# PARTICIPANT INFORMATION SHEET AND CONSENT FORM

## PARTICIPANT INFORMATION SHEET

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| **Title** | An open label phase 1b study to characterise the pharmacokinetic/pharmacodynamic relationship and safety of MMV367 in healthy adult participants experimentally infected with blood stage *Plasmodium falciparum* |
| **Protocol Number** | MMV_MMV367_22_01 |
| **Sponsor** | Medicines for Malaria Venture (MMV) |
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| **Version / Date** | Version 3.0/ 14 July 2023 |

### 1. Introduction

You are invited to take part in this study because you are assumed to be healthy, aged 18 to 55 years old, and have not previously had malaria.

This Participant Information Sheet and Consent Form tells you about this study. It explains the tests and treatments involved and will help you decide if you want to take part in this study.

Please read this information carefully. You are encouraged to ask questions until you are sure that you fully understand the study, its benefits and risks, and the study requirements. Before deciding whether or not to participate in the study you can also discuss any of these details with a relative, friend, or your doctor.

Participation in this study is voluntary. You may refuse to take part or withdraw from this study at any time and without any prejudice to being considered for any future trials or treatment at UniSC Clinical Trials or Queensland public hospitals. You may be withdrawn from the study if the doctors feel it is best for you, or if you do not comply with the requirements of the study. The study sponsor can also stop this study at any time for clinical or administrative reasons.

If you decide you want to participate in the study, you will be asked to sign the consent section.

## 2. What is the purpose of the study?

Malaria is an infectious disease caused by *Plasmodium* parasites that are carried by *Anopheles* mosquitoes. Natural malaria infections occur when an infected mosquito bites a human and injects the malaria parasite into the blood. Millions of people around the world become sick and approximately 619,000 die from malaria each year, particularly in Africa and South East Asia, since *Anopheles* mosquitoes are mostly found in hot and humid regions of the world. *Anopheles* mosquitoes are not found in South East Queensland, but can be found in far north Queensland. Fortunately, malaria was eliminated from Australia in the 1980's.

Current approaches to controlling malaria around the world are failing because the malaria parasites have become resistant to the antimalarial drugs we have available (this means the parasites are no longer killed by the drugs or they take longer to be killed by the drugs). This is why we need to develop and test new antimalarial drugs.

Medicines for Malaria Venture (MMV; a not-for-profit organisation developing new drug treatments for malaria, and GSK plc (a global pharmaceutical company) are working together to develop MMV367, a new test medicine to treat malaria. The Clinical Research Organisation involved in monitoring the study and acting as the local sponsor is Southern Star Research (SSR; Sydney, Australia).

MMV367 was found to be very effective at killing malaria parasites in the laboratory and in animal models.

Antimalarial drugs are usually tested in clinical trials in patients who live in regions of the world where malaria is common and who have been naturally infected with malaria (that is, a malaria infected mosquito has bitten them). However, this process can be lengthy and logistically difficult. One way of speeding up this process is to test the drugs in healthy volunteers who have been deliberately given malaria under controlled experimental conditions. To do this, we infect healthy adult volunteers by injecting them with a small number of malaria parasites (we call this a malaria inoculum).

The purpose of this study is to test the antimalarial activity of MMV367 in healthy volunteers who are experimentally infected with malaria parasites. In this study we will be investigating *Plasmodium falciparum* 3D7 (called *P. falciparum* 3D7 for short). We hope to enrol up to 18 healthy male or female adults who have never had malaria. The results of this study will determine whether MMV367 can be tested in malaria endemic regions, and help decide which doses of the drug should be tested in these trials.

## 3. What does participation in this study involve?

If you choose to participate in this study, you will be deliberately infected with malaria parasites (malaria inoculation). Malaria parasites contained within human red blood cells will be injected into a vein and we will closely monitor the growth of the parasites in your blood over the course of the study by collecting regular blood samples and conducting very sensitive laboratory tests.

You will be admitted to the clinical unit (UniSC Clinical Trials, Morayfield) in the evening of the seventh day after malaria inoculation, and stay for 4 nights to ensure your doctor can closely monitor you for safety purposes. You will be given a single dose of MMV367 after an overnight 8 hours fast as an oral suspension (liquid) to swallow 8 days after malaria inoculation. By this time, you may have early symptoms of malaria, which may include headaches, fever, aches, and pains. During your stay within the clinical unit, the study team will also collect frequent blood samples from you to measure the number of parasites in your blood and to measure the concentration of MMV367 in your blood.

