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IRAS project ID: 330788

NRES Committee South Central

Berkshire 23/SC/0364

PARTICIPANT INFORMATION SHEET: BIO-004

Group 3 only

Understanding how the immune system responds to repeated malaria infections

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 involves. Please read the following information carefully. You can discuss it with friends, relatives and your GP (General Practitioner/family doctor) if you wish. Take time to decide whether or not you wish to take part.

- **Part 1** tells you about the purpose and the design 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** gives 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 can ask us any questions at your screening visit. You can also contact us on the email address at the top of the page. This information booklet has been reviewed by four members of the Oxford Vaccine Centre's patient and public involvement (PPI) team. The PPI team make sure the information is presented in a way that is clear and understandable.

Who can take part?	Healthy adults aged 18–45 (full criteria inside)
Total participants	3-5 participants
Study aims	**Overall study:** To understand how the body's cells that help to fight infection (T-cells) learn to tolerate repeated malaria infections. **Group 3 (i.e. your group):** To provide healthy bone marrow samples (no malaria infection) to compare to bone marrow samples of participants (i.e. Group 1 and Group 2) undergoing malaria challenges.
Study site	Centre for Clinical Vaccinology and Tropical Medicine (CCVTM) and Oxford Experimental Medicine Clinical Research Facility (EMCRF), Churchill Hospital, Oxford, OX3 7LE
Expenses and payment	Approximately £260
Risks of participation	There is a small risk of pain, bleeding and infection following a bone marrow test. We will monitor the safety of all participants closely. A full discussion of risks starts on page 12.
Benefits of participation	Participating in this study will not benefit you directly. It will help our research into changes in the immune response to malaria after repeated infections. A better understanding of this may help us develop more effective strategies to reduce the global burden of malaria disease and malaria deaths.

Visit schedule	Group 3: Screening appointment, 1 x bone marrow procedure, 1 x telephone appointment over approximately 3 months

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PART 1: THE PURPOSE AND DESIGN OF THE STUDY

Why are we conducting this study?

Malaria is an infectious disease caused by the *Plasmodium* parasite and is a major public health problem in many parts of the world. Malaria is spread by the bite of an infected mosquito. There are five species of the Plasmodium parasite that are known to cause malaria in humans. Of these five species, Plasmodium falciparum causes the most sickness and death globally, with an estimated 241 million cases of malaria and 619,000 deaths worldwide in 2021. *Plasmodium vivax* accounts for more than half of all malaria cases in the Americas and South-East Asia; globally, around 14 million annual cases present a significant clinical and economic burden. Most of the deaths from malaria occur in children under five living in Africa, with infants under 1 year being at the highest risk.

A significant study conducted in Tanzania showed that while the number of malaria parasites in the blood remained constant over the first few malaria infections of life, the risk of severe disease and hospitalisation decreased significantly with each infection. This study concluded that rather than killing the malaria parasite, the immune system developed the ability to 'tolerate' the presence of the parasite in the body, which reduced the damage caused during repeated infections. This was an important finding, however the way that the immune system tolerates the malaria parasite remains unknown.

In order to better understand how the immune system adapts to tolerate the malaria parasite after repeated infections, we are recruiting participants (Group 1 and Group 2) to undergo three malaria challenges. In a 'malaria challenge', study participants are injected with a small amount of malaria-infected blood under carefully regulated conditions in order to cause malaria infection. This is important as we will know the exact moment of infection and will be able to track the immune response that follows. This is difficult to do when studying infections that occur naturally. We are also recruiting a small number of participants to be 'healthy controls' (Group 3). This is the group you will be recruited to, and this information sheet will give you more information about your group in particular. Participants in your group (i.e. Group 3 participants) will not be infected with malaria but will help us establish what is 'normal' in order to understand the results.

