make a decision and give you time to think about whether or not you want to sign up for this study.

Talk to someone else. You may want to discuss your decision about whether to sign up with your family, friends, your regular doctor, or someone else. You can show them this document to help them talk about the study with you.

Talk to someone about your rights as a participant. If you want to talk about the study with someone who is not part of the study team, talk about your rights as a research participant, or report problems or complaints about the study, you can contact the UW Human Subjects Division at hsdinfo@uw.edu or call 206.543.0098.

Additional information about research purpose.

Worldwide, about 229 million people become sick and about 409,000 people die from malaria each year. Malaria is a disease caused by an organism, called a parasite, that is spread to people primarily through bites from infected mosquitoes. Currently, there are no vaccines approved by the US-FDA to help prevent malaria infections.

What is the PfSPZ-LARC2 Vaccine that is being tested in this study?

The investigational vaccine called PfSPZ-LARC2 Vaccine, stands for *Plasmodium falciparum* sporozoite late-arresting, replication competent vaccine. *Plasmodium falciparum* is one type of a malaria parasite. A sporozoite is the stage in the life cycle of the parasite that the mosquito injects into a person during a mosquito bite. The PfSPZ-LARC2 Vaccine was developed by a company called Sanaria Inc. It is made from malaria parasites (sporozoites) that have been genetically modified (their DNA has been changed) so they should not grow into the bloodstream and cause malaria infection. Before being given, it is diluted ("watered down") in a solution of two US-FDA approved products - saline and human serum albumin (HSA). HSA is a human protein normally found in the blood.

The PfSPZ-LARC2 Vaccine has not been approved by the US-FDA. This is the first study in which it will be given to humans. A previous version of this vaccine was given as part of another study and was shown to protect many people against malaria. It also appeared to be safe and well tolerated (meaning that the subjects did not have much pain or other side effects with the injections). This new version of the vaccine being used in this study may be even better at preventing malaria, but we are still trying to determine how well and how long it works.

What is the product used for malaria or Controlled Human Malaria Infection (CHMI)?

We will test if the vaccine works to prevent malaria by injecting you with malaria using a product called PfSPZ Challenge (7G8). Like PfSPZ-LARC2 Vaccine, the PfSPZ Challenge (7G8) is made up of malaria parasites (sporozoites). The difference is that the PfSPZ Challenge (7G8) is not genetically modified (its DNA has not been changed). This means that the PfSPZ Challenge (7G8) is infectious and can cause malaria if injected into humans. PfSPZ Challenge (7G8) is given in the vein just like PfSPZ-LARC2 Vaccine. PfSPZ Challenge (7G8) has not been approved by the US-FDA. However, the PfSPZ Challenge (7G8) has been given in other malaria challenge studies and has been safe.

What is the product used to treat malaria or CHMI?

If you develop malaria, it is curable and can be treated with medication atovaquone/proguanil (also called Malarone®) or artemether/lumefantrine (also called Coartem®). These medications will be available to you during the study. These are standard FDA-approved medications for malaria treatment.

Additional information about who can be in this study

To be in this research study, you must be:

- 18-45 years of age and in good health; your vital signs and laboratory tests must be within normal ranges.
- Able to attend all study visits and willing to provide contact information that can be used by study staff throughout the entire study.
- Willing to to use birth control or practice abstinence from sexual intercourse.
- Willing to not travel at certain times during the study and not donate blood for three years after the study is over.
- Willing to take malaria treatment medicine.
- Able to pass a written Assessment of Understanding quiz about the study.

You cannot be in this research study if you:

- Have received a malaria vaccine in a prior clinical study.

- Have received live vaccines within 4 weeks or non-live vaccines within 2 weeks of the first study injection.
- For infectivity controls, have received live vaccines within 4 weeks or non-live vaccines within 2 weeks of the CHMI.
- Have a history of malaria infection within 2 years before joining in this study.
- Have a had your spleen removed, or have a history of sickle cell disease, non-fever seizures, or complex fever seizures.
- Have ever had a severe, life-threatening allergic reaction to a vaccine.
- Plan to have major surgery between your first injection and 28 days following CHMI.
- Have allergies to Malarone® or Coartem® or any parts of the study products
- Have taken part in a vaccine study less than 4 weeks before enrollment or plan to participate in other vaccine or other drug research studies while in this study.
- Plan to travel greater than 100 miles from clinic during the injection visits (month 1-3) and CHMI visits (months 5-7) while in the study.
- (For persons of child-bearing potential): Currently pregnant, breast-feeding, or plan to become pregnant during your participation (one year).
- Have an increased risk for heart disease, an abnormal heart test, or test positive for malaria, HIV, Hepatitis B or C. Low potassium and or low magnesium levels may also exclude you from the study.
- Currently taking or plan to take medicines that may interact with the study vaccine or malaria treatment medications. The study team will share a detailed list of medications you should avoid during the study.
- History or family history of abnormal heart rhythms.