After your 4-night stay within the clinical unit, you will be allowed to leave if you are well enough. If you are feeling unwell, the medical team may decide to extend your stay in the clinic for your safety. You will be

requested to return to the clinical unit (Southbank clinic) for further tests on specific days over the next 2 weeks.

We expect the dose of MMV367 will initially reduce the number of parasites in your blood, and any symptoms of malaria you may have will improve within a few days. However, the dose of MMV367 you receive might not kill all the malaria parasites in your blood. Therefore, you will be given definitive antimalarial treatment before the study is complete. Definitive antimalarial treatment consists of one or more antimalarial medications that we know will completely clear all malaria parasites from your blood. These medications are all approved in Australia for the treatment of malaria.

The timing of the definitive antimalarial treatment will depend on the growth of parasites monitored in your blood and any symptoms of malaria you may be experiencing. However, the definitive antimalarial treatment will occur no later than 24 days after you were infected with malaria parasites.

During the entire study, your health will be monitored by a study team who are experienced in conducting malaria volunteer infection studies.

Typical procedures that will be performed during the study include:

- **CANNULATION:** Insertion of an indwelling cannula into a vein in your forearm. This may cause minimal discomfort. A cannula is a small, flexible tube that allows blood to be collected easily and injections to be given without the need for repeated needle insertions for each blood sample or injection.
- **PHYSICAL EXAMINATION:** Medical examination of your body and measurement of your weight and height.
- **MEDICAL HISTORY:** Check of medical issues or procedures you have had in the past**.**
- **DEPRESSION QUESTIONNAIRE:** A written questionnaire to determine if you may be suffering from depression.
- **MEDICATIONS:** Check of medications you may be taking now or in the past.
- **VITALS:** Measurement of body temperature, heart rate, rate of breathing, and blood pressure.
- **BLOOD SAMPLING:** Collection of blood samples (with a cannula or a needle) for medical tests to assess your health (including viral hepatitis and HIV testing), and to measure the number of parasites and concentration of MMV367 in your blood.
- **COVID-19 TEST:** A swab from your nose will be taken to test for COVID-19. If you test positive you will not be allowed to continue in the study.
- **URINE SAMPLING:** Testing of your urine to assess your health (e.g., kidney function and abnormal presence of sugar).
- **URINE DRUG SCREEN:** Testing of your urine for drugs of abuse (e.g., cannabis and cocaine). If you test positive you will not be allowed to continue in the study.
- **ALCOHOL BREATH TEST:** If you test positive you will not be allowed to continue in the study.
- **ELECTROCARDIOGRAPH (ECG):** ECGs involve attaching leads to your chest to record the electrical activity of your heart
- **PREGNANCY TEST:** For females, pregnancy testing and/or follicle stimulating hormone testing for postmenopausal status, as required. Tests may be done from blood or urine.

Note: Please be aware that if blood tests reveal that you have HIV (also called the “AIDS virus”) or viral hepatitis, the laboratory conducting the test is required under the *Queensland Public Health Act 2005* to inform the Queensland Health Department of these results. Your name will be kept anonymous. However, if requested by the Queensland Health Department, the laboratory may disclose your name to the Chief Executive of the Queensland Health Department. If you are found to have HIV or viral hepatitis, you will be referred to appropriate counselling and/or medical services. The clinical unit will also be informed of these results (as for all the data collected during the study) but will not disclose your identity to any third party.

## 4. What is the duration of the study?

The total duration of your participation in the study is a maximum of 8 weeks from screening until the end of the study. This includes the initial screening period of up to 4 weeks and participation in the trial (approximately 4 weeks).

This study is divided into the following phases:

- Screening and confirmation of eligibility visits to the Southbank clinic (up to 4 weeks before malaria inoculation).
- Malaria inoculation at the Southbank clinic (Day 0).
- Malaria monitoring follow-up by phone (Day 1 to Day 3) and daily visits to the Southbank clinic (Day 4 to Day 7).
- Start in-patient stay at the Morayfield clinic (Day 7 PM).
- MMV367 administration (Day 8).
- End in-patient stay at the Morayfield clinic (Day 11 AM).
- Outpatient visits to the Southbank clinic up to approximately 3 times per week (Day 12 to Day 24).
- End of study visit at the Southbank clinic (Day 27).

Over the course of the study, you will have to visit the Southbank clinic up to approximately 15 times, and the Morayfield clinic once (for the 4 night inpatient stay).

On the malaria inoculation day (Day 0), you must remain at the Southbank clinic for at least 1 hour after you are injected with the malaria parasites. After that time, if your vital signs are normal, you will be free to leave the clinic.