This study will assess:

1. Changes in the immune (T-cell) response after three infections with P. falciparum malaria (Group 1 only)
2. Changes in the immune (T-cell) response after two infections with P. falciparum malaria followed by one infection with a different species of malaria, P. vivax (Group 2 only)
3. Changes in the bone marrow following the first malaria infection (Group 2 only) compared to the third malaria infection (Group 1 only). We will do this by taking samples of bone marrow through a procedure called a 'bone marrow test'. We will compare the bone marrow samples from Group 1 and Group 2 with your healthy bone marrow samples: **i.e. bone marrow from participants who have not had a malaria infection (Group 3)**
4. Whether the immune (T-cell) response to vaccination is changed by repeated malaria infection – we will use the yellow fever vaccine to answer this question as this vaccine is known to stimulate a T-cell response. (Groups 1 and 2 only)

It is hoped that the results of this study will help inform strategies to reduce the frequency of severe disease and death among children in parts of the world where the burden of malaria is high.

Do I have to take part?

No. It is up to you to decide whether or not to take part. Your decision will not result in any penalty, or loss of benefits or access to medical care to which you are otherwise entitled.

If you are eligible for the study, you will have the opportunity to ask the study team any questions you have to help you decide whether you want to take part. You will then be asked to sign a consent form.

You are free to withdraw from the study at any time without giving a reason. However, we would ask that you discuss this with a member of the study team before making this decision. We may also 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 to not participate in the study, or a decision on your part to withdraw from the study, will have no effect whatsoever on your employment/student status at the University.

What will happen if I decide to take part?

After you complete the pre-screening questionnaire, you will be invited to a screening appointment.
If you are eligible and you decide to take part in the study, you would then be enrolled into **Group 3 only**.
The details of the study visits are given later in this information sheet; however, in summary:

- Your screening appointment may take place up to 3 months before the bone marrow procedure. At this appointment, the study team will check your eligibility by asking you questions, doing an examination and taking blood samples. We will then check your blood results after the visit.
- Your group of participants (**Group 3**) will undergo a bone marrow test only. You will NOT undergo a malaria challenge. You will NOT receive a yellow fever vaccine. The purpose of this group is to provide healthy bone marrow samples for comparison with Group 1 and Group 2.
- 7 days after the bone marrow procedure you will receive a phone call from one of the study team. This is to check that you are feeling okay after the procedure.
- Your total study time will be maximum **3 months.** This is calculated from the screening appointment until the completion of the bone marrow test and the telephone review appointment.

Visits will take place in the Centre for Clinical Vaccinology and Tropical Medicine (CCVTM) and the Oxford Experimental Medicine Clinical Research Facility (EMCRF). This is at the Churchill Hospital in Oxford. The CCVTM clinic is wheelchair accessible. If you have other accessibility needs, please contact us to discuss them. We will try to meet your needs wherever possible.

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

Am I eligible to be involved in the study? Group 3 only.

In order to be involved in the study you must be:

- A healthy adult aged 18 to 45 years
- Able and willing to meet all study requirements
- Willing to allow the Investigators to access volunteer's electronic medical records or discuss the volunteer's medical history with their GP
- Willing to refrain from blood donation during the study period
- Able to travel to CCVTM (Churchill Hospital)

You cannot take part in this study if:

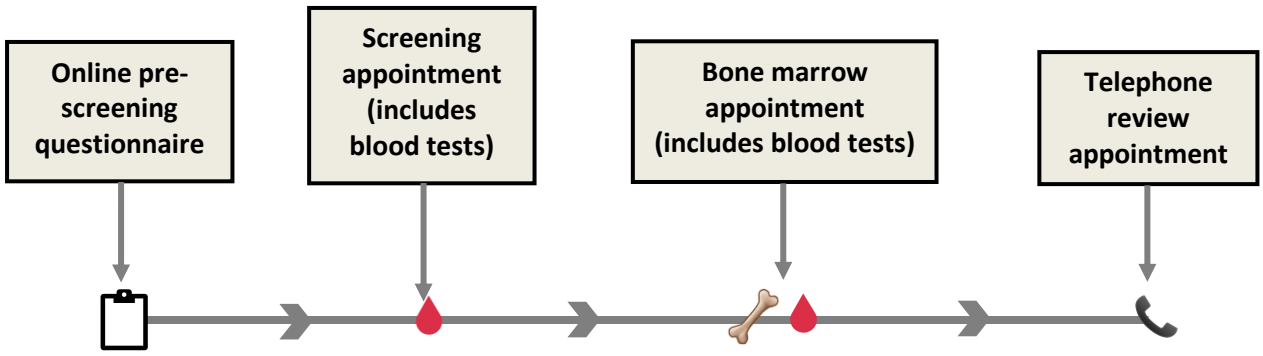
- **You have had malaria before or previously participated in a malaria challenge study**
- **You have previously received a malaria vaccine (e.g. as part of a clinical trial)**
- **You have travelled to an area with malaria transmission in the last 6 months, or, you are intending to travel there during the study period**
- You have received any blood products in the last three months. This includes a blood transfusion or immunoglobulins
- You have had any other vaccine in the past 30 days or plan to have any other vaccine during the study period
- You are taking part in another study using an experimental treatment
- You have problems with your immune system. This includes taking any medication that supresses your immune system
- You have a confirmed or suspected bleeding disorder (e.g. haemophilia)
- You take blood thinning medications (e.g. heparin, warfarin, apixaban, edoxaban)
- You have an allergy to local anaesthetics (e.g. lidocaine)
- You have difficult intravenous access (i.e. it is not possible to take blood from you within three attempts)
- You are pregnant, breastfeeding or intend to become pregnant during the study
- You have a history of cancer (except for basal cell carcinoma of the skin and cervical carcinoma in situ - these are not exclusion criteria for the study)
- You have a history of a serious mental health condition that may affect your taking part in the study
- You have any other serious long-term illnesses requiring hospital follow-up
- You have sickle cell anaemia, thalassemia or any other blood condition that might affect susceptibility to malaria infection
- You drink on average more than 25 units of alcohol a week. A pint of beer is two units, a small glass of wine 1 unit and a shot of spirits one unit
- You have injected recreational drugs at any time in the last 5 years
- You have Hepatitis B, Hepatitis C or HIV infection
- There are any other reasons that the study doctors think you should not join the study

If enrolled in the study, you may be temporarily excluded from undergoing the bone marrow test if:

- You are feeling unwell on the day of your bone marrow test.
- You have a fever (temperature >37.5°C).

Mild conditions do not automatically stop you joining the study. An example could be childhood asthma which is well controlled. If you are unclear whether you are eligible, you can contact the study team who will be able to advise you.

What will happen at the study visits?



Pre-screening questionnaire

Firstly, you will be asked to complete an online pre-screening questionnaire. This questionnaire takes 3-5 minutes and will ask questions to check if you are eligible to be considered for this study. It will also ask for your permission for us to check your medical records and contact you about the study.

If you are potentially eligible, we will then invite you by telephone or email to a face-to-face screening visit. If you only complete the online screening your data will not be kept beyond the end of the study.

Screening visit

The screening visit can take place up to 3 months before the study starts. The screening visit can last up to two hours, however, there will be an opportunity for a short break. The purpose of the screening visit is for you to discuss the study with us and decide if you still wish to take part. We will also ask you to sign a consent form. You will have an opportunity to ask any more questions about the study at this point.

After signing the consent form:

- You will be asked some medical questions.
- A doctor will examine you.
- Blood samples (16mL, approximately 1 tablespoon) and a urine sample (for individuals who are able to get pregnant) will be taken for testing. These test results will need to be normal for you to be enrolled in the study.

The blood tests will look at:

- Your blood count (for example, to check if you are anaemic).
- Your liver and kidney function.
- Whether you have Hepatitis B, Hepatitis C, HIV. You will not be able to enrol in this study if any of these are detected.
- Whether you have antibodies to cytomegalovirus (CMV) or Epstein-Barr virus (EBV), indicating past exposure to these common viral infections. This is because these viruses can affect how your body's immune system behaves.