Additional information about research procedures

In this study, up to 22 participants will be enrolled who will receive 3 injections of either the PfSPZ-LARC2 vaccine or placebo.

Group	# of Participants	Injection Type	Dosing Days	CHMI Day
Group 1	3	PfSPZ-LARC2	Days 1, 29, and 57	Day 169
Group 2	1	Placebo	Days 1, 29, and 57	Day 169
Group 3	12	PfSPZ-LARC2	Days 1, 29, and 57	Day 141
Group 4	6	Placebo	Days 1, 29, and 57	Day 141

Infectivity controls: If any participants in the placebo group have to drop out of the study, they will be replaced with a new participant. If you are selected as an infectivity control, you will not receive any injection of study

vaccine or placebo and will only receive CHMI. You will have a study visit before CHMI to make sure you are eligible.

Overview of Study Procedures: This study will include several phases which are described in detail below.

- **Screening/pre-injection phase**: Screening will be done up to 90 days before your first injection and again the day before your first injection. You will receive information about the research study, have an opportunity to ask questions and be guided through the informed consent process. You will be asked questions on your health and have a physical exam and blood tests done to see if you are eligible to take part in this study.
- **Injection phase**: If you are eligible for the study based on your Screening visit, you will be put into one of the study groups. You will be followed for the next 3-4 months depending on which group you are assigned to. You will receive your injections and be asked questions about your side effects, health and have physical exams (if needed) and blood tests done.
    - You will be randomized into one of the four study groups. Two of the four study groups will receive the PfSPZ-LARC2 Vaccine, and two groups will receive a placebo.
- **Malaria Challenge Phase**: Approximately 2-3 months after all the injections have been completed, all participants will receive the CHMI (infectious malaria parasite). You will be followed for the next month in the clinic, asked questions about your side effects, health and have a physical exam (if needed) and blood tests done.
- **Malaria Treatment Phase**: After receiving the CHMI, all participants will be treated for malaria. You will be asked questions about your treatment, health and have physical exams (if needed) and blood tests done.
- **Post-malaria treatment phase**: Approximately 3 months after the malaria treatment phase all participants will be called. You will be asked questions about your health. Three months after that visit, you will come back to the clinic for a final visit and be asked questions about your health, have a physical exam (if needed) and blood tests done.

Detailed Description of Study Procedures:

Screening Visit (90 to 2 days prior to injection): The procedures and tests during this visit will allow us to know if you are eligible to take part in the study.

- We will collect information about your sex, date of birth, and race and ethnicity.
- Medical history and current and recent medications will be reviewed.

- A physical examination will be performed. We will also collect your height, weight, and vitals (blood pressure, heart rate, and temperature). We will calculate your Body Mass Index (BMI) and your cardiovascular risk.
- Electrocardiogram (ECG): This is a painless test in which we will stick pads (known as leads) to your chest, arms, and legs. It shows us the "electrical activity" of the heart and the results can provide warning signs for heart disease.
- Blood draw (24 mL or approximately 1.6 tablespoons): Testing will include a complete blood count (CBC), liver and kidney function tests, and glucose (a type of sugar in your blood), HIV, hepatitis B, hepatitis C. We will also make sure you do not currently have malaria by testing for malaria parasites (malaria safety monitoring). We will also use some of the blood for research tests.
- Blood pregnancy test for those who are of child-bearing potential. If you have a positive pregnancy test, you will not be allowed to participate in this study.
- Assessment of Understanding (AoU): After reviewing this consent form with the research staff, you will complete a short quiz that shows your understanding of the study. You must achieve a score of 80% (at least 8 out of 10 questions correct) to be allowed to participate. If you do not score 80% on your first try, we will review the study with you to help you more fully understand. You will have an opportunity to take the quiz again. If you get less than 80% the second time, you will not be allowed to participate in the study.

If any of the screening lab results show abnormal values, we will contact you to discuss this. We will also provide referrals to a health care provider if needed and give you copies of the tests to take to your health care provider.

***Pre-Injection Visit (7-2 days prior to injection)*:** If you are eligible for the study based on the results of the Screening Visit, you will be seen for a Pre-injection visit in which the following procedures will be performed.

