MALI ADULT ENROLLMENT CONSENT FORM

Title of Research Project:
Controlled Human Malaria Infection models for evaluation of *Plasmodium falciparum* transmission-blocking interventions in healthy Malian adults

FMPOS Protocol #: 2021/335/CE/USTTB
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Site: Sotuba and surrounding area, Mali, West Africa

Participant's Name: _____
(first) *(last)*

Participant's Census ID Number: _____

PURPOSE OF STUDY

Malaria is a disease that affects many people in Africa, including in Mali. Malaria is caused by small germs, called parasites, that are carried by some mosquitoes. When a person is bitten by this kind of infected mosquito they get malaria. Most malaria infection causes mild symptoms such as fever or headache or sometimes no symptoms at all, but malaria can also be serious and kill men, women, and children. If a mosquito bites someone who is infected with malaria, it can carry the malaria parasites to someone else, causing them to become sick as well. If researchers can discover a safe vaccine that stops malaria being passed from one person to the next, it would be a very important thing for millions of people.

We are asking you to take part in a study in which we will simulate how malaria parasites are transmitted from people to mosquitoes. In this study we will first infect you with malaria parasites by an injection directly into your vein using a sterile needle and a syringe. Once these parasites have grown sufficiently, we will allow uninfected mosquitoes to bite you, to see if the malaria parasites can be passed to these mosquitoes. In this study we will not test any malaria vaccine, but in the future we will use this method to test vaccines that stop humans passing malaria to mosquitoes.

Most likely, we expect **that the malaria parasites will start to grow in your blood and that they may make you feel sick with symptoms of malaria.** But there is also a chance that the parasites

do not grow or that you do not feel sick with symptoms of malaria. This is because you live in an area with lots of malaria, and you have probably already developed natural protection against malaria infection over the years.
To be safe, we will monitor you very closely and take a small amount of blood almost every day to look for malaria parasites. As soon as you develop symptoms of malaria or the malaria parasites grow to a high level in your blood, we will treat you with medicines to kill or control the malaria parasites. After this we will continue to monitor you and may treat you again. This is described in more detail below. It will be very important for you to keep your scheduled clinic visits to ensure that you are diagnosed and treated quickly before moderate symptoms of malaria develop.

The Malaria Research and Training Center (MRTC) at the University of Bamako is leading this research project in Mali. We are working with scientists from Radboud University Medical Centre (RUMC) in the Netherlands and the National Institute of Allergy and Infectious Diseases (NIAID) in the USA. The sporozoites used for infection (PfPSZ Challenge) are produced by Sanaria, Inc. in the USA and the blood-stage parasites used for infection come from the Queensland Institute of Medical Research (QIMR) in Australia.

Your participation in this part of the study is extremely important as it helps researchers understand if this model can work in areas where malaria occurs commonly and if it can be used in the future to predict how malaria vaccines can work to stop the spread of malaria parasites.

It is your choice whether or not to participate in this study. If you decide to participate, you can change your mind and withdraw from the study at any time. If you decide to withdraw from the study later, please inform any member of the study team. This decision will not affect your participation in other studies. We will tell you about any new findings that may affect your decision to participate in the study.

STUDY PROCEDURES

Now we will explain the study and ask you if you want to participate.

You MAY be able to enroll in the study now if you are:

- male and between ≥18 and ≤50 years of age
- in good general health
- living in or around Sotuba
- willing and able to provide proof of identity
- available for the length of the study and willing to comply with all study procedures, including:
    - not travelling outside of the area during the entire study period

  - attending all study visits and willing to sleep in appropriate accommodation during most of the study
  - not donating blood during the study or until 6 weeks after the end of the study
- willing to take a human immunodeficiency virus (HIV), hepatitis B (HBV) and hepatitis C (HCV) test
- willing to allow your blood samples to be stored, as described below
- able to answer at least 80% of test questions about the study correctly

You <u>CANNOT</u> be in this study if you:

- have a medical or other problem which would make it more risky for you to participate in the study
- have received a malaria vaccine or very recently received other vaccines or blood products (if you have *ever* had a blood transfusion, please mention this to the study doctor)
- use or have used certain medicines which make it more risky for you to participate in the study, or which might affect the study results
- have lab results which may make it risky for you to participate in the study
- have had a severe allergic reaction or are allergic to certain anti-malarial drugs, to latex or to mosquito bites, or have recently participated in another study

(If you are uncertain about any of these things, please discuss them with the study doctor!)

