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IRAS project ID: 1008352

REC REF: 23/SC/0386

PARTICIPANT INFORMATION SHEET: VAC096

A study to assess the safety and immune response following vaccination with R21/Matrix-M™: a candidate malaria vaccine

We are inviting you to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it would involve. Please take time to read the following information carefully and discuss it with friends, relatives and your General Practitioner (GP/doctor) if you wish.

- **Part 1** tells you the purpose of the study.
- **Part 2** tells you if you are eligible to take part and what will happen if you take part.
- **Part 3** tells you about any possible risks and benefits of taking part.
- **Part 4** tells you more information about how the study will be carried out.

Ask us if there is anything that is not clear or if you would like more information. You will be able to discuss the study with us if you attend a screening visit, and we're happy to answer queries before this too. You can contact us using the email address or telephone number at the top of the page. Take time to decide whether or not you wish to take part.

Who can take part?	Healthy adults aged 18-50 years old (full criteria inside)
What vaccine is being tested?	Malaria vaccine: R21/Matrix-M™
Total participants	36 participants
Study aims	To test the safety and immune responses to R21/Matrix-M™ when administered in a new escalating-dose schedule
Trial site	(insert trial site)
Expenses and payment	Up to £2475
Risks of participation	Short-lived post vaccine symptoms such as arm pain and fever may occur. A full discussion of risks, including potential, rare but serious reactions is contained within (page 8). As this is the first time this multi-dose schedule has been assessed in people, we will monitor the safety of all participants closely.
Benefits of participants	Participating in this trial will help our research into the development of a safe and effective vaccine against malaria.
Visit schedule	15-21 visits over 12 to 24 months

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PART 1: THE PURPOSE OF THE STUDY

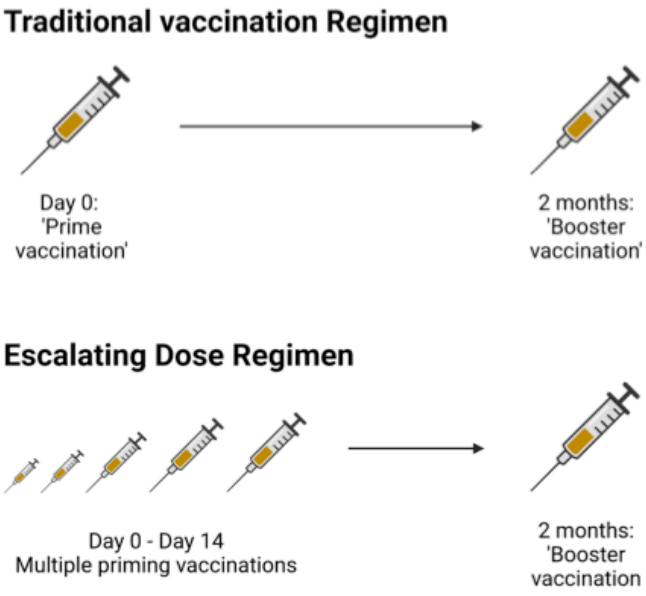
Why are we conducting this study?

Malaria is an infectious disease caused by a parasite which is spread by the bite of an infected mosquito. There were around 240 million cases of malaria and 627,000 deaths worldwide in 2020. Most of the deaths were in children under five years old living in Africa. There is a great need for a safe, effective malaria vaccine. This is because the range of effective medicines for treating malaria is limited and commonly used medicines are becoming less effective. Researchers around the world, including at the University of Oxford, have been investigating malaria vaccines for many years.

The World Health Organisation recently recommended the use of one malaria vaccine, known as 'RTS,S'. This is being given to young children in certain African countries. However, this vaccine is not yet widely available and is only partially effective. The University of Oxford has developed a similar malaria vaccine called 'R21'. This vaccine is administered with an adjuvant called 'Matrix-M™' (an adjuvant is an ingredient added to improve the body's immune response to a vaccine). This vaccine has been given to more than 5000 individuals, including African infants and children. Side effects from R21/Matrix-M™ have been mild and short-lived. Studies have shown the vaccine to be more effective than RTS,S, protecting a higher proportion of infants against malaria. We think the vaccine works by inducing the body to make antibodies which protect against the malaria parasite. However, four doses of R21/Matrix-M™ are required in order to achieve this protection, and there are concerns that the protection may be short lived as antibody levels are known to fall without further vaccination.

We are trying to find new ways of administering R21/Matrix-M™ so that higher antibody levels are made which last for longer. If successful, this could mean that vaccinated individuals are protected from malaria for longer and that fewer doses of vaccine are required to protect an individual. This would reduce the cost of vaccination meaning that more people could be protected.

Multiple doses of vaccine are often needed for a vaccine to protect against disease. Commonly each dose of a vaccine is the same and administered a number of months apart ('**Traditional Vaccination Regimen'** in the Figure 1). However, recent animal studies have shown that if the first vaccine dose is split and administered in multiple doses over a short period, where each dose is bigger than the preceding dose, then higher levels of antibody which last for longer are induced. This type of vaccination administration regimen is called an '**Escalating dose regimen**.'



In this study, we want to assess if administering R21/Matrix-M™ in an '**escalating dose regimen'** will lead to increased antibody levels which last for longer. This study will be the first time R21/Matrix-M™ has been administered in an escalating dose regimen.

In this study participants will either be given R21/Matrix-M™ administered in a 'traditional vaccination regimen' or an 'escalating dose regimen.' We will then compare data from all individuals to understand;

1. The side effects seen with each vaccination regimen.
2. How the human immune response to the vaccine is affected by the administration regimen.