- Review of medical history and review of current and recent medications. We will provide you with a list of medications to avoid during the study.
- A targeted physical examination will be performed if needed based on symptoms.
- Vital signs will be collected (blood pressure, heart rate and temperature).
- Blood Draw (98.5 mL or 6.7 tablespoons) for safety labs and research tests.
- A study team contact card will be given to you in case you need to contact the study team. We will also review your contact information. We will ask for the names and phone numbers of two emergency contacts. These emergency contacts may be called if we are not able to contact you after the injections or CHMI. We will confirm the two emergency contacts by calling them during the visit.

Pre-injection Phone Call (day before injection): The day before your first injection visit, we will call you to confirm that you are still eligible and to make sure that you are still able to follow the study visit schedule. The study team will also ask about any recent changes to your medical history and current medications.

Injection Visits (Days 1, 29 and 57): You will have the following procedures completed at your injection visits.

- Group Assignment: At the first injection visit, you will be randomly assigned (like flipping a coin) to your study group. You will receive either an injection with the PfSPZ-LARC2 Vaccine or placebo, depending on your group assignment. Neither you nor the study team will know what injection you receive.
- Medical History and current medications will be reviewed.
- A targeted physical examination will be performed if needed based on symptoms.
- Vital signs will be collected (blood pressure, heart rate, and temperature).
- Urine pregnancy test for those who are of childbearing potential. If your pregnancy test is positive, you will not be allowed to participate in this study.
- Blood draw (55.5 mL or 3.75 tablespoons) for malaria safety monitoring and research tests. There will not be a blood draw on Day 1, your first injection day.
- PFSPZ-LARC2 Vaccine or placebo will be injected into your vein in your arm.
- Observation: For your safety, after each injection, you will be observed in the clinic for least 30 minutes. We will look at the injection site and watch for any severe allergic signs that may need to be treated while you are still in the clinic.
- Memory Aid Questionnaire: You will record how you feel for 7 days after each injection on a paper form given to you. If you develop signs or symptoms that concern you, please contact study investigators immediately. We will ask that you bring the completed memory aid with you to the follow-up visits after each injection.
- We will give you a study team contact card so you can reach a study investigator 24 hours a day if needed. We will ask you about any changes to your emergency contact information. The study team will remind you about the importance of following the study schedule.

Post-Injection Follow-Up Visits: The visit schedule after each injection is shown in the table below.

Post Injection Visit Schedule	
Dose	**Follow-up Visits on Study Day**
Dose 1	Day 2, 5, 6, 8, 9, 11, 13, 15, 17, 20, 27
Dose 2	Day 34, 36, 38, 43
Dose 3	Day 62, 64, 66, 71, 84

At each post-injection visit, the following procedures will be performed:

- Your injection site will be checked.
- Medical History and current medications will be reviewed.
- A targeted physical examination will be performed if needed based on symptoms.
- Vital signs will be collected (blood pressure, heart rate, and temperature).
- You will be asked about possible side effects or other medical problems that you might be experiencing.
- Your memory aid will be reviewed.
- Blood Draw ((2- 86.5 mL or ½ teaspoon to approximately 6 tablespoons) volume depends on the collection time point) for malaria safety monitoring, safety labs, and research tests.

Pre-PfSPZ Challenge (7G8) (CHMI) Visit (1-3 days before challenge): The following procedures will occur:

- Medical history and current medications will be reviewed to confirm that you are still eligible to take part in the study.
- A targeted physical examination will be performed if needed based on symptoms.
- Vital signs will be collected (blood pressure, heart rate, and temperature).
- You will be asked about possible side effects or other medical problems that you might be experiencing.
- Urine pregnancy test for those who are of child-bearing potential. If your pregnancy test is positive, you will not be allowed to participate in this study.
- Blood draw (94.5 mL or 6.4 tablespoons) for malaria safety monitoring, safety labs, and research tests.
- We will review your contact information. We will also review (and confirm by calling) the contact information for your two emergency contacts. The contacts will only be used if we are not able to reach you. If we cannot reach you or your emergency contacts after CHMI, we may need to call emergency services to help find you.
- The study team will remind you about the importance of following the study schedule.