<u>Screening:</u>

The screening process determines if you can participate in the study. This screening process may take several visits. If the visit is completed more than 4 months before your first study visit, we may have to repeat some of the tests. At your screening visit we will run tests on your blood to look for signs of illness or infection in your blood, kidneys, and liver and also test for HIV, HBV, or HCV. We will tell you all your test results and we will explain the possible meaning of these results to you. We will not store blood from this screening visit and we will use it only to find out if you can take part in this vaccine study.

We require all volunteers to have an ECG (electrocardiogram) test to look at the electrical activity through your heart. In order to complete the ECG we will need to put stickers on your skin on your chest, hands, and feet.

We may use some of your test results to help find out what normal results are in Malian adults and to check for malaria parasite and other infections in this area of Mali.

In the event that we discover a chronic illness and/or HIV, HBV, or HCV during the course of screening, the study will not reimburse long-term treatment and care, but we can refer you for continuing care.

Malaria infection:

In this study we will use different forms of live malaria parasites to infect volunteers. The forms of parasites carried by mosquitoes are called 'sporozoites'. About one week after these sporozoites enter the human body, they reach the blood where they grow inside red blood cells. These 'blood-stage' parasites are the ones that can cause symptoms of malaria. In this study we will infect volunteers *either* with sporozoites *or* directly with blood-stage parasites. In all cases we will inject the malaria parasites directly into your vein using a sterile needle and a syringe.

There are multiple groups within this study, called "Cohorts". We will infect volunteers in Cohort 1 with blood-stage parasites. We will infect volunteers in Cohort 2 with different, but related, blood-stage parasites. We will infect volunteers in Cohort 3 with sporozoites ('PfSPZ Challenge'). In all cases we will inject these live infectious malaria parasites directly into a vein, using a sterile needle and syringe.

Within each cohort, we will first inject 3 volunteers with a low number ('dose') of malaria parasites. If this does not cause safety problems, but results in insufficient malaria in the blood, we may inject 3 new volunteers in each cohort with a higher dose of malaria. If this also does not cause safety problems, but still results in insufficient malaria in the blood, we may inject 3 additional volunteers in Cohort 2 with the highest dose of malaria. Finally, we may inject an additional 7 volunteers in each cohort with the best dose of malaria. Apart from the form and dose of malaria parasites that we will inject, we will treat volunteers in each Cohort almost identically. **You cannot choose which Cohort you will participate in, or which dose of parasites you will receive.**

As described above, injection of live infectious malaria parasites may cause these parasites to grow in your blood and this may cause symptoms of malaria. To be safe we will therefore monitor you very closely and take a small amount of blood almost every day to look for malaria parasites. As soon as you develop symptoms of malaria, we will treat you with a medicine against malaria called piperaquine. We will also treat you with piperaquine if the level of parasites in your blood becomes too high, even if you do not have symptoms of malaria. It will be very important for you to keep your scheduled clinic visits to ensure that you are diagnosed and treated quickly before moderate symptoms of malaria develop.

The piperaquine medicine will kill most of the parasites in your blood, but not all. We will therefore continue to monitor you. If the level of parasites again becomes too high, or if you again develop symptoms of malaria, we will treat you again with piperaquine. Meanwhile, we will keep checking the malaria parasites in your blood. Once the parasites have developed sufficiently, we will allow uninfected mosquitoes to feed on you. To do this, we will hold two cups, each containing 30 mosquitoes, against the skin of your forearm or lower leg so the mosquitoes can bite you. We will do this on up to 3 different days.

The study will last up to 8 weeks, but we may end the study early if you develop high levels of malaria in your blood or symptoms of malaria for a third time. We may also end the study early if the malaria parasites do not grow in your blood at all, or if the study doctor thinks it is important for your health. In any case, at the end of the study, we will treat you with another antimalarial medication called artemether-lumefantrine (Coartem), which is approved and commonly used in Mali. We will also treat you with an extra medicine called primaquine. This combination of medicines will ensure that all the malaria parasites in your blood are killed at the end of the study.

The infectious malaria parasites used in this study have been used before in many other studies. The sporozoites (PfSPZ Challenge) have been used in many studies in Africa (including in Mali), Europe and the USA. The blood-stage parasites have been used in studies in Australia and Europe, but not yet in Africa. In total, thousands of volunteers have participated in these kinds of studies.

All volunteers will be seen in clinic almost every day to check for malaria parasites in the blood, ask about your health and any symptoms you may be experiencing. We will also take blood periodically to look for any side effects from being exposed to malaria parasites and to look at your immune response to this exposure. Each clinic visit will last about 30 minutes to 2 hours and we will ask you how you are feeling and examine you. If you are carrying malaria parasites, we may ask you to give some additional blood to see if the parasites in your blood can infect mosquitoes and for research to look at your parasites more closely and at your immune system response to the malaria parasite. At most clinic visits we will take blood.