We will do this by giving participants between two and six doses of R21/Matrix-M™. We will then do blood tests and collect information about any symptoms that occur after vaccination.

As part of this study, we also want to study the **body's immune response in the lymph nodes** close to the vaccination site. Lymph nodes (or lymph glands) are small lumps of tissue that contain white blood cells. They are part of the body's immune system and play an important role in the body's response to vaccination. Animal studies using cells from lymph nodes have provided important information to help us understand how to improve the immune response to vaccination. In this study, we will take samples from participants' axillary (arm pit) lymph nodes, to help us better understand the effect of varying vaccine regimen on the immune response. These samples will be taken using a procedure called fine needle aspiration, which is described in more detail on page 13.

What are the vaccines being tested?

R21 is a protein vaccine, and **Matrix-M™** is a saponin based vaccine adjuvant.

R21 is a protein particle, which is produced by combining a protein from Hepatitis B with the circumsporozoite protein (CSP) of the malaria parasite. This is not a live vaccine and so there is no chance of catching malaria from vaccination. CSP is a protein required by the malaria parasite to get into liver cells. We are hoping to make the body develop an immune response to this protein, in order to stop the malaria parasite from getting into liver cells. R21 has been found to be safe and well tolerated, but can cause

temporary side effects, as detailed in the section titled "What are the risks of taking part in the study?" on page 12.

Matrix-M™ has been given to tens of thousands of volunteers in other vaccine trials. It has been shown to be safe and well tolerated. This includes trials of vaccines for malaria, COVID-19 and influenza. Matrix-M™ has now been approved for use in the UK as part of Novavax's COVID-19 vaccine.

R21 combined with Matrix-M™ has not been administered in an escalating dose regimen to humans before.

Do I have to take part?

No. It is up to you to decide whether or not to take part. Your decision not to take part will not result in any penalty, or loss of benefits to which you are otherwise entitled. You are free to withdraw at any time without giving a reason. However, we may ask you to return to the clinic for follow up for safety reasons.

For University of Oxford staff or students: The University does not urge, influence, or encourage you to take part in this research study. Your decision not to participate in the study, or a decision on your part to withdraw from the study, will have no effect whatsoever on your employment or student status at the University.

What will happen if I decide to take part?

This study involves having between two and six doses of R21/Matrix-M™ depending on what group you are in. You will be followed up with regular clinic visits and blood tests (see detailed visit schedule on page 10).

Visits will take place at insert study site and any relevant information re location/access. You will be asked to complete an online diary to record any symptoms you experience after each vaccination and lymph node sampling.

Length of research

You will be involved in the trial for a minimum of 12 months from the date of your first vaccination and attend 15-19 clinic visits depending on the group you are enrolled in. There is the option to continue in the study and be followed-up until 24 months after the first vaccination. This would involve attending two further clinic visits (see detailed visit schedule on page 10).

PART 2: WHO CAN TAKE PART AND WHAT WILL HAPPEN?

Am I eligible to take part in the trial?

You may be eligible to take part in the trial if you are aged 18-50 years, in good health, and able to meet all of the study requirements, including attending all of the scheduled visits.

You must also be willing to let us access your electronic NHS medical records and discuss your medical history with your GP.

You **cannot** take part in the study if:

- You have previously had malaria or a malaria vaccine, or have travelled to an area with malaria in the last 6 months
- You have an allergy that may be worsened by being in the study.
    - This includes previous severe allergic reaction to any vaccine, allergy to any part of the study vaccination, or an allergy to the local anaesthetic lidocaine
- You have a significant physical or mental health condition that requires regular visits to the doctor, or might make it inadvisable for you to take part in the study*.
    - This includes problems with your immune system, previous cancer, unusual or excessive bleeding, auto-immune conditions, hepatitis B or C or HIV infection
- You have taken medication to suppresses your immune system in the last 6 months
- You have received any blood products in the last 3 months (e.g. immunoglobulins or a blood transfusion)

Whilst in the trial, **you must not:**

- Have a vaccine within 30 days of receiving a study vaccine (apart from COVID 19 vaccination)
- Take part in another study using an experimental treatment
- Travel to an area with malaria
- Plan to be pregnant or breastfeeding
- Donate blood

Before you can take part in the study, you will attend a screening appointment with a doctor, who will ask you questions about your health and lifestyle and examine you to assess whether it is appropriate for you to take part in the study. Participation is at the discretion of the investigators.

*Mild conditions may not exclude you from taking part. If you are unsure whether you are eligible, please contact the study team for further information.

Is there anything else to think about?

Blood Donation
Under current UK regulations, volunteers will not be able to donate blood during the study.

Pregnancy and Contraception
The potential effect of the vaccine used in this study on an unborn baby is unknown. If you are able to

become pregnant then you will be asked to use an effective method of contraception for the time you are part of the study. Condoms alone are not considered effective enough.

Acceptable forms of contraception include:

- Established use of hormonal contraceptives. This includes the pill, mini-pill, contraceptive injection or implant.
- Placement of an intrauterine device or intrauterine system. These are also known as the copper coil or hormone coil (e.g. Mirena coil).
- Vasectomy (male sterilisation), if this is your only partner.
- Complete abstinence from any sexual relationships in which you may become pregnant. Periodic abstinence and withdrawal methods are not acceptable.

A urine pregnancy test will be done at screening, just before each study vaccination, before lymph node sampling, and at the day 365 visit.