PfSPZ Challenge (7G8) (CHMI) Visit: At the CHMI visit, all the pre-CHMI procedures will be repeated (except there will be no blood draw) and the following additional procedures will occur:

- PFSPZ Challenge (7G8) (infectious malaria parasites) will be injected into a vein in your arm.
- Observation: For your safety, after the CHMI injection, you will be observed for least 30 minutes in the clinic. We will look at the injection site and watch for any severe allergic signs that may need to be treated while still in the clinic.
- Memory Aid Questionnaire: You will record how you feel for 7 days after the CHMI on a paper form given to you. If you develop signs or symptoms that concern you, we ask you to contact the study team immediately. We will ask that you bring the completed memory aid with you to the follow-up visits.

- You will be instructed to contact the study staff immediately if you develop any signs and/or symptoms that may be related to malaria. Below are some important reminders:
    - It takes at least 7 days to develop malaria after being infected by the malaria parasite. From 7 until 28 days after you receive PfSPZ Challenge (7G8), YOU MAY DEVELOP MALARIA. During this time, we ask that you avoid areas with mosquitos to avoid potentially spreading malaria.
    - Symptoms of malaria may include but are not limited to fever (oral temperature of more than 38°C (more than 100.4°F)), feeling feverish, shaking, sweats, cough, headache, dizziness, tiredness, joint or muscle aches, nausea, vomiting, abdominal pain, diarrhea, chest pain, shortness of breath, and heart palpitations.
    - The type of malaria parasite used in PfSPZ Challenge (7G8) is curable. You will be treated with Malarone® or Coartem®.

Post CHMI Follow-Up Visits: The visit schedule after each injection dose is shown in the table below.

CHMI Visit	Follow-up Days
Beginning 7 days after CHMI	Day 7, 8, 9, 10, 11, 12, 13, 14
Following 8 days of daily visits	Day 15, 18, 21, 24, 28

These visits are very important so that we can monitor your health and safety. The following procedures will occur:

- Medical history and current medications will be reviewed. We will also ask if you have any signs or symptoms of malaria.
- A targeted physical examination will be performed if needed based on symptoms.
- Vital signs will be collected (blood pressure, heart rate and temperature).
- You will be asked about possible side effects or other medical problems that you might be experiencing.
- Blood draw (2 mL or 1/2 teaspoon) to check for malaria parasites in your blood (malaria safety monitoring). If you start to develop signs or symptoms that could be due to malaria infection, you may have additional 2 mL (1/2 teaspoon) of blood drawn. Based on the results of malaria testing and symptom review, the following will occur:
    - Positive malaria test result: If you have a positive malaria test you will be treated with Malarone® or Coartem® at the clinic daily for 3 days until you have completed the treatment course and no longer have symptoms. On your first day of treatment and 7 days after treatment, we will draw a small amount of blood (7 ml or ½ tablespoon) for safety labs and malaria safety monitoring. 7 days after treatment, we will collect a small amount of blood for research tests. If your malaria test is still

positive 8 days after starting treatment, you will be asked to come to the clinic daily for blood draws (malaria safety monitoring) until the infection has cleared.

- Negative malaria test results: If you do not develop malaria symptoms within 28 days after the CHMI and your blood tests are still negative for malaria, you will still be treated for malaria as described above.

- Malaria-like symptoms: If you develop any malaria like symptoms AT ANY TIME after CHMI, it is important that you notify the study staff immediately so we can determine whether you need to follow up in the clinic.
- A total blood volume of up to 35 mL (about 2.4 tablespoons) may be collected for safety monitoring and research tests over the course of all CHMI follow-up visits.

90 Days Post CHMI Phone call: We will call you 90 days (3 months) after your CHMI Visit to ask about any changes to your health.

180 Days Post CHMI Visit: You will have an in-clinic visit 180 days (6 months) after CHMI Visit. The following procedures will occur:

- Medical history review and targeted questions to see how you are feeling.
- A targeted physical examination will be performed if needed based on symptoms.
- Vital signs (blood pressure, heart rate, and temperature).

Early Termination Visit: If you decide to withdraw from the study you may be asked to do the following, depending on when you withdraw:

- If you received the PfSPZ-LARC2 Vaccine or placebo injection, you will be asked to return to the research clinic for a final safety follow-up visit 28 days after your last injection.
- If you received CHMI, you will receive a complete course of malaria treatment medication starting no sooner than the seventh day after CHMI administration. You will be given standard treatment at the clinic daily for 3 days until you have completed the treatment course and no longer have symptoms.
- You will also be asked to return to the research clinic for a final safety follow-up 28 days after CHMI Procedures at the final follow-up visit may include:
  - Medical history and current medication review, and targeted questions to see how you are feeling. We will also ask if you have any signs or symptoms of malaria.
  - A targeted physical exam will be performed if needed based on symptoms.
  - Blood will be collected for testing if you choose to withdraw from the study within 28 days of a visit with a planned blood draw.