The urine test will look at:

- Pregnancy (if you are able to become pregnant)

If any of your tests 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 and offer to refer you for further investigation/treatment. If you test positive for Hepatitis B or C, we are required to notify the UK Health Security Agency of this result. It is important for us to do these tests prior to enrolment in the study for two reasons: first, to establish that you fulfil the criteria of a 'healthy adult control', and secondly, to ensure your participation in the trial procedures will be safe.

Some people may test positive for Hepatitis C virus because they have previously taken part in a Hepatitis C vaccine study. You may still be able to take part in our study if this applies to you. In this case, we will contact the team who ran the Hepatitis C vaccine study. We will only do this with your written consent (clause 27 of the informed consent form). 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. We will check your Hepatitis C status with them before enrolling you in this malaria study.

Bone marrow test

As part of this study, we want to try and understand how immune cells are influenced by malaria infection and how they develop immune "memory". Many of these important immune cells live in the bone marrow. Bone marrow is the spongy material found on the inside of most bones and it is where most of the cells in your blood are made. This includes white blood cells, which are an important part of your immune system. In order to examine these cells more closely, we would like to perform a procedure called a bone marrow aspiration and biopsy.

During this procedure, we will take a small sample of bone marrow from your pelvic bone. This bone forms part of the hips and can be reached with a small needle at the lower back area where it is close to the skin surface (Figure 1). You will have the opportunity to discuss the procedure with the study doctor at the screening appointment. You will also have an opportunity to ask the person performing the procedure questions on the day of the procedure.

Before the procedure starts, we will perform some pre-procedure checks (including physical observations) and blood tests. You will then be asked to lie on your side with your knees bent up and your clothing loosened to expose your back at the top of your pelvic bone. Your skin will be cleaned with an antiseptic solution to reduce the risk of infection. Local anaesthetic will then be injected into the skin over the back of the pelvic bone to numb the area where the sample will be taken. Once the area is numb, a needle will be passed through the skin into the bone and a sample of liquid marrow (up to 20ml, just over 1 tablespoon) will be drawn up into the syringe. This is called a bone marrow aspirate. In addition to the liquid marrow, we would also like to take a very thin 1 or 2cm core of bone marrow in one piece to look at the structure of your bone marrow under a microscope. In order to do this, the person performing the procedure will insert a second needle into the same numbed area to take this sample. This is called a bone marrow biopsy. During the procedure, you may experience some discomfort and a "pressure-like" sensation where the needle is being inserted. This usually gets better after the procedure is finished. A video containing information about the bone marrow test can be viewed here: https://youtu.be/tI7m2y_secI.

After the procedure is complete, a small dressing will be placed over the site of the procedure. You should wait 24 hours before removing the dressing or bathing the area. You will be asked to rest in clinic for around half an hour and have refreshments after the test is finished. A member of the study team will check your

dressing and explain how to look after the area where the bone marrow was taken. You will then be able to go home.

You will only be asked to undergo **one** bone marrow test during the study period.

It is important to be aware that the bone marrow procedure in this study is very different to the procedure that you may have heard of relating to the donation of "stem cells". Donating stem cells (e.g. for a bone marrow transplant in the treatment of certain blood cancers) involves a much larger volume of bone marrow and often requires a night in hospital. The procedure we are performing in this study is much simpler, quicker to perform, and is a routine investigation in outpatient clinics of hospital specialists in the diagnosis of certain infections and blood disorders.

This is an image of a person getting a bone marrow test.

The person is lying on his or her side on a hospital bed with the lower back exposed.

The image demonstrates how the needle would be inserted by a medical professional through the skin and outer layer of the hip bone. The needle would pass into the centre of the bone, where the bone marrow sample would be extracted.