If you do become pregnant whilst in the study, you must inform a trial doctor immediately.
We will not give you any further vaccinations, but will continue follow-up until 3 months after the birth.

Private Insurance
If you have private medical insurance, you should contact your insurance company before participating in this trial. Involvement may affect the cover provided.

Malaria Protection
You should not assume that the experimental vaccine you receive in this study will give you any protection against malaria. Make sure you visit your GP or a travel clinic before travelling to an area where malaria is found. You should follow their advice on prevention measures.

What will happen at the visits?

Screening Visit
First, we will need to check whether you are eligible to join the study. Following an online pre-screening questionnaire, we will contact you by telephone or email. You will have an opportunity to ask any more questions about the study at this point. We will also arrange for you to attend a screening appointment.

The screening appointment takes place up to 3 months before the study starts. It can last up to 1.5 hours, with an opportunity for a short break. The purpose of the screening visit is for you to discuss the trial with us and decide if you still wish to take part. If you do, we will ask you to sign a consent form.

After signing the consent form:

- You will be asked some medical questions.
- A doctor will examine you.
- Blood and urine samples will be taken for testing. These test results will need to be normal for you to be enrolled in the study.
- If you are able to become pregnant then you will also have a urine pregnancy test.

The blood tests will look at:

- Your blood count (for example, to check if you are anaemic).
- Your liver and kidney function.
- How well your blood clots (to make sure lymph node sampling will be safe).
- Whether you have hepatitis B, hepatitis C or HIV. This is because these conditions can affect your body's response to the vaccines we are assessing.

If any of your test results are not normal, we will let you know and may arrange for a repeat test. With your consent, we may also report any abnormal results to your GP.
Hepatitis B and C are 'notifiable diseases'. This means that we are legally required to report any new diagnosis to the UK Health Security Agency. This may be done via the testing laboratory or your GP.

Some individuals may test positive for Hepatitis C virus due to previously taking part in a Hepatitis C vaccine study. If this applies to you and you wish to take part in our study, with your written consent, we will contact the team responsible for the Hepatitis C vaccine study. We will check your Hepatitis C status with them before enrolling you in this malaria vaccine study.

Vaccination visits
The table below shows each group and the vaccinations they will receive. Each vaccination will be R21 administered with the Matrix-M™ adjuvant. The dose of vaccine will vary according to the group.

Groups 1 and 2: Participants will receive 6 vaccinations with R21/Matrix-M™ in total. The first five doses of vaccines will be an **escalating dose regimen**, where 5 doses of vaccines are administered over 14 days, with each dose greater than the preceding dose. The total dose of vaccine administered across these five doses will equal the same as the 'full dose' of R21/Matrix-M™. Participants in Group 1 will then receive a full dose of R21/Matrix-M™ 2 months after the first vaccination. Participants in Group 2 will receive a full dose of R21/Matrix-M™ 6 months after the first vaccination.

Group 3: Participants will receive 2 vaccinations with R21/Matrix-M™ in total as a part of a '**traditional vaccination regimen**.' Both of these doses will be the full dose of R21/Matrix-M™. The second vaccination will be administered 2 months after the first vaccination.

The study doctor will talk to you about which group you would be enrolled in. This will depend on when you enrol in the study and your availability.

Group	Vaccine on Day 0	Vaccine on Day 3	Vaccine on Day 7	Vaccine on Day 10	Vaccine on Day 14	Vaccine on Day 56	Vaccine Day 168
1	1/20 Full Dose 	1/13 Full Dose 	1/8 Full Dose 	¼ Full Dose 	½ Full Dose 	Full Dose 	
1	1/20 Full Dose 	1/13 Full Dose 	1/8 Full Dose 	¼ Full Dose 	½ Full Dose 		Full Dose 
3	Full Dose 					Full Dose 	

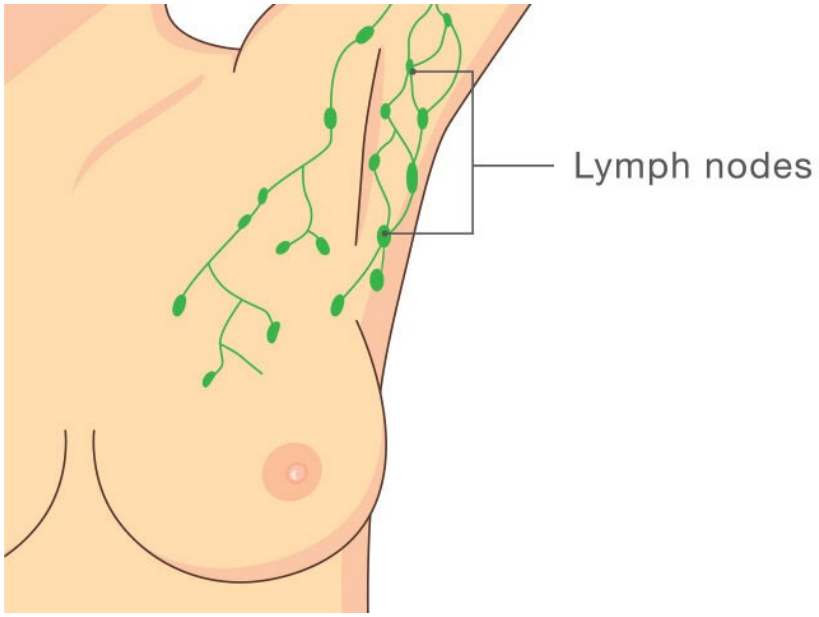
Each vaccination will be given into the muscle of the same upper arm. You can choose which arm you have vaccinated. We will ask you to wait in clinic for 30 minutes after each vaccination to check there are no immediate problems. We will also show you how to use the electronic diary. A paper diary will be