Potential benefits of the study.

There is no known benefit from taking part in this study, however, society may benefit from information learned in this study and development of a malaria vaccine. This is a research study and does not replace standard treatment or therapy for malaria. You may benefit from having physical exams and routine blood tests, including HIV and hepatitis B and C.

Potential risks or side effects of the study.

In this part of the consent form, we describe the side effects that we expect from the tests, procedures, and treatments in this study. The PfSPZ-LARC2 Vaccine and PfSPZ Challenge (7G8) could cause side effects we do not know about yet.

Risks of Blood Drawing:

Blood will be drawn from a vein in your arm using a needle. You may experience discomfort from the needle stick, swelling or bruising, and there is a very small risk of infection at the site of the needle stick. You may feel dizzy and/or faint and may develop a fast heartbeat during blood collection.

Risks of PfSPZ-LARC2 Vaccine and CHMI:

The risk of the study can be minimized by giving the vaccine first to only three participants and reviewing their side effects before enrolling the rest of the participants in the study. These first 3 participants are called sentinels and will be a part of our study. Side effects, if present, are usually short term and often do not require treatment. We will give you a memory aid to record how you are feeling, and we will also be checking for side effects during your study visits.

Side effects of any vaccine can be grouped into 3 types—immediate reactions, local reactions at the injection site and general reactions. These are described below:

- **Immediate reactions:** Occur shortly after the injection is given. Although rare, an allergic reaction to the vaccination can be very serious, including anaphylaxis. They can even cause death if not treated. You will be observed in the research clinic by the trained staff for 30 minutes following each injection and follow-up with the staff in the days following.
- **Local reactions:** Occur at the site of injection. They include bruising or leaking of the vaccine into tissues around the vein. Local reactions may appear as pain, redness, tenderness, swelling, a hard bump under the skin, itching, and bleeding, and arm motion limitation (including the forearm).
- **General reactions:** may include fever, chills, fatigue, irritability, dizziness, headache, nausea, vomiting, chest pain, abdominal pain/tenderness, diarrhea, muscle or joint pain, generalized rash or itching skin, abnormal safety labs, or lymph node swelling in your armpit. Chest pain, palpitations, or shortness of breath have been reported but are rare.

These products contain Human Serum Albumin (a solution made from human plasma). Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. However, no cases of transmission of viral diseases have ever been reported with Human Serum Albumin (HSA). There is also the possibility that unknown infections agents may be present in such products.

If you receive the placebo or are selected for the infectivity control group, or if you receive the vaccine but it does not completely protect you from CHMI, you will get malaria infection after the CHMI. There is also a small possibility that you could get malaria at the time of injection if the vaccine is incompletely weakened. However, because we are following you so closely during the study, the chance of serious illness or death from malaria infection is very small. We use an approved, ultrasensitive malaria blood test as well as a backup microscope test to diagnose blood-stage malaria. The malaria blood test we use can detect infection often before people have any symptoms. Therefore, if you do have an infection, we are often able to diagnose and treat you before you have symptoms.

Risk to Placebo (Saline) Injection

These risks are the same as the local reactions described above.

Risks of Malaria Treatment:

Malarone®: include (1) common side effects: nausea, vomiting, abdominal pain, loss of appetite, diarrhea, headache, cough, dizziness, sleeplessness, weakness and, (2) rarely, a condition where the blood produces a lower-than-normal amount of healthy red blood cells (anemia), mouth sores, fever, swelling in your limbs and hair loss.

Coartem®: include (1) common side effects: abdominal pain, nausea, vomiting, loss of appetite, chills, cough, heart palpitations, fever, headache, muscle pain, joint pain, sore throat, nose congestion, shortness of breath while exercising , dizziness/vertigo, sleeplessness, enlarged liver or spleen, elevated liver tests, itchy skin or rash, easy bruising, tiredness and weakness; and (2) rare serious side effects: bleeding significant enough to cause a black stool and blood in the urine, pain on urination, changes in hearing, chest pain, seizures, hypersensitivity reaction, fast heart beats, and skin blisters.

If you require treatment with any other anti-malarial drug, you will be provided with a detailed list of side effects associated with that medication.

If treatment is not started or taken correctly, a serious malaria infection may cause kidney, liver or brain injury (seizures, coma), and lead to death. It is very important that you follow all study instructions, take the mediation prescribed, attend all the visits, and not travel outside the Seattle, WA area during the CHMI.