You will be required to stay within the Morayfield clinic for 4 nights, from the evening of Day 7 until the morning of Day 11.

In the unlikely event that you still have symptoms or laboratory tests reveal any abnormalities on the day of the planned end of study (Day 27), you may be asked to return to the Southbank clinic a few times so we can make sure these issues are resolved.

## 5. How will I be compensated for my time?

If you are eligible to be enrolled in the study, you will be reimbursed $25.00 for each scheduled phone contact, $150.00 for each outpatient visit at Southbank, and a rate of $750.00 per night for your in-clinic stay at Morayfield. The total payment for participants who complete the entire study will be approximately $5,000. The exact amount you receive will be dependent on the number of out-patient visits you are required to attend (this will be influenced by the timing of your definitive antimalarial treatment). All payments are in Australian dollars.

We may recruit extra volunteers who will attend the clinic on the first malaria inoculation day, but may end up not taking part. These volunteers are called reserves. Reserves only participate if one or more volunteers are withdrawn by the study doctors or if they withdraw themselves before they are given the malaria inoculation. You will be told if you are a reserve volunteer on the first malaria inoculation day. All reserves are reimbursed for their time in the recruitment process, even if they do not end up participating in the study. If you are a reserve participant, and do not complete the entire study you will be reimbursed $150.00 for each outpatient visit.

Regardless of whether you withdraw early or complete the study, you will be reimbursed after the end of study visit via electronic funds transfer directly into your bank account. Should you withdraw from the study before the final visit you will receive a partial payment according to the number of visits you have attended.

Reimbursement figures are calculated from a formula that provides for the reimbursement of time, travel costs, the number of visits you make to the clinic, and your inconvenience. This reimbursement is not made for undergoing risk nor is it to compensate you for any loss of earnings as a result of your participation. If you decide to withdraw early from the study or you are withdrawn from the study by a member of the study team, you will receive pro-rata payment.

We will not make deductions for any taxes from these payments — you are solely responsible for reporting this payment in your tax return and for the payment of any taxes due.

To obtain valid clinical data and to follow up your safety, it is best that you complete the study where possible.

Your participation in this study does not entitle you to a payment or compensation for any commercialisation of the intellectual property associated with or discovered during the conduct of this study.

There are no additional costs associated with participating in this study. All medications, tests, and medical care required as part of the study will be provided to you free of charge. Any meals provided to you during your stay at the Morayfield clinic will be free of charge.

## 6. What are my obligations and responsibilities during the study?

For your safety, you will need to be contactable at all times by mobile phone and available for the duration of the study. It is a condition of this study that you must identify and provide contact details of a support person who is aware of your participation in the study and is available to provide assistance if required at any stage during the study. With their permission, we ask you provide contact details of this support person. Should the study team not be able to contact you for more than 36 hours local police support will be requested to locate you so you can receive definite antimalarial medication.

In order to provide maximum protection for your health, the study will be under the direct supervision of a doctor and will be conducted by trained personnel. Please provide us with all the information about your current and past health (medical history) at the screening visit. We need this information to protect your health.

It is very important that you come to all the clinic visits at your scheduled time. Call the study staff immediately if you have a problem getting to the clinic on time. It is very important that you follow instructions from the study staff because delaying treatment may lead to serious outcomes, including coma or death, if you are not treated.

You MUST contact the study staff at any time (even at night) if you develop a fever of 38°C or higher or you are experiencing symptoms that are moderate or severe or affecting your ability to complete activities you usually do. You must come to the clinic if the staff ask you to, for your own health and safety.

If you choose to participate in this study, you must also observe the following restrictions:

<u>Medicines</u>

- You must not take prescription or non-prescription drugs, herbal supplements, or receive any vaccinations in the 2 weeks (or longer depending on the drug) before the day you are inoculated with malaria or during the study unless approved by the study staff (e.g., the use of contraceptives and hormonal replacement therapy will be permitted).
- You must immediately contact the study staff if you need to take any prescription or other medication not given to you by the study staff.

- Recreational drug use is not permitted during the study. Urine testing for evidence of drug use will be undertaken during screening, on the day of malaria infection, and on the day of MMV367 administration.
- If you are experiencing malaria symptoms during the study and need a symptomatic treatment, we prefer that you take ibuprofen (e.g., Nurofen®) as treatment and avoid taking paracetamol (e.g., Panadol®) unless agreed first with the study doctor. It is best to avoid paracetamol because it may worsen the liver inflammation that is sometimes observed with the malaria infection.