available if you are unable to use the electronic diary. We will ask you to record your symptoms and measure any redness at the injection site following vaccination. For this, you will be given a thermometer and tape measure to take away. For participants in Groups 1 and 2, you will be asked to complete the electronic diary from the day of the first vaccination until 7 days after the 5th vaccination (i.e. from Day 0 until approximately Day 21). You will also be asked to complete an electronic diary for 7 days from the date of your 6th vaccination (on Day 56 or Day 168). For participants in Group 3, you will be asked to complete an electronic diary for 7 days following your 1st and 2nd vaccinations. We will also give you a phone number for the emergency study doctor, who can be contacted 24 hours a day, in case of any concerns.

We may ask to photograph your vaccination site. You can choose whether or not to agree to this when you sign the consent form. Your face will not appear in any such photographs. Only the vaccination site and your unique trial number will be visible. These photographs may be shown to other professional staff, used for educational purposes or included in a scientific publication.

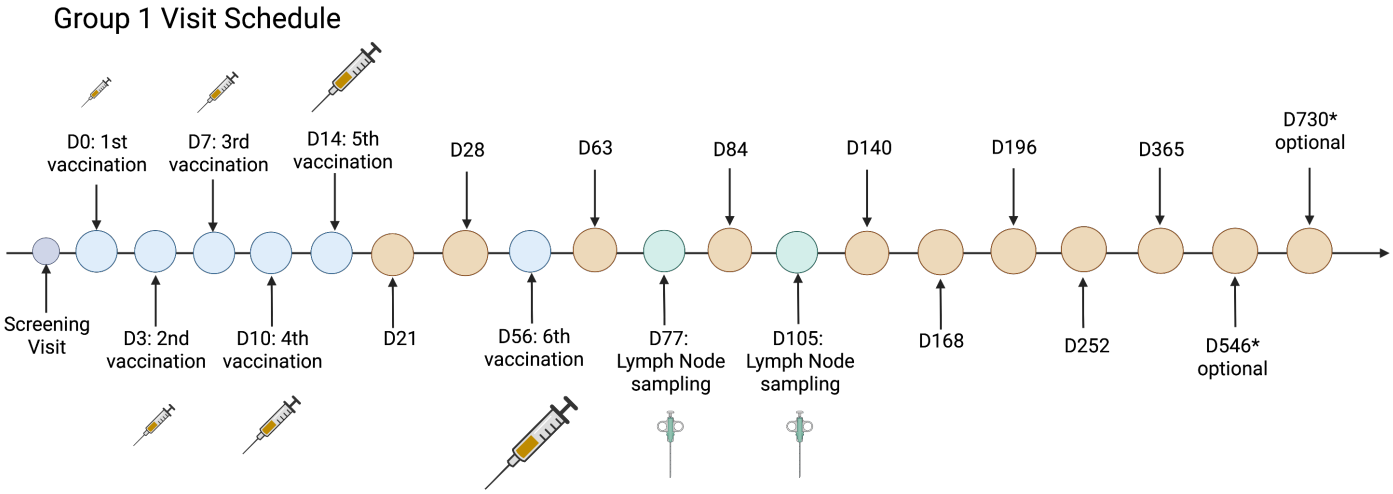
Lymph Node Sampling

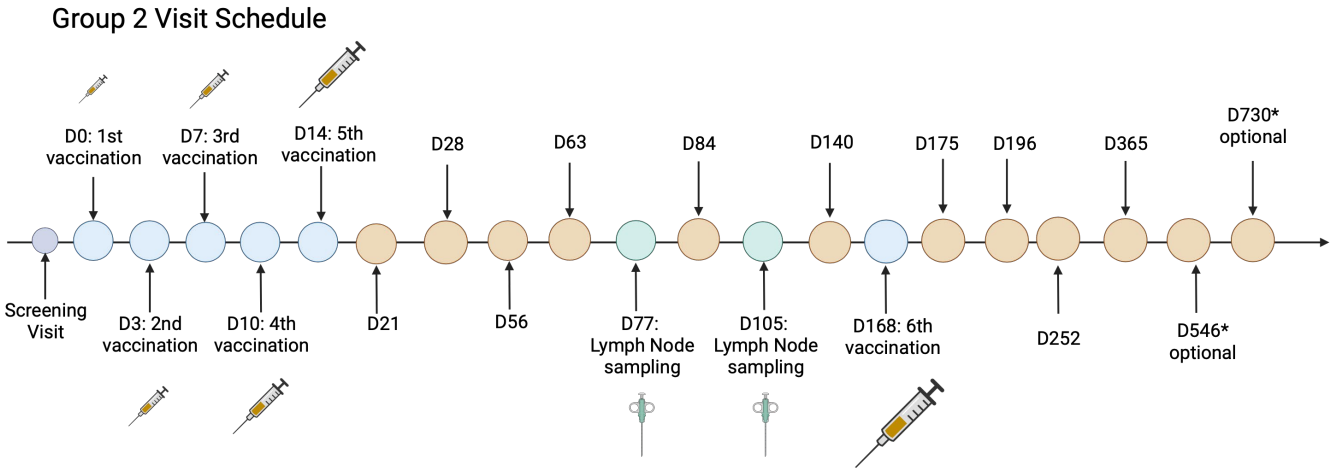
Lymph nodes from the arm pit (axilla) of the arm where vaccinations were given will be sampled in all participants. This will take place twice; on Day 77 and Day 105 after the first vaccination. Sampling will be performed using a procedure called a **'fine needle aspiration'** (FNA) by an experienced doctor. Before the procedure, the doctor will examine your axilla to feel for lymph nodes. They will then use an ultrasound machine to visualise the lymph nodes. The doctor will use a small needle to introduce local anaesthetic into the skin above the lymph node. When the skin is numb, they will introduce a longer needle through the skin into the lymph node, guided by the ultrasound images. They will then collect cells from the lymph node by passing the needle back and forth gently. Ultrasound images from the lymph node sampling will be saved and stored using your unique trial number, as a record of the procedure. The FNA procedure will take about 45 minutes. You will be asked to stay in the clinic for 60 minutes after the FNA to check there are no immediate complications. We will ask you to record your symptoms following the FNA in an electronic diary for 7 days following each FNA. We will give you the phone number for the emergency study doctor, who can be contacted 24 hours a day, in case of any concerns.