If you do not take all your malaria treatment medication, you could get sick with malaria a second time. This could occur at any time up to 1 year after you get malaria the first time. If, during that 1 year after you participate in this study, you develop symptoms that might be caused by malaria, contact the study team or tell your personal healthcare provider that you participated in this study.

We will have over the counter medications available for you in case they are needed for any malaria symptoms, such as acetaminophen (Tylenol) and/or ibuprofen (Motrin). A study staff member will make sure you are not allergic to the medications before we give them to you.

Reproductive risks:

The PfSPZ-LARC2 Vaccine may involve unknown risks to an embryo, fetus (unborn baby) or nursing infant.

For participants of childbearing potential (are not surgically sterilized or one year post-menopausal):

- You cannot join this study if you are pregnant, planning to become pregnant, or breast-feeding.
- You must use an effective method of birth control or abstain from sexual intercourse for at least 30 days prior to your first study visit until 60 days after your last injection or 28 days post CHMI, whichever is later. If you choose to no longer practice abstinence, you must agree to use another birth control method below. Birth control methods include:
    - monogamous relationship with partner who has been vasectomized for 180 days or more prior to your first study visit
    - intrauterine contraceptive device (IUD)
    - birth control pills
    - diaphragm or condom in combination with contraceptive jelly, cream or foam
    - implantable or injectable birth control such as Implanon® or Depo-Provera®

For participants who can cause a pregnancy:

- You agree to refrain from sperm donation from the first injection until 60 days post last injection or 28 days after CHMI, whichever is later.
- You use condoms with a partner of childbearing potential from first study visit to 60 days after last injection or 28 days after CHMI, whichever is later.

If you or your partner become pregnant after joining this study, you must notify the study staff immediately. Your participation in this study will end. The study staff must share this information with Sanaria, Inc, within 72 hours of being notified and with the UW Institutional Review Board (IRB), a group of people who review research studies to protect the rights and welfare of research participants.

We will ask for your permission to continue scheduled safety follow-up visits and to complete an end-of-study visit, as scheduled. We will ask you to share pregnancy details and outcomes with us or allow study staff access

to your medical records so that staff can review your pregnancy and outcome details, including medical records for your infant.

Non-physical risks:

- You might not be able to work at certain points during the study due to frequent clinic visits or illness.
- Certain information about you, such as personal information, and laboratory data might be released by accident. This risk is very low, because we keep personal information private.

What additional safety measures would I need to take while in this study?

- Some medicines can prevent malaria parasites from growing or can interfere with malaria medicine. For example, you should not take any antibiotics, unless it is absolutely necessary, beginning 2 weeks before each injection date and at least 2 months after receiving CHMI. If your personal healthcare provider prescribes an antibiotic for you, please inform one of the study clinicians, preferably before you begin to take it. The study clinician will talk to your personal healthcare provider about possibly using a different antibiotic, if necessary, which would not interfere with the study. We will provide you with a list of medications to avoid while on the study.
- You should not travel outside of the Seattle, Washington area during the injection period and until 28 days after receiving the CHMI. Let the study staff know about planned travels so we can coordinate your visits. We ask that you do not travel to any areas of the world with malaria during the entire study.
- After participating in this study, you should not assume that you are protected from malaria in the future. After completing the study, if you plan to travel to a malaria area, you should talk to your healthcare provider about how to prevent malaria infection and follow their standard guidance.
- You should not donate blood or plasma while participating in this study. Federal Regulations also do not allow blood donations for 3 years after infection and treatment for malaria.

How will we protect the information you provide?

We will protect your confidentiality. We will store your name and other identifiable information separate from the study data. Paper documents containing personal information about you will be maintained in locked file cabinets. Computerized information will be kept in password-restricted files.

Access to your identifying information will be limited to certain members of the study team and any individuals from the UW, the Food and Drug Administration (US-FDA), Sanaria, Inc., National Institutions of Health (NIH) (the sponsor of the study), the Fred Hutchinson Cancer Center (FHCC), or other agencies that may need to audit study records. When we publish the results of this study, we will not use your name. If we learn you intend to harm yourself or others, we must report that information to the appropriate authorities.

The link between your identifiers and the research data will be destroyed after the records retention period required by state and/or federal law.

We will keep your contact information and may contact you in the future to ask if you would like to participate in other studies. Your contact information will be kept confidential and will not be shared.