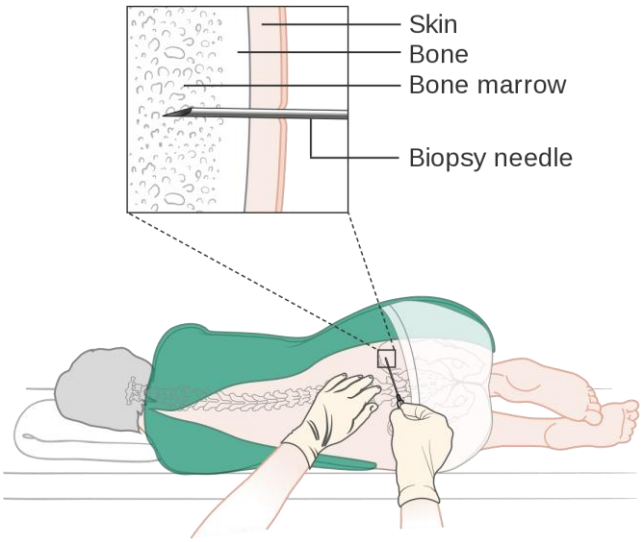


Figure 1: Diagram showing bone marrow test procedure (Image source: Wikimedia Commons)

You will be reminded about the procedure close to the time when we will provide you with some refresher information and give you plenty of time to ask questions.

Telephone review appointment

7 days after your bone marrow test, we will contact you be telephone to perform a quick review. This is to make sure you do not have any symptoms (e.g. such as pain/aching) following the bone marrow procedure, or any questions for the study team. This will be your final study appointment.

Is there anything else to think about?

Blood Donation

If you are a blood donor, we ask that you do not donate blood during the study period due to the additional

blood volume that will be taken during the study.

Medications

Your health and well-being is much more important than the study. If you need any medication, then you should take it. However, it is very important that you let us know **before** you start any treatment.

Pregnancy and Contraception

If you are able to become pregnant, you will be asked to use a highly effective method of contraception. This will be required from when you start the study until the end of the study. This would be approximately 3 months: i.e. from screening appointment until bone marrow test. Condoms alone are not considered effective enough.

Acceptable forms of contraception include:

- Hormonal contraceptives. This includes the pill, mini-pill, contraceptive injection or implant or transdermal patch.
- 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 relationship in which you may become pregnant. Periodic abstinence and withdrawal methods are not acceptable.

A urine pregnancy test will be done at screening.

Private Insurance

If you have private medical insurance you should contact your insurance company before taking part in this study. Involvement may affect the cover provided.

Expenses and Payments

You will be compensated for:

- Screening appointment	£110
- Bone Marrow appointment	£150 per visit

If you choose to leave the study early, or are withdrawn, you will be compensated according to the length of your participation. The reimbursement provided are considered to be reasonable amounts to cover the costs of participating in this research.

Group No.	Time in Study (approx.)	Clinic Visits	Maximum Volume of Blood Taken (ml)	Compensation Amount
3	~3 months	1. Screening appointment 2. 1 x Bone marrow test 3. Telephone follow up appointment	63*	£260

*This is equal to approximately 4 tablespoons of blood

The reimbursement provided is considered reasonable to cover the costs of participating in this research and, as such, should not have any consequences for tax purposes. However, as the amounts detailed above include compensation for both directly incurred expenses (e.g. travel) and other involvement payments, you may wish to discuss your individual circumstances with HMRC. Participants who are receiving welfare benefits are advised seek advice from their provider.

Further information is available at:
1. HM Revenue and Customs (HMRC) EIM71105 - Research volunteers, lay participants and participants in clinical trials https://www.gov.uk/hmrc-internal-manuals/employment-income-manual/eim71105
2. National Institute for Health and Care Research (NIHR) Payment guidance for members of the public considering involvement in research https://www.nihr.ac.uk/payment-guidance-members-public-considering-involvement-research

We may recruit 1–2 'back-up participants' in addition to the 3-5 planned participants in Group 3. These participants will be asked to be available to take part in the study at short notice. This is in case another participant is unavailable at the last minute.

What do I have to do?