Food and beverages

- While in the Morayfield clinic, you must only consume the standard meals provided.
- You will be required to fast for at least 8 hours before your screening visit and before you are administered MMV367 (Day 8 AM). After you are given MMV367, you will be required to remain fasted for an additional 4 hours.
- You must not eat any food that contains poppy seeds in the 24 hours before the following time points because it may result in a positive urine drug test: screening visit, malaria inoculation day (Day 0), and day of admission to the clinic (Day 7 PM).
- You must not drink or eat any beverages or food that contain alcohol (e.g., beer, wine, and mixed drinks) during your in-patient stay at the clinic and 24 hours before the following time points: screening visit, malaria inoculation day (Day 0), and day of admission to the clinic (Day 7 PM).
- Additionally, you should not drink more than 2 standard drinks of alcohol per day at other times during the study.
- You must not consume quinine containing foods/beverages (e.g. tonic water, lemon bitter) throughout the study.
- You must limit consumption of any beverages or food that contain xanthine bases (e.g., Red Bull, coffee, chocolate) throughout the study. You should not consume more than 400 mg caffeine per day, equivalent to more than 4 cups of coffee.

Exercise

- You should avoid strenuous exercise and not increase your regular exercise activity during the study.
- When you are confined in the Morayfield clinic, you will not be allowed to do any activity that is more vigorous than walking.

Smoking

- Smoking will not be permitted during this study.
- This includes the use of e-cigarettes, vaping, and other nicotine use.

Sexual activity and contraception

Males:

- If you are not surgically sterile or with a female partner that is not surgically sterile, you must agree to use a double method of contraception including condom plus diaphragm, or condom plus intrauterine device, or condom plus stable oral/transdermal/injectable hormonal contraceptive by the female partner, from the time of informed consent through to 94 days after MMV367 administration (approximately 4 months in total).
- If abstinent, you must agree to start a double method of contraception if you start a sexual relationship with a female partner during the study, and through to 94 days after MMV367

administration.

- You should not donate sperm or father a child from the time of informed consent until 94 days after MMV367 administration.
- If your partner becomes pregnant within 94 days from MMV367 administration you must inform the study doctor immediately. For the sake of safety, it is important for the sponsor and the study doctor to follow-up on the pregnancy until the end, to check if there are any effects on the child.

Females:

- If you are of childbearing potential, you must be using an insertable/injectable/transdermal or combination oral contraceptive combined with a barrier contraceptive from the time you give informed consent through to 34 days after MMV367 administration.
- If abstinent, you must agree to start a double method of contraception if you start a sexual relationship with a male partner during the study, through to 34 days after MMV367 administration.
- You must not be planning in vitro fertilisation (IVF) within the required contraception period.
- If you become pregnant within 34 days from MMV367 administration you must inform the study doctor immediately. For the sake of safety, it is important for the sponsor and the study doctor to follow-up on the pregnancy until the end, to check if there are any effects on the child.

Travel

- You must not travel to areas where *Anopheles* mosquitos are present (which includes far north Queensland and some areas of Africa, south-east Asia, and South America) during the study.
- Please discuss any travel plans you have with the study doctor.

Blood donation

- You will be unable to donate blood to The Australian Red Cross Lifeblood or other blood donation service for 12 months after you complete the study.
- Additionally, there is a chance that after this 12 month exclusion period the blood donation service may only allow you to donate plasma if they detect malaria antibodies when they test your blood. Plasma is a component of blood where the blood cells have been removed.
- There are no health concerns for you associated with having malaria antibodies in your blood (you may or may not have these antibodies).
- If blood donation is important to you, we encourage you to discuss these issues with the study doctor before you decide to take part in this study.

## 7. Is there any benefit for me to participate in the study?

You will not receive any direct personal benefit from participating in this study, except for information about your general state of health. Participating in this study will not protect you from developing malaria in the future if you travel to a country where malaria is common. You should follow recommendations from your health care provider to prevent malaria when you travel.

Information collected during the study may be useful for treating patients with malaria in the future.

## 8. What are the risks and disadvantages of taking part in this study?

Potential risks of receiving red blood cells from a donor

This study involves the injection of malaria parasites into your blood that are contained in human red blood cells. These red blood cells were collected from a volunteer who got malaria when they were bitten by an

infected mosquito. This raises several possible risks:

- Risk of infection with viruses or organisms (other than malaria) contained in the blood from another person. This risk is considered small for several reasons. Firstly, the donor was screened and tested negative for the presence of active blood borne infections. Also, the Australian Red Cross Lifeblood removed white blood cells from the donor blood to lower the risk of a transfusion-transmissible infection. Lastly, the volume of blood associated with the malaria inoculum is many thousands of times smaller than in a transfused unit (i.e., a relatively lower risk of infection). No blood borne infections have been reported in any of the 400+ participants who have received the *P. falciparum* 3D7 malaria inoculum in previous studies.