You will be in a private exam room for all your visits, but it is possible that you will be in the clinic with other participants at the same time.

Reporting Requirements. Per state regulations, if the hepatitis or HIV tests are positive, the study team must report the information to the Washington State Department of Health.

Certificate of Confidentiality

To help us protect your privacy, we have a Certificate of Confidentiality (Certificate) from the NIH. Study staff cannot provide to any person not connected with the research your name, or any materials that have identifiable, sensitive information about you, unless permitted by a legal exception, such as state and national laws that require reporting of some contagious diseases. The most important protection provided by the Certificate is that the study staff cannot be forced to provide any of your identifiable, sensitive information, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, such as if there is a court subpoena, without your permission.

The study staff will use the Certificate to resist any demands for information that would identify you.

Your information protected by the Certificate may still be disclosed or used when the information:

1. is disclosed to people connected with the research; for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the FDA. This does not include disclosure for use during legal proceedings as noted above;
3. is necessary for your medical treatment and you have consented to this disclosure;
4. is for other scientific research as allowed by applicable federal regulations;
5. is disclosed with your consent.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing and dating below you consent to those disclosures. As previously noted, reporting sexual abuse or assault if you are under 18 years of age is required by law and will become part of your medical record, but not your research record.

What if you want to stop being in this study, or if the researcher decides you should no longer participate?

While you are taking part in this study, we may learn new information about malaria infection or prevention. If this happens, we will contact you about the new information so you can decide if you want to stay in the study.

If you decide you want to stop being in this study, be sure to contact the study team. You may be withdrawn from the study at any time without your consent by the study clinician if it is believed to be in your best interest, if you are not able to perform all the study procedures, or for administrative reasons, such as the study is stopped, or we have reached the required number of participants for the study.

How will we test, store, and share your information and samples?

Laboratory Testing of Samples. The blood specimens collected from you will be used for research tests of the immune response to the study vaccine. These tests will measure how your body developed an immune response to the study vaccine. We will also look at how different cells of your immune system help to fight malaria. The results of these tests are useful only for research purposes. Your individual results will not be available to you or your regular doctor and will not be placed in your medical record.

Samples for these research tests may be sent to a central storage facility or sent directly to the research testing laboratories. These samples will not be labeled with your name or initials, or any other information that could readily identify you. These samples will be labeled only with a barcode and a unique tracking number (ID code) to help protect your confidentiality. Staff at the central storage facility and research testing laboratories will not know your identity, or even the study identifier you were assigned. However, the study staff who enrolled you will keep a list in a secure area with your name, contact information and the ID code (called a code key) that can link the samples to you, if needed. Access to the code key is limited to study staff working at the research clinic where your samples were collected.

Leftover Samples and Secondary Research.

After all tests required for this study are complete, we will save leftover samples and information (identified only by ID codes) for possible secondary research instead of throwing them away**.** Secondary research is research that is not part of this study but will be performed in the future. You will not be told about this future research. Secondary research will be limited to malaria research and may help us understand how the vaccines work or to develop new tests.

Blood samples will be stored indefinitely at a site determined by the National Institutes of Health (NIH). Leftover samples will be labeled only with a barcode and an ID code (not with your name, initials, or any other

information that could readily identify you). These leftover blood samples will be stored with the same confidentiality measures used for the main specimens.

Leftover blood samples and information may be shared with other study doctors/institutions for secondary research. We may remove the codes from your information or samples so that we cannot identify you and use these in other research. These de-identified samples and information may be shared with other researchers without your additional consent. It is also possible that in the future we may want to use or share study information/samples that might identify you. If we do, a review board will decide whether or not we need to get additional permission from you. Leftover blood samples will be used only for research purposes. This may include reproducing or growing your cells.

We will not conduct any genetic research testing on your samples.

If these blood samples are tested in the future, the results may be published. The publication will not contain any information about you that would allow someone to determine your identity.

The samples we collect as part of this research may be used for commercial profit, such as developing new tests or products. There is no plan to share this profit with you.

You will be asked at the end of the consent form to agree or not to secondary research use of your leftover blood samples and information collected for this study. There are no benefits to you in the storage and future research use of your blood samples and information. The results of any future research testing will be kept confidential in the same way as the results of other testing done for this study. The results of any future research will not be available to you or your regular doctor and will not be placed in your medical record.