If you become sick at any time, we want you to come to the clinic so that we can examine you. You do not have to wait for your scheduled visit. A study doctor will be available at the study clinic 24 hours a day throughout the study period. If you are sick from malaria, you will be treated and can continue in the study unless the clinician determines you are too ill to be in the study any further.

If you develop a rash or other injection site issues, we may ask to take a photo of this finding. These photographs will not include your face.

If you are in the study, we will make a card with your name you to keep, so that we can be sure to identify you correctly. This will also contain study (contact) details to inform other healthcare providers and in case you or any healthcare providers needs to contact the study team.

RISKS AND DISCOMFORTS

These are some of the risks and discomforts you may have if you participate in the study.

Blood Draws

- Can cause pain, bruising, bleeding, sometimes lightheadedness or fainting, and rarely infection. The frequency and amount of blood that will be required for this study should not put you at risk for anemia or compromise your overall health. The total amount of blood you will give *during the entire study* will be less than the amount that people can safely give in one go for blood donation.

Study Medications - *Antimalarial Medications*

- All medicines used to treat malaria in this trial have an excellent safety record. Some common side effects for each of the drugs are listed below.
- Volunteers with known bad reactions to the medicines used in this study are not allowed to be in the study.

piperaquine (PPQ)

- The most commonly reported side effects of PPQ include: headache, changes in the electrical activity of the heart, fast heartbeat, weakness and fever. Uncommon side effects include: loss of appetite, cough, nausea, vomiting, diarrhoea, abdominal pain, changes of heart rhythm, liver abnormalities, itching, muscle or joint ache, dizziness and fitting, but generally these effects do not require people to stop using the drug.

artemether/lumefantrine (AL, Coartem)

- The most commonly reported side effects of AL include: headache, loss of appetite, dizziness, weakness, muscle pains, and joint pains, but generally these effects do not require people to stop using the drug.

primaquine (PQ)

- The most commonly reported side effects of PQ include: nausea, vomiting, heartburn and stomach cramps. In some people use of high doses of PQ can cause a drop in levels of red blood cells, but at the dose used in this study this should not occur.

Experimental Malaria Infection

Injection of blood-stage parasites or sporozoites (PfSPZ Challenge)

- Reactions at the site of the injection may include pain, redness, itching, bruising, pain with moving the arm, small lumps, and/or swelling. Other side effects like fever, chills, upset stomach, vomiting, loss of appetite, headache, diarrhea, tiredness, and muscle or joint pain may also occur, even several weeks after injection. These symptoms may be severe and may require a medication such as paracetamol. Typically these symptoms go away after 1 dose of this kind of

medicine. Some of these symptoms may be due to a mild malaria infection thus you will be evaluated promptly for diagnosis.

- Injection with blood-stage parasites may in theory cause your body to create an immune response against some other people's red blood cells. This risk is considered extremely low, and has in fact never yet been seen following parasite injection.
- With any injection of a study product there is a small chance that a sudden, severe allergic reaction can occur, which can cause death. This reaction can start by tongue swelling, feeling lightheaded, or having trouble breathing. Because of this, you will be watched carefully for at least 30 minutes.

Malaria infection

- You may develop symptoms of malaria infection. The most common symptoms of malaria infection include headache, tiredness, muscle aches, back pain, joint aches, generalized body aches, fever, sweats, and chills. Less common side effects include upset stomach, vomiting, diarrhea, abdominal discomfort, cough, and dizziness.
- Infection with malaria in this study is diagnosed early and we will treat you quickly if you develop symptoms of malaria or if the level of parasites in your blood becomes too high. Also you may also have symptoms of malaria after treatment has started.
- Because the malaria infection in this study is treated early, it probably does not cause any permanent damage to your organs or long term medical problems. However, malaria infection that is not treated can cause severe illness including possible kidney, liver and/or heart problems, seizures, coma and even death.
- In order to avoid complications of malaria, it is extremely important that you follow the recommendations of the study staff and complete all required study visits and take all the drugs.
- You cannot give malaria to others, but there is a small risk you could give malaria to mosquitoes that bite you. You will be required to sleep with a bed net every night when on study, and use insect repellant if directed.