- Risk that you could have a 'transfusion reaction'. The risk of a transfusion reaction is unlikely. This is because of the extremely small quantity of donor blood in the malaria inoculum, and because the white cells have been removed from the donor blood in the inoculum. Nevertheless, you will be monitored closely for one hour after you are given the malaria inoculum.

- Risk that you could develop antibodies (a protein that can protect the body from foreign organisms, such as bacteria and viruses) to the donor red blood cells that may make blood transfusion more difficult in the future is very small. This is because the donor of the red blood cells had blood group O Rh (D) negative blood. People with this blood group are considered 'universal donors', because people who receive even large volumes of blood from them are unlikely to develop red blood cell antibodies. Nevertheless, as a precaution, you will be tested for red blood cell antibodies at your screening visit and at the end of study visit. Women of childbearing potential have a small additional risk of developing red cell antibodies that could cause problems during pregnancy. Women of childbearing potential have participated in several malaria challenge studies with no known issues to date.

<u>Potential risks associated with the malaria infection</u>

- Untreated *P. falciparum* malaria infection can be fatal. However, as long as you take the definitive antimalarial treatment as directed by the study staff there is minimal risk of you developing a severe malaria infection. The study doctor will closely monitor the number of parasites in your blood (by taking blood samples) and also closely monitor you for malaria symptoms. The definitive antimalarial treatment can be given at any time during the study to ensure your safety and it will completely cure you of malaria.

- More than 400 healthy volunteers have been given the *P. falciparum* 3D7 malaria inoculum in previous studies to test antimalarial drugs. Severe malaria was not observed in any of these volunteers. Symptoms commonly reported by these participants have included: headache, fever, fast heart rate, muscle aches, sweating, nausea, stomach pain, and fatigue. Additionally, laboratory testing of blood samples has commonly found decreased white blood cell counts, and in a few cases, increased levels of liver enzymes. These abnormal laboratory results have all been temporary, returning to normal levels over a few days or weeks. Two participants developed unexpected cardiac events in a previous study, although an independent cardiologist concluded that these conditions were present before the participants were infected with malaria.

<u>Potential risks associated with the study drug (MMV367)</u>

To assess the potential risk of treating humans with MMV367, non-clinical (i.e. animal) studies were conducted in two species (rats and dogs). Risks based on animal studies:

- In animal tests with single doses of MMV367, no effects were noted on the nervous system (brain) function. Small increases in blood pressure and heart rate were seen at the highest tested doses in dogs, and small changes to heart monitoring (ECG) and a small drop in body temperature were seen in rats. Changes in breathing were noticed in rats at the highest tested doses.

- In animals given daily doses of MMV367 for 7 days, reduced food intake, weight loss, and changes in cells in the adrenal glands (glands above the kidneys which make hormones) were seen in rats. In dogs, vomiting and reversible weight loss were seen at the mid-to-high dose level. The side effects observed in rat adrenal glands are believed to be stress-related, and not directly caused by MMV367.

Risks based on human studies:

- MMV367 was evaluated for the first time in male and female healthy adult volunteers in a "First-In-Human" study recently completed in the UK. In this study, a total of 47 volunteers were administered MMV367 (at various doses from 100 mg to 1500 mg) or a matched placebo. While the results of the study are still blinded (i.e., we do not know yet who received the test medicine MMV367 or the placebo), 2 adverse events – both of mild intensity - were considered as related to either MMV367 or placebo treatment.

- The reported side effects in this initial human study were one report of abdominal pain and one report of stomach pain (in the same volunteer).

- The highest possible dose of MMV367 you might receive if you decide to participate in this study will be 1500 mg administered as a single dose in a fasted state. This dose was previously tested in the First-In-Human study and was considered safe and well tolerated.

- As with any new test medicine, there may be side effects or risks associated with MMV367 that are unknown.

- You should notify the study staff immediately if you experience any of the side effects specified above, or any other side effects during the study.

- All drugs, including MMV367, have the potential to cause severe isolated reactions, such as an allergic reaction, which may be life-threatening.

Risks related to Pregnancy:

- There is little information available about the effect of MMV367 on an unborn child and so currently we don't know if it may cause a risk to the baby as it grows during pregnancy. Taking the study drug may involve some risks to a human unborn baby or nursing infant. Therefore, you cannot join this study if you are pregnant, if you are planning to become pregnant in the next two months, or if you are breast-feeding.