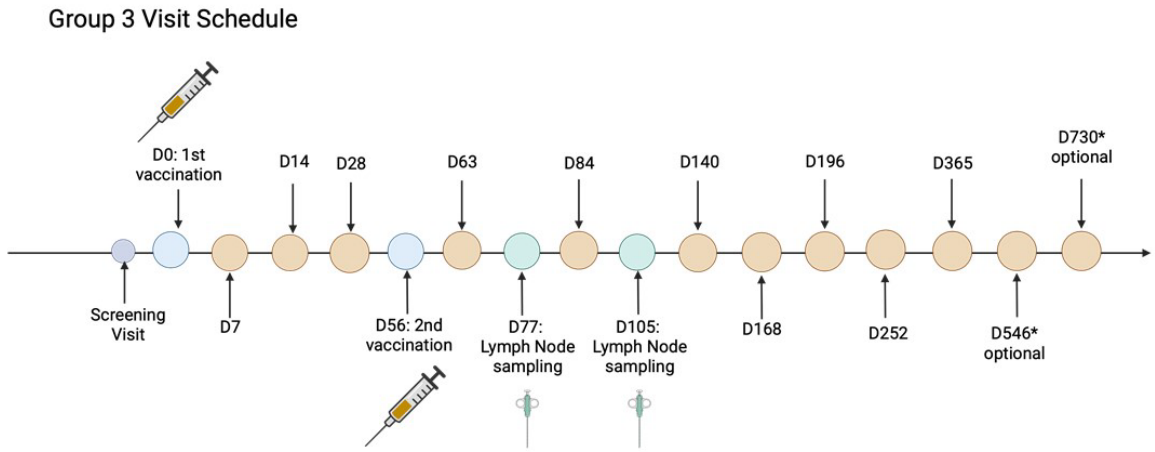


Schedule of Visits: Circles denote in-person clinic visits. Visits include a medical assessment and examination of a doctor if needed. We will also take your temperature, pulse and blood pressure, as well as blood tests at most visits. You may also be invited for an unscheduled visit if there is a medical need; for instance, if you have a severe or unexpected side effect.

All lymph node sampling visits will take place at the Oxford site. Lymph node samples are a much smaller volume than blood and more complicated to obtain. Reducing the transit time to the lab, in Oxford, will help us to preserve the quality of these valuable samples. Bristol volunteers will have transport to Oxford arranged and will be compensated for the additional time commitment.







Expenses and payments

You will be compensated for:

- Screening visit £75
- Travel expenses (enrolled volunteers) £30 per visit (if travel to the trial site costs more than £30 additional reimbursement may be offered)
- Time required for visit (enrolled volunteers) £40 per hour
- Inconvenience of blood tests £20 per blood donation
- Lymph node sampling £150 per FNA
- Diary completion (only if completed every day): £30 per diary

Volunteers travelling from Bristol to Oxford for lymph node sampling will be compensated for a whole day (8 hours) and will have transport from Bristol provided.

The overall compensation will be between £1995 - £2475* depending on your Study Group, as shown in the table below. The amount of compensation is calculated according to your time spent in clinic visits, which varies between groups. If you choose to leave the study early, or are withdrawn, you will be compensated according to the length of your participation. This will be calculated based on the figures above. **Compensation payments received in this trial may have an impact on your entitlement to benefits.**

Group No.	Maximum time in Trial (approx.)*	Maximum no. of Clinic Visits*	Maximum compensation amount*
1	24 months	20	£2385**
2	24 months	21	£2475**
3	24 months	17	£1995**

*Includes optional visits at days 546 and 730

**Volunteers from Bristol who have two lymph node sampling procedures in Oxford will receive an additional £500 (£250 per visit), to compensate for the extra time required.

What do I have to do?

- You **must** attend all the visits that are outlined above (NB the clinic visits on Day 546 and Day 730 following first vaccination are optional).
- If you are able to become pregnant you **must** use effective contraception for the duration of the study.
- You **must not** donate blood during the study.

PART 3: RISKS AND BENEFITS

What are the risks of taking part?

Blood Tests
The total volume of blood taken during the study depends on the group. The amount taken at each visit will vary between around 15mLs (about a tablespoon) to a maximum of 67mLs (about 4 and half tablespoons). The volume of blood being taken over the course of the trial should not cause any problems in healthy people. There may be some temporary mild discomfort. This may include bruising and tenderness at the site where the blood is taken. You may feel faint as a result of collecting blood.