You may change your mind about secondary research and withdraw consent for the storage and use of your samples or information at any time. You will need to contact the study staff using the contact information listed on page 1 of this form. Your samples will be removed from future use when this vaccine study is completed. Only stored samples with an ID code and not used in this research can be removed or destroyed. Research that has already begun using your samples cannot be withdrawn. For example, if some research with your samples and information has already been completed, the information from that research may still be used. Also, if the samples and information have been shared already with other researchers, it might not be possible to withdraw the samples and information.

Will you get to know your research results?

We will give you the results of your urine pregnancy, malaria tests, and the safety labs as soon as the results are available.

You will be notified to which group you were randomized, PfSPZ-LARC2 Vaccine or placebo, before you complete the study.

Other information about this study.

Being in this study is voluntary. This means that you can refuse to sign up. It also means that if you do sign up, you can decide to stop being in the study at any time without penalty.

We are receiving financial support from the NIH and study drug from Sanaria, Inc.

If there is an emergency, call 911 right away or go to the emergency room as soon as you can. If you have been injured or otherwise harmed by participating in this study, contact Dr. McClelland (8:00am-5:00pm) or the 24-hour emergency line listed on page 1 of this consent form. You will be treated or referred for treatment. Information about your problem or injury may be collected directly from you, or with your written permission, from the health care providers who treated you.

Costs: There will be no charge to you for the research tests, procedures, and malaria treatment while taking part in this study.

Research-Related Injury: In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH or the Federal Government. The costs of the treatment may be billed to you or your health insurance just like other medical costs, it may be covered by Sanaria, or it may be covered by the UW's discretionary Human Subjects Assistance Program (HSAP), depending on a number of factors. Sanaria will cover the cost of medical expenses for unanticipated injuries that result directly from your receipt of PfSPZ Vaccine or PfSPZ Challenge (7G8) (CHMI). HSAP coverage may be requested by the researcher by following established procedures. If you wish to request HSAP coverage yourself, contact the researcher or the UW Human Subjects Division at hsdinfo@uw.edu or 206-543-0098. Ask the researcher if you would like information about the limits and conditions of the HSAP. The UW does not normally provide any other form of compensation for injury. However, the law may allow you to seek payment for injury-related expenses if they are caused by malpractice or the fault of the researchers.

The study does not compensate you for disability, time lost from work or school, loss of a job, or other costs to you or your family. You do not waive any right to seek payment by signing this consent form.

You will receive compensation. You will be compensated for your participation in this study as noted in the table below. If you decide to stop being in the study before finishing all the visits, you will receive a partial payment based upon the study procedures/visits you completed.

It may take up to 4 weeks to receive your payment. Payments may be batched. Parking validation or bus tickets will be provided for each study visit.

Procedures	No. of Visits	Compensation per Visit ($)	Maximum Total Compensation ($)
Screening	1	75	75
Pre-Injection	1-2	100	200
Injections	3	200	600
Post-Injection Follow-Up	16-20	75	1500
Pre-CHMI	1	100	100
CHMI	1	250	250
Post-CHMI Initial Malaria Monitoring Phase	Up to 13	50	650
Post-CHMI Follow-Up	2	100	200
Unscheduled visit	N/A	50	--
Total *			**3,575**

*The number of visits will depend on your group assignment. Not all visits may be required of each study participant. Participants will be paid the maximum total for participation in each segment of the study. Total compensation will be unique for each participant. Payment amounts may be more than the planned maximum amounts if unplanned visits (e.g. evaluation of adverse events) are required.

If you earn $600 or more in subject payments from the University of Washington during a calendar year, the UW will report this to the Internal Revenue Service as Miscellaneous Income. This means we will ask you to provide us with your Social Security number.

In order to process your payment, we must enter your name, contact information for payment (e.g., email address or mailing address), and social security number into the UW's financial system. Your name and participation in this study will be visible to employees who handle financial transactions for the UW.

A description of this clinical study will be available on https://clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Consent presenter statement

By signing this consent form, I am attesting that I have provided the participant with information about this study. The participant has been given sufficient time to consider participation and I have answered any questions they had. The participant indicated that they understand the nature of the study, including risks and benefits of participating.

Participant's statement

By signing this consent form, I confirm that the study has been explained to me and I volunteer to participate in the research. I have had a chance to ask questions. If I have questions later about the research or feel I have been harmed by participating in the study, I can contact a member of the research team or the UW Human Subjects Division using the information listed above. I will receive a copy of this consent form.

Printed name of participant	Signature of participant	Date

☐ I give permission for the study team to use my leftover samples and information for secondary research. _____ (Initials and date)

☐ I do **not** give permission for the study team to use my leftover samples and information for secondary research. _____ (Initials and date)