- All women of childbearing potential willing to be enrolled in a clinical study with MMV367 will have pregnancy tests at screening and during the study and will be requested to follow specific contraception rules.

<u>Potential risks associated with the definitive antimalarial medications</u>

- The definitive antimalarial medication you are most likely to be given to completely clear all malaria

parasites from your blood before you complete the study will be Riamet® (three-day oral course). You may also be given Primacin® (single oral dose), which specifically kills the form of the malaria parasite transmitted to mosquitoes. There are also backup antimalarial medications (Malarone® and intravenous artesunate) available in case you cannot take Riamet® for any reason (e.g. you are allergic to it, or are vomiting and cannot take oral medications). All of the definitive antimalarial medications are approved for use in Australia to treat malaria. However, all medications have possible side effects. You will be given written information that lists possible side effects of the definitive antimalarial medications.

- It is important to understand that any medication, including the medications that you will be taking in this study, could possibly cause a serious life threatening or fatal allergic reaction. Allergic reactions may result in swelling of the face, lips, tongue, throat, and vocal cords, difficulty breathing, skin rashes, seizures, loss of consciousness, and shock. Death may result from heart and lung failure in very rare cases. We will closely monitor you for any symptoms and signs of allergic reaction. As a precaution, a management plan for possible allergic reactions has been developed by the study doctors.

Potential risks associated with other study procedures

- There is some risk of pain, local bruising, and infection at the site where blood is drawn for laboratory tests. This is particularly the case where multiple blood samples will need to be collected. The study doctor and study staff are very skilled in blood collection, but this study is not suitable for people afraid of needles or of having their blood collected. There is also a small risk of a fainting episode, which can occur as a reaction to donating blood. We will ensure that the maximum amount of blood drawn over any consecutive 30-day period does not exceed 470 mL, which is similar to the amount drawn in a single blood donation to the Australian Red Cross Lifeblood.

- We will conduct electrocardiographs (ECGs) by placing electrodes (adhesive tabs attached to wires) on the skin of your chest to check the electrical activity of your heart. Occasionally, there is minor skin irritation while the electrodes are attached and hair-pulling when the electrodes are removed.

- Testing for COVID-19 involves placing a swab (like a very long Q-tip) in your nose to collect cells and secretions. The swab will go into your nasal cavity, above the roof of your mouth. This can cause discomfort and stuffiness in your nose, and it may cause your eyes to tear up temporarily, you may experience a nosebleed and/or a gag reflex.

## 9. What will happen to my test samples?

Samples of your blood and urine obtained for the purposes described above will be transferred to nominated national or international laboratories for testing. These samples will not identify you by name, but only by your study number (code), initials, and perhaps your date of birth. These coded samples will be stored according to the laboratory's testing requirements for the duration required to complete the tests. The samples will then be destroyed as per the laboratory's procedures.

A small sample of your blood taken on the day of malaria infection, and at the end of the study, will be stored indefinitely at QIMR Berghofer Medical Research Institute (Brisbane, QLD) in case future confirmation of your safety results is required.

You will also be asked if you agree for the study team to collect additional blood samples which will be stored for use in future malaria research. Your decision about whether or not you agree will not affect your participation in this study or other studies. If you agree to these additional blood samples being collected,

you will be asked to sign a separate informed consent form.

**10. What happens if new information arises during this research study?**

If any new information becomes available, you will be informed of any newly identified risks to which you may be exposed and that may affect your willingness to participate in this study. If you decide to continue with the study, you may be asked, under certain circumstances, to sign an updated Participant Information Sheet and Consent Form.

**11. What if I withdraw from this research project?**

Your participation in this study is voluntary and you may withdraw from the study at any time. You can withdraw from the study by letting a member of the study team know.

IMPORTANT: If you wish to withdraw from the study after being infected with malaria, you must return to the clinic to receive appropriate definitive antimalarial treatment. This is for your own safety. Untreated malaria can be fatal.

If you withdraw during the study, any data collected up to the point you withdraw from the study may still be used. Under certain conditions, a study investigator may withdraw a volunteer. Reasons include a volunteer becoming pregnant, not complying with the study requirements, becoming ineligible to participate, or having any clinical or laboratory condition that would mean their continuation in the study would not be in their best interest.

**12. What will happen to information about me?**

The Australian Government *Privacy Act (1988)* stipulates that companies and organisations that collect personal information about you must show that information to you if you wish to see it. Below we tell you how to request a copy of your personal information. Please read this carefully. If you have any questions, please ask the study doctor.