- You **must** attend all the visits outlined in Part 1 of this information sheet
- If you are able to become pregnant, you **must** use highly effective contraception until the end of the study period.
- You **must not** donate blood between the screening appointment and bone marrow test

What alternatives are present?

Your alternative is not to take part in this study.

PART 3: RISKS AND BENEFITS

What are the risks of taking part?

The potential risks are as follows:

Blood Tests

At most of the study visits, we will be taking at least one sample of blood from study participants. The amount of blood we will take at each appointment will vary; this may range from approximately 16mL (approximately 3 teaspoons) to 47mL (approximately 3 tablespoons). If the study team have a lot of difficulty taking blood from you during the screening appointment, you may be deemed ineligible for the study.

The maximum blood volume that we expect to draw from participants in Group 3 is 63 mL. The volume of blood being taken over the course of the study 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. You may feel faint as a result of collecting blood. We will only send the results of your blood tests to your GP if you wish us to and will not report them to anyone without your permission.

As we carry out several medical tests throughout the trial, it is possible that we pick up previously unknown health issues (e.g. high blood pressure, abnormal blood results). If abnormal results or undiagnosed conditions are found during the study, these would be discussed with you and, if you agreed, your GP would also be informed of these results. Sometimes incidental medical findings might require your GP to carry out further investigations such as blood tests, scans or referral to specialists.

In the UK, healthcare professionals are legally obliged to report any new suspected cases of hepatitis B and hepatitis C to the UK Health Security Agency (UKHSA). If you are found to have hepatitis B or C, we will be required to send a report to the UKHSA, including your personal contact information. It's important to note that you cannot opt out of this due to UK reporting requirements.

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

- Your full blood count, liver and kidney function, serum cholesterol
- Blood borne infections (HIV, Hepatitis B & C, EBV, CMV)
- Thalassaemia, sickle cell anaemia and other conditions that affect the blood
- Immune cell analysis (to look at how these compare to people with a malaria infection)
- Genetic analysis of your cells (to look at genes that are expressed)

Bone Marrow Test

The bone marrow test is a safe procedure, however, there are a few important risks that you should be aware of.

Local anaesthetic (such as lidocaine) is very safe and serious side effects are very rare. You may experience “stinging” from the local anaesthetic when it is being injected. You may also have some bruising where the local anaesthetic was injected, but this usually gets better within a few days. Occasionally, people can experience an allergic reaction to local anaesthetic. **If you have a known allergy to local anaesthetic, you will not be able to take part in the study.** Very rarely, local anaesthetic can cause damage to the tissue it is injected into (known as “necrosis”). Very rarely, people can experience symptoms such as dizziness, headaches, blurred vision and muscle twitching. These are very rare side effects of local anaesthetic and not likely to occur during this procedure. Only a small amount will be injected using a small needle,

therefore minimising the risk of injury, and the person performing the procedure will be experienced in injecting this medication.

Sometimes people find the bone marrow test procedure very uncomfortable, despite the injection of local anaesthetic. If this is the case for you, we can provide you with a pain-relieving gas called **Entonox** (a mixture of nitrous oxide and oxygen, more commonly known as 'gas and air') during the procedure to make it more comfortable. Entonox is delivered through a handheld mouthpiece which allows you to control how much of the gas you breathe in. It has a few side effects including drowsiness, dizziness and nausea, and can also give you a dry mouth. The effects of Entonox wear off very quickly, so, you will be able to drive home if you attended the visit by car. Entonox will only be administered by a trained individual.

Some discomfort during the bone marrow test is common, however, if you are experiencing a lot of discomfort during the procedure, please let the person performing the procedure know. **You can ask for the procedure to be stopped at any time.**

Mild pain/discomfort following the procedure is also common but typically does not last very long (usually less than 24 hours). In particular, you may feel an achiness in your back after the local anaesthetic wears off. This is usually relieved with paracetamol.