Risks of Specific Interest

- ***Heart Problems.*** There is no known specific heart risk for healthy volunteers receiving experimental malaria infection injected sporozoites (PfSPZ Challenge). Heart problems when individuals have clinical malaria are extremely rare but can happen. Due to a few individual reports of heart problems in study volunteers undergoing malaria infection by mosquito bite or blood-stage parasites, we will not

include individuals with an existing heart problem. We will screen for heart problems by asking about your medical history and that of your direct family. We will also ask you about any symptoms of heart disease and perform an ECG on you.

- ***Liver problems.*** In some volunteers undergoing experimental malaria infection in Europe and Australia, blood tests have shown temporary liver abnormalities. We think these abnormalities are a normal response to malaria infection and treatment and they go away again by themselves. Such abnormalities are generally not seen in studies in Africa in volunteers who have previously had malaria. To be on the safe side, we will not include volunteers who are at risk of liver disease and we will check in your blood for signs of liver damage.
- ***Blood problems.*** One volunteer in Australia developed very low levels of white blood cells after experimental malaria infection. This was probably also a response to the malaria infection. It has not been seen in studies in Africa. If you have symptoms of malaria infection during the study we will check levels of your white and red blood cells.

Genetic Testing

- There is the possible risk that we discover a genetic characteristic that may suggest a risk of disease for you or your family or that we discover undisclosed family relationships.

Other Risks

- It is unknown if the experimental malaria infection may alter your response if you ever have malaria infection in the future. We will inform you of any significant health effects and serious side effects if they occur in other subjects.
- There may be side effects from the experimental malaria infection with blood-stage parasites or sporozoites (PfSPZ Challenge), even serious or life threatening risks that we do not yet know about. We will monitor you for all side effects including any new symptoms. Please tell your study team about any side effects you think you are having. This is important for your safety.

ALTERNATIVE TO PARTICIPATION IN THIS STUDY

Your alternative is not to participate in this study.

BENEFITS

You will not receive any direct benefit from being in this study. You will not receive a malaria vaccine. Your participation in this study is important to simulate how malaria parasites are transmitted from people to mosquitoes, so that in the future researchers can use this kind of

study to test vaccines and drugs that prevent malaria parasites being passed on to other people. The information we learn will help in the development of a vaccine to prevent transmission of malaria parasites, which would be used in Mali and in other parts of the world where malaria is a problem.

NUMBER OF PEOPLE IN THE STUDY

A maximum of 42 male adults between the ages of 18 to 50 will be enrolled into the study.

DURATION OF STUDY FOR EACH PARTICIPANT

Participants will be in the study for a maximum of 8 weeks. How long and often you will be seen during the study will depend on if or when you develop malaria.

COMPENSATION

If you participate in this study, you will be given compensation in kind (for example, rice or millet) or cash equivalent to a total value of approximately USD $6 - $162 or CFA 3,000 – 78,000. How much you are compensated will depend on how many visits you complete, if you have unscheduled visits with research blood draws, and how long you are in the study.

CONFIDENTIALITY

We will keep your health information private. We will keep all files with information that could identify you in locked cabinets. We will mark samples of blood that we collect from you with a number that tells the study team that it is your blood. We will not mark these samples with your name.

People responsible for making sure that the research is done properly may look at your study records. This may include people or their representatives from the Malaria Research Training Center (MRTC) at the University of Bamako, RUMC, NIAID, Sanaria Inc., QIMR, the Mali regulatory body, the United States Food and Drug Administration (FDA) and the World Health Organization. All of these people will also keep your identity private as much as possible.

COMPENSATION FOR INJURY

If you are enrolled in this study, you will receive free medical care for acute illnesses during the duration of the study (maximum of two months) at the Sotuba study clinic. We will provide treatment for malaria and other illnesses to you according to the standard of care that is available in Mali, and it will be free. We cannot provide treatment for chronic illnesses. We will refer you for care if needed. A study doctor will be available at all times while you are in the

study to check on you and treat you for any short-term health problems, and for any problems resulting from your participation. Insurance is available to take care of you in case of injury or illness related to this study.

STORED SAMPLES AND FUTURE RESEARCH

We may take extra blood and tissue samples and store them for future research. These samples will help us learn more about malaria or other health problems. The research tests we will use may not be like medical tests. We may not know how the results relate to your care. Therefore, we may not put future test results in your medical record or study chart. However, if you ask, someone on the study team will discuss the test results with you. We will not share these test results with your private doctor unless you ask us to do so. The blood that is stored will be what is left over from the tests that are done during the study. Some of these tests will tell us about how your body fights malaria. Your blood will be stored at the MRTC in Bamako, at RUMC in the Netherlands, or at NIAID in the United States.