This study is being conducted under Australia's regulatory agency, the Therapeutic Goods Administration (TGA). All records will be kept for a minimum of 15 years. All information obtained during this study, including clinic and hospital records, personal information and research data, will be kept confidential. Your personal information specifically relating to your health before, during your participation and when you finish the study will be recorded on forms by the study doctor and study staff.

UniSC Clinical Trials keeps all forms on which your personal information is recorded. If you wish to see these forms, you may ask staff to show them to you. UniSC Clinical Trials does not forward any study records showing your personal details to the sponsor organisation; only information taken from your records (which will be coded by your study number and in some cases your initials, sex, and year of birth) is sent to the sponsor. However, you may contact the sponsor if you wish to see what information they hold about you in relation to this study.

The forms containing your name may be inspected by sponsor representatives, the government agencies (such as Queensland Health and the TGA), and the QIMR Berghofer Medical Research Institute Human Research Ethics Committee to ensure study conformity with the TGA requirements. However, such non-anonymised records will only be accessible at the clinical site and cannot leave the clinic. The representatives of these organisations all comply with privacy standards.

During the study, a copy of your personal information will be made. All data that may directly identify you (e.g., your name, contact details, date of birth) will be removed from this copy and the new dataset will be given a numbered code (such as 123456). This is known as your 'Coded data'.

Once it is coded, linking it to you is only possible through a code list. The code list is kept secure and confidential by the study site and is not shared with others. Data that directly identifies you will not leave the study site.

Your coded data will be shared with:

• The Sponsor, GSK and/or trusted third parties and/or institutions working for the purposes of this study (who are contractually bound to protect your coded data). UniSC Clinical Trials will protect your coded data and will only share it as described in this consent form.

• Health agencies, such as the TGA, the US Food and Drug Administration (FDA), European Medicine Agency (EMA) or others, who review and approve new medicines. These agencies will be granted direct access to your information. This is so they can verify clinical study procedures and/or data.

A description of this study will be available in the public clinical trial registry www.clinicaltrials.gov. This website will not include information that can identify you. You can search this website at any time.

A report of the study may be submitted to government agencies (including the TGA).

It is expected that the results of this study will be published in a scientific journal, and that all data obtained will be made freely available to the scientific community for the purpose of future scientific work. This data will be shared in such a way that you cannot be personally identified. The following data may be shared:

- Your study number
- Race and ethnicity
- Age
- Gender
- Body weight and height
- Results of laboratory tests performed from blood and urine samples collected during the study
- Results of safety tests such as ECGs, vital signs, and physical examinations
- Medications taken prior to the study and during the study
- Medical conditions prior to the study and during the study

Your personal details including name, initials, date of birth, address, or contact details will not be shared under any circumstances.

If you do not agree with the use of your data as described in this form, you cannot join this study.

What is a data controller?

A data controller collects and processes personal information. It determines why and how it is processed.

Medicines for Malaria Venture (MMV) is the data controller for this study. If you have any queries which are related to personal coded information, please contact privacy@mmv.org.

### 13. What happens if I become sick or if I am injured during the study?

Your health and wellbeing is our primary concern. If you suffer any injuries or complications as a result of this study, you should contact the study staff as soon as possible and you will be assisted with arranging appropriate medical treatment. The study doctor or your GP will provide usual or customary care, or arrange hospitalised medical care. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

In the event of loss or injury as a result of the proper conduct of the study, the parties agree to be bound by the Medicines Australia Guidelines for "Compensation for Injury Resulting from Participation in a Company-Sponsored Clinical Trial". You will receive a copy of these Guidelines. You do not give up any legal rights to compensation by participating in this study, including any rights to take legal action as a result of injuries or loss not covered by the Guidelines. The sponsor has adequate insurance in place.

You may be able to seek compensation through the courts.

It is the recommendation of the independent ethics committee responsible for the review of this study that you seek independent legal advice before taking any steps towards compensation for injury.

### 14. Who is organising and funding the research?

This research study is sponsored by Medicines for Malaria Venture (Geneva, Switzerland). The study is being jointly funded by Medicines for Malaria Venture and GSK plc (London, UK). The local sponsor is Southern Star Research Pty Ltd (Sydney, Australia). The sponsor is paying UniSC Clinical Trials to conduct the study. No member of the research team will receive a personal financial benefit from your involvement in this study (other than their usual wages).

### 15. Who has reviewed the research study?

The study has been reviewed and approved by the QIMR Berghofer Medical Research Institute Human Research Ethics Committee (HREC number EC00278), in accordance with the *National Statement on Ethical Conduct in Human Research (2007)*, incorporating all updates. The *National Statement* has been developed to protect the interests of people who participate in human research studies.