We will give you a copy of your blood test results if you ask for them. We will only send the results to your GP if you wish us to and will not report them to anyone without your permission.

If abnormal results or undiagnosed conditions are found in the course of the study these will be discussed with you. If you agree, your GP will also be informed. For example, a new diagnosis of anaemia might be made. Any newly diagnosed conditions will be looked after by your GP within the NHS.

At different time points throughout the trial, we will take blood samples for the following tests:

- Your blood counts, liver and kidney function and the ability of your blood to clot.
- Blood borne infections (HIV, hepatitis B & C).
- Genetic analysis of your cells (to look at patterns of genes that can affect the immune system).
- Immune responses to vaccination. This may include production of specific antibodies called monoclonal antibodies.

Vaccination Side Effects
Once vaccinations have been given, they cannot be undone. It is therefore important you understand the potential risks of the vaccine before you join the study.

R21/Matrix-M™ has been given to more than 5000 individuals to date. The most common side effects experienced by volunteers who have received a '**full dose**' of R21/Matrix-M™ are described below:

- Injection site pain. This is most likely mild. However, there is a chance this could be moderate or severe in intensity.
- Redness, swelling, itching and warmth at the vaccine site. Symptoms are likely to be mild if present. However, there is a chance this could be moderate or severe in intensity.
- A 'flu-like' illness within 24 hours of vaccination that usually resolves within 48 hours. This can include headache, muscle aches, joint aches, feverishness, tiredness, nausea and feeling generally unwell. The majority of general symptoms are likely to be mild. There is a small possibility of moderate or severe symptoms occurring.

We expect that most symptoms will be mild. However, some may be moderate or severe. Symptoms should last no more than a few days.

The first five vaccinations given to participants in Groups 1 and 2 over 14 days will be an **escalating dose regimen**. The total dose of vaccine administered across these five doses will equal the 'full dose' of R21/Matrix-M™, with each individual dose only a fraction of a full dose. We think that participants receiving these doses will experience only minor side effects, similar to those described above, which are short lived. We will review the side effect you experience closely and will only give the next vaccine in the escalating dose regimen if the side effects from the last vaccine are mild in severity, and stable or improving. **However, it is important to appreciate that this escalating administration regimen has not**

be assessed in humans before. This means there is a chance you could experience a side effect different in nature, or more severe than those described.

Lymph Node Sampling side effects

Fine needle aspiration (FNA) of lymph nodes is a simple procedure that is usually well tolerated, with minor side effects that are short lived. Local anaesthetic is used to numb the skin over the lymph node – this can give a short-lived stinging sensation. After this, the doctor will use ultrasound scan to visualise the lymph node. Ultrasound is painless. The doctor will then introduce a longer needle into the lymph and collect cells by passing the needle back and forth gently. This should not be painful, but you may feel a pulling sensation. After the procedure, you may experience tenderness at the sampling site, as well as bruising and swelling, which is likely to be mild and resolve within a few days.

Severe Reactions

With any vaccination or medication there is a low risk of serious reactions. These may be related to the nervous system or the immune system.

Severe allergic reactions to vaccines or medications (anaphylaxis) are very rare but can be fatal, if not immediately treated. Therefore, we will have doctors qualified in the management of anaphylaxis at each vaccination and lymph node sampling appointment. Appropriate equipment and medication will also be present.

Reactions in the nervous system are also extremely rare. However, vaccines can cause an illness called Guillain-Barré syndrome. This is an illness in which people can develop severe weakness. It may be fatal. However, these reactions have not previously been seen with the type of vaccine used in this study.

If you experience unexpected symptoms, or become in any way concerned, you should contact one of the study doctors. At your first vaccination visit, you will be given the phone number for the emergency study doctor, who can be contacted 24 hours a day, in case of urgent concerns.

Taking part in a vaccine study in the context of COVID-19

We now have over 3 years' experience conducting trials in the context of COVID-19 infection. We have developed procedures to keep our volunteers safe and trials running. As the public health situation evolves, we may change some of these procedures, in line with the most up-to-date guidance from the UK Health Security Agency (UKHSA) and the UK Government. If you volunteer, we can discuss the up-to-date policy and volunteer requirements with you when you visit.

Of note, the results of any COVID-19 swab tests done as part of this study must be passed on to UKHSA. This includes tests that are negative. This is because COVID-19 is a 'notifiable disease' and this is a legal requirement.

If you are self-isolating when you are due to attend a clinic visit, please let us know. We will try to re-schedule clinic visits to another time.

Clinic visits

- (insert site) has policies in place for social distancing measures and face mask use. These are updated regularly. We will let you know what the current policies are. Both study staff and participants will need to follow these policies.

COVID-19 vaccination

- Please inform us if you have an appointment for COVID-19 vaccination during the trial. You will be able to receive a COVID-19 vaccination if it is given at least 14 days before or 7 days after any malaria

trial vaccinations. The malaria vaccinations can be fitted around any COVID-19 vaccination. Where possible, we would like you to receive the COVID-19 vaccine on the opposite side to the arm vaccinated with R21/Matrix-M^{TM} in this study.

There may be other risks, or side effects, which are unknown at this time.

What are the possible benefits of taking part?

This study will not benefit you. The information gained from the trial might help to prevent malaria infection and disease in those who live in areas where malaria is common, and in travellers. There are other malaria vaccines in various stages of development.

PART 4: OTHER INFORMATION ABOUT THE STUDY

What if relevant new information becomes available?