By agreeing to participate in this study, you do not give up any rights that you have regarding access to and disclosure of your records. For further information on those rights, please contact Prof. Issaka Sagara (Tel: +223 2022-8109 or Tel: +223 6675-3731).

Labeling of Stored Samples

We will label your stored samples with a code that only the study team can link to you. We will keep any information that can be traced back to you private to the extent permitted by law.

Future Studies

Other investigators may want to study your stored samples. If so, the study team may send your samples to them without any information that can be traced to you. The study team may also share information such as your gender, age, health history, or ethnicity. In some cases, an Institutional Review Board (IRB) will review new research that uses your samples. The IRB is a committee that oversees medical research studies to protect volunteers' rights and welfare.

Investigators will use your samples *only* for research. We will not sell them. Future research that uses your samples may lead to new products, but you will not receive payment for these products. Some future studies may need health information (such as smoking history or present health status) that we don't already have. If so, the study team may contact you for this information and to obtain permission to access your medical records.

Genetic Testing

Some of the blood drawn from you as part of this study may be used for genetic tests. Genetic tests can help researchers study how health or illness is passed on to you by your parents or from you to your children. Any genetic information collected or discovered about you will be

kept confidential. Records containing this information will be kept on password-protected computer systems and in locked and secured locations. We will not release any information about you to people outside of the study without your written permission. Some genetic information, such as the name of your diagnosis, may be on your study chart. Researchers who will have access to genetic information about you will take measures to maintain the confidentiality of your genetic information.

Some of the blood drawn from you as part of this study may be used for a test for HLA type, which is a genetic test of markers of the immune system. For research, HLA testing might be used to try to identify factors associated with the development or severity of diseases. Some HLA types have been associated with an increased risk of certain diseases like arthritis and other rheumatologic problems. However, simply having those HLA types doesn't mean you will develop these diseases.

Following genetic testing, your sequence data may be shared in a public database for other investigators to benefit from it. However, no personal, identifiable information will be shared in this process, as the shared results will be coded with no link back to you.

Benefits

In general, future research that uses your samples will not help you, but it may help us learn what causes malaria or related conditions. This research may also help us learn how to prevent or treat malaria.

Risks

The risk is that someone may take information from your medical records without your permission. The chances of this happening are very low. If this information becomes available, you may face discrimination when you apply for insurance or a job. You may also have similar problems if you share the information yourself or allow us to release your medical records.

Making Your Choice

The choice to let us store your samples for future research is up to you but you will not be eligible to participate if you do not want your samples stored for future research. If you agree to let us store your samples now, you can change your mind later. If you wish to withdraw your consent for your samples to be used in future research, please contact us and say that you do not want us to use your samples for future research.

QUESTIONS

If you want to talk to anyone about this research study because you think you have been hurt by being part of the study, or you if have any other questions about the study, you should tell the study team. They will ask the Principal Investigator, **Prof. Issaka Sagara** (Tel: +223 2022-8109) or (Tel: +223 6675-3731) or **Prof. Mahamadou S Sissoko** . (Tel. (+223 7507-5836) to talk to you.

Also, you can contact the people at the **Faculty of Medicine of Pharmacy and Odonto-Stomatology (FMPOS) Ethical Review Committee** at Point G, Bamako (Tel: 2022 52 77) for example, the President of the Ethics Committee, **Pr. Mamadou Marouf Keita (Tel 66 72 20 22)**; or the Permanent Secretary, **Pr. Mahamadou Diakité**, (Telephone: 2022 52 77, Cell: 76231191) to answer questions you may have about being part of this study and your rights as a research participant.

A description of this trial will be posted on Clinical Trial Registry. The website will include a summary of the results of the trial; and will not include any information that can identify you.

If you have any questions about this research study, you may ask someone on the study team. You can also ask questions in the future if you do not understand something that is being done to you.

If you agree you to participate in this study, please sign or put your fingerprint below.

_____ Date: ___ / ___ / __
Signature or fingerprint of volunteer *dd mm yy*

_____
Name of volunteer

_____ Date: ___ / ___ / ___
Signature of Investigator *dd mm yy*

_____

Name of Investigator

Complete if participant is illiterate:

Witness to Consent Interview

On the date given next to my signature, I witnessed the consent interview for the Research Study named above in this document. I attest that the information in this consent form was explained to the subject, and the subject indicated that his/her questions and concerns were adequately addressed.

Name of Witness _____
(first) (last)

Signature of Witness _____ Date: ___ / ___ / ___