### 16. Who should I contact if I have questions?

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this study or if you have any medical problems which may be related to your involvement in the study (for example, any side effects), you can contact the Principal Investigator Dr. Bridget Barber on 0424 737 153 or the clinic as listed below:

**General contact details**

| | |
|---|---|
| During Business Hours | (07) 5430 2956 |
| After Hours | 0401 226 709 |

For matters relating to research at the clinic at which you are participating, the details of the clinic complaints officer are:

**Complaints officer contact**

| | |
|---|---|
| **Name** | Office of the Deputy Vice Chancellor (Research and Innovation) |
| **Address** | University of the Sunshine Coast, Sippy Downs Drive, Sippy Downs, QLD 4556 |
| **Telephone** | (07) 5459 4446 |

If you have complaints about any aspect of the study, including the way it is being conducted, or any questions about being a research participant in general, then you may contact:

**Reviewing Human Research Ethics Committee (HREC) approving this research**

| | |
|---|---|
| **Reviewing HREC name** | QIMR Berghofer Medical Research Institute HREC |
| **Telephone** | 07 3362 0117 |
| **Email** | HREC.Secretariat@qimrberghofer.edu.au |

In the event of a severe medical emergency, please call **000**.

## INFORMED CONSENT FOR STUDY PARTICIPATION

| | |
|---|---|
| Protocol Number | MMV_MMV367_22_01 |
| Study Title | An open label phase 1b study to characterise the pharmacokinetic/pharmacodynamic relationship and safety of MMV367 in healthy adult participants experimentally infected with blood stage *Plasmodium falciparum* |
| Version / Date | Version 3.0/ 14 July 2023 |

| | Participant Initials |
|---|---|
| I have read this participant information sheet. I understand the purpose of the study, the study requirements and the risks of participating in the study. I have had the opportunity to ask questions and my questions have been answered. I hereby give my informed consent to be a participant in this study. | |
| I understand that potential adverse reactions could be caused by the malaria infection, the study drug (MMV367), and the definitive antimalarial medications. I have been given a copy of the Consumer Medicines Information leaflet for Riamet® and Primacin®. If I require Malarone® or intravenous artesunate, I will be given a copy of the Consumer Medicines Information leaflet or other written information for those medications. | |
| I understand that I must be contactable and that I must provide contact details of a support person (with their permission) from the time I am injected with the malaria parasites until I have completed the study. | |
| I understand that if I have a General Practitioner, I may choose to inform them about my study participation. | |
| I understand that when I sign this consent form, I authorise representatives of the sponsor and members of the Human Research Ethics Committee or regulatory authorities to access my study-related medical records. They may need to access my records to verify the clinical study procedures and/or data. | |
| I realise that the information obtained from this study, including the results of all tests upon myself, will be held in both computerised and manual filing systems. The case report form for this study will not identify me by name. These anonymised records may be used for product registration purposes and thus may be made available to health authorities worldwide, and they may be sent overseas for processing by either sponsor personnel or a third party. | |
| I understand that all data obtained in this study may be published and shared freely with the international scientific community for the purpose of future scientific research. I understand that this data will be shared in such a way that I will not be able to be personally identified. | |
| I understand that I am free to withdraw from the study:<br>• at any time<br>• without having to give a reason for withdrawing, and<br>• without affecting my future medical care. | |
| Because untreated malaria is a potentially fatal illness, I understand that if I wish to | |

| | |
|---|---|
| withdraw after being infected with malaria, I will need to be treated with appropriate definitive antimalarial medications. **I understand that for my protection I MUST take the full course of these definitive antimalarial medications to clear the malaria parasites.** | |
| I understand that I am free to discuss my participation in this study with project staff | |
| I understand that if I have any concerns and/or complaints about the study, I may contact the Chairperson of the QIMR Berghofer HREC via the Secretary (07 3362 0117). | |
| I am aware that I will receive a copy of this fully signed Informed Consent Form. | |

**Participant:**

| Full name | Signature | Date | Time |
|---|---|---|---|
| | | | |

**I, the undersigned, have fully explained the relevant details of this study to the participant named above.**

**Investigator or delegate:**

| Full name | Signature | Date | Time |
|---|---|---|---|
| | | | |

***Reminder: A copy of this signed consent form must be given to the participant.***

The QIMR Berghofer Medical Research Institute - Human Research Ethics Committee, in accordance with the National Health and Medical Research Council's guidelines, has approved this study.