Sometimes, during the course of a research project, new information becomes available. If this happens, we will tell you about it. We will discuss whether you want to or should continue in the study. If you decide to continue in the study, you will be asked to sign an updated consent form. On receiving new information, we might consider it to be in your best interests to withdraw you from the study. Your participation in this study may also be stopped at any time by the study doctor or the Sponsor, without your consent, for other reasons.

What will happen if I don't want to carry on with the study?

You are free to withdraw from the study at any time, without giving a reason. This will not result in any penalty, or loss of benefits to which you are otherwise entitled. Your data collected and samples taken will continue to be used unless you state otherwise. You may request that your samples and research data are destroyed at any time during or after the study, although once the study data is fully anonymised it will not be possible to withdraw this. Your compensation would be paid as a proportion of the total compensation, according to the length of your participation.

What if there is a problem?

If you are harmed as a result of taking part in this study, the study doctor can advise you of further action. If necessary, they will refer you to a doctor within the NHS for treatment. The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this trial. We will provide compensation for any injury caused by taking part in this study. We will pay compensation where the injury probably resulted from:

- A drug being tested or administered as part of the trial protocol
- Any test or procedure you received as part of the trial

Any payment would be without legal commitment. (Please ask if you wish more information on this). We would not be bound by these guidelines to pay compensation where the injury resulted from a drug or procedure outside the trial protocol or where the protocol wasn't followed.

The Investigators recognise the important contribution that volunteers make to medical research. They make every effort to ensure your safety and well-being. In the event of harm being suffered, while the University will cooperate with any claim, you may wish to seek independent legal advice to ensure that you are properly represented in pursuing any complaint.

Complaints procedure

If you wish to complain about any aspect of the way in which you have been approached, or treated during the course of this study, you should contact your local trial team (contact details at the end of this document). You may also contact the University of Oxford Research Governance, Ethics and Assurance (RGEA) office (phone: 01865 616480, email: RGEA.Sponsor@admin.ox.ac.uk)

Will my taking part in this study be kept confidential?

All information that is collected about you during the course of the research will be coded with a study number and kept confidential. Personal details will be stored securely and separately from the research data.

Responsible members of the University, independent monitors and the regulatory authorities may be given access to data for monitoring and/or audit of the study. This is to ensure that the research is complying with applicable regulations.

In order to arrange lymph node sampling appointments, personal data (name, date of birth) will be shared securely between clinical study staff in Bristol and Oxford. This will be the minimum amount of data required for the procedure to be safely done.
With the exception of COVID-19 tests, any other information about you that leaves the clinic will have your name and address removed so that you cannot be identified from it. Your information is stored electronically on a secure server. Any paper notes are kept in a locked filing cabinet.

Involvement of the General Practitioner/Family doctor (GP)

In order to enrol into this study, you will be required to sign a form to say that you consent for us to view your electronic NHS medical records and contact your GP. This is to inform them that you are interested in being involved in the study. We will also check there are no medical reasons that would make your taking part in the study inadvisable. Your GP may be asked to share information about your medical history and give access to any other medical records as needed. The researchers will not enrol you in the trial if they have concerns about your eligibility or safety. We will write to your GP to let them know whether or not you are enrolled in the study. We will also write to let them know whether or not you completed the study, so they can update your medical records accordingly.

Prevention of 'Over Volunteering'

Volunteers taking part in this study must not be receiving investigational medications or vaccines in another study at the same time. In order to check this, you will be asked to provide your National Insurance or Passport number. This will be entered into a national database which helps prevent volunteers from taking part in too many clinical trials. More information can be found at *www.tops.org.uk*. Your national insurance or passport number is also required to allow the processing of compensation payments. Please bring this information with you to the screening visit.

What will happen to any research samples I give?

The results of any COVID-19 swab tests done as part of this study must be passed on to UKHSA. This includes tests that are negative. We will pass on your details (name, date of birth, contact details, ethnicity, NHS number) and date of diagnosis and symptom onset if applicable. This is because COVID-19 is a 'notifiable disease', and this is a legal requirement in the UK.

Some of your samples (e.g. blood, lymph node) will be analysed in Oxford University research laboratories. Blood tests for your general health will be carried out in an NHS laboratory. Some cells from your samples may be used to produce specific antibodies ('monoclonal antibodies'), which could be used for commercial activity in the future. Other tests to look at the response of your body to the vaccine will be done with collaborating laboratories in the UK and in other countries, including those outside Europe. Any samples or data sent to NHS laboratories or collaborating labs will be assigned a study code, rather than your name/personal details (i.e. will be pseudo-anonymised).

If you consent, some of your leftover samples will be stored indefinitely at the University of Oxford. This will be coded with a study number. Your personal details will also be stored securely, until the sample is depleted or destroyed. In line with the Human Tissue Act, personal data will be stored separately from the sample itself, or any research data.

The samples may be used for further related research, including the study of the human body's immune response and/or vaccine research. Any such future research will have an appropriate ethical review. You may request that remaining samples are destroyed at any time. If you decide not to consent to storage of your leftover samples, they will be disposed of at the end of the study. Taking part in this study will not be affected by your decision whether to allow storage and future use of your leftover samples.

Urine samples will be disposed of immediately after testing.

Will any genetic tests be done?

Yes. Some samples will be used to look at the pattern of your genes that can affect the immune system. As these tests are not done to look at your health, we would not give you these test results.

What will happen to my data?

Data protection regulations require that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford, as sponsor, is the data controller. This means that we, as University of Oxford researchers, are responsible for looking after your information and using it properly.

We will use information from you and your medical records in order to undertake this study. We will use the minimum personally-identifiable information possible. The University of Oxford will keep identifiable information from participants collected during the study initially for 5 years after the study has finished. Once the study has been completed, all documents will be archived in a secure facility. In addition, we will securely store the pseudo-anonymised research data and any research documents with personal information, such as consent forms, initially for 25 years after the end of the study. The need to store this information for longer, in relation to licensing of the vaccine will be reviewed every 5 years. Files will be confidentially destroyed when storage is no longer required. For effective vaccines that may be licensed, secure storage of research data may be required for at least 25 years after the end of the study, subject to changes in clinical trials regulations. In addition to the scientific data, we will also store documents containing personal information that you provide when registering for the trial (including contact details), medical information and signed consent forms during this archiving period.

The study team will use your name and contact details to contact you about the research study. We will also make sure that relevant information about the study is recorded for your care, in relation to your health during the study, and to oversee the quality of the study. At the end of the study, unless you consent otherwise, your personal details will not be used to contact you other than for exceptional circumstances concerning your safety. If you consent to take part in another study at the Oxford Vaccine Centre, personal information and medical information including blood test results may be accessed to avoid unnecessary repetition.

Your information may also be shared with partners working with Oxford University. This information will be identified only by the unique trial number, and you will not be personally identifiable. All data received will be kept securely by these parties in line with all regulatory requirements. De-identified safety data will be shared with the local ethics committee, UK Medicines and Healthcare products Regulatory Agency (MHRA) and independent Data Safety Monitoring Committee to enable them to monitor the trial. They will also be shared with the manufacturers of the vaccine and the adjuvant (Serum Institute of India and Novavax).

Your bank details will be stored for 7 years in line with University of Oxford's financial policy.

If you test positive for the hepatitis C virus due to previous involvement in a hepatitis C vaccine study, with your written consent, we will contact the team responsible for the hepatitis C vaccine study as described previously. A copy of this consent will be held by both ourselves and the team responsible for the hepatitis C vaccine study. They will hold your form in the same way they described when you originally joined the study.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in

order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at: https://compliance.web.ox.ac.uk/individual-rights

Monitors
Independent external monitors will be used in this study to ensure we are complying with the clinical trial regulations. Monitoring staff will conduct a site visit to prepare and set up the clinical trial prior to recruitment as well as conduct monitoring visits to check the information in source documents (e.g. blood test results and GP letters). In most documents you will only be identified by a study ID number, but they will see some documents which would identify you (e.g. the consent form). They will not retain any data which could identify you personally. For remote monitoring to occur they may require secure online access to electronic documents but will not download or copy them. The monitors will comply with the University of Oxford's Information Security Policies, which are documented in the agreement with the University of Oxford.

What happens when the research study stops?
If you have any queries or concerns once the study is over, please do not hesitate to get in touch with us.

The data we collect in this study will be shared with the funder (Bill & Melinda Gates Foundation). It may be made open to the public so that others can learn from it. If data are shared publicly, they will not be linked to you personally.

The results of this research study may be presented at scientific meetings or conferences and published in a scientific medical journal. This may not happen until 1 or 2 years after the study is completed. If you contact the researchers in the future, you can obtain a copy of the results. You will not be identified in any report or publication.

The anonymised data from this study will be shared with the partners who are organising and funding this research work. Data from this study may be used to file patents, licence vaccines in the future or make profits in other ways. You will not be paid for any part of this. Data from this study may be used as part of a student post-graduate degree, for example a MD or PhD.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Taking part in future vaccine related research
With your consent, we would like to keep your contact details after your participation in this study is complete. This is so we may inform you of opportunities to take part in future vaccine-related research. This is entirely optional. Taking part in this study will not be affected by your decision whether to allow storage of your contact details beyond your participation in this trial.

Your details will be stored electronically on a secure server. Only authorised individuals at (insert study site) will have access to it. We will not, under any circumstances, share your contact details with any third-party institutions without your permission. Being contacted does not oblige you to agree to take part in future research. You can ask us to have your contact details removed from our database at any time.

Who is sponsoring, organising and funding the research?

The study is organised by the University of Oxford. The study is funded by the Bill & Melinda Gates Foundation and coordinated by the Jenner Institute at the University of Oxford. Neither your GP nor the researchers are paid for recruiting you into this study.

The Chief Investigator, Professor Sir Adrian Hill, has a patent relating to the R21 vaccine used in this study. While Professor Hill therefore has a potential conflict of interest, the integrity of the trial is maintained by samples being analysed by non-clinical researchers who cannot link them to individuals (thereby ensuring no bias), as well as the monitoring of safety by an independent Data Safety Monitoring Committee.

Oxford researchers and staff, including investigators on this trial protocol, and Serum Institute of India staff may benefit from a share of any future royalties received as a result of development of a new indication, formulation or regimen for licensure of the malaria vaccine.

Who has reviewed the study?

This study has been reviewed by the National Research Ethics Service Committee [name] and has been given a favourable ethical opinion. A Research Ethics Committee is an independent group of people who review research to protect participants' interests.

It has also been reviewed by the Medicines and Healthcare Products Regulatory Agency (MHRA), the government body that monitors medical products in the UK.

Thank you for reading this information sheet. If you are interested in taking part in the study, please contact the study team at your local study site to arrange a screening appointment.

Contact details for further information:

Volunteer Recruitment Co-ordinator

Insert contact details