A small amount of bleeding can occur after the procedure, however, this usually stops after applying firm pressure over the dressing. In extremely rare circumstances, bleeding can continue from the site of the procedure and the blood can get trapped in the muscle around your bone causing pressure. This is called compartment syndrome and is a very rare complication of the bone marrow test. In order to reduce the risk of this complication, you will have a blood test at screening to check that your platelet counts in your blood are within the acceptable range for the procedure. Platelets are important cells that help your blood clot. If your platelet count is too low, we will postpone the bone marrow test for 1-2 days and re-check your platelet count to ensure that it is within an acceptable range before performing the procedure. It is important to note that this procedure is commonly carried out in people with low platelets without complication. One study found that out of more than 13,500 bone marrow tests performed in the UK in one year, there were only 9 episodes of bleeding, so this risk is very low.

There is also a small risk of infection at the site of the bone marrow test, however, extreme care will be taken to keep the procedure sterile in order to minimise this risk, including the use of antiseptic to clean the skin and the use of sterile equipment.

In very rare circumstances, the needle used can pierce a blood vessel or an organ in your abdomen. This is an extremely rare complication of this procedure, however, the person performing the procedure will be able to recognise the signs and manage this complication if it occurs.

To minimise the risk of any complications from the bone marrow test, the procedure will only be performed by a fully trained individual. If there are any clear reasons why we should not perform to bone marrow sampling on the day, then the procedure will be delayed until these have resolved and the procedure can be safely performed. Following the procedure, every participant will have 24 hour telephone access to an on-call study doctor who can advise if there are any concerns relating to the procedure.

What are the possible benefits of taking part?

This study will not directly benefit you. The information gained from the study might help us to better understand how to prevent severe disease and death among thousands of infants who live in areas where malaria is common.

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 may be asked to sign an updated consent form. On receiving new information, we may 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 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 data are destroyed at any time during or after the study until analysis begins. 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 study.

The Investigators recognise the important contribution that study participants 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 study team (contact details at the end of this document). You may also contact the University of Oxford Research Governance, Ethics and Assurance (RGEA) office on 01865 616480 or the director of RGEA, email RGEA.Complaints@admin.ox.ac.uk. The RGEA office can also be contacted if you have questions about your rights as a study participant.

Will my taking part in this study be kept confidential?

Personal details will be stored securely and separately from the research data. Responsible members of the University 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. Your information will be stored electronically on a secure server and any paper notes stored securely in a secure location at the study site.

Involvement of the GP (General Practitioner/Family doctor)

In order to enrol into this study you will be required to sign a form to say that you consent for us to contact your GP. This is to inform them that you are interested in being involved in the study. We will check there are no medical reasons that they are aware of that would make your taking part inadvisable. Your GP may be asked to share information about your medical history and give access to any other medical records as needed. You will not be enrolled in the study if your GP has 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 on to a national database which helps prevent volunteers from taking part in too many clinical studies. If you are a non-UK citizen, you will need to provide your Passport number to be entered onto this database. More information can be found at https://www.hra.nhs.uk/about-us/committees-and-services/the-over-volunteering-prevention-system/. Your national insurance or passport number is also required to allow processing of compensation payments.

What will happen to any research samples I give?

Clinical safety blood samples are sent to local NHS laboratories and follow local sample labelling requirements (which may include personal identifiers). As part of processing the clinical safety blood samples, the laboratories may be required to add the results to your medical records.

Samples sent to research laboratories for processing will not have personal identifiers (they will be identified by study number and participant number only).
Your blood and bone marrow samples will primarily be analysed in research laboratories at the University of Oxford and the University of Edinburgh. They may also be analysed at other collaborating research institutions in the UK and other countries. Your blood and bone marrow samples will be handled in accordance with the relevant national and regional guidance (e.g. Scotland and England) and the principles of the Human Tissue Act.

With your consent, some of your leftover blood and bone marrow samples may be stored indefinitely at the University of Oxford and/or the University of Edinburgh for use in future research. These will be coded with a study number. Your informed consent form will also be stored securely (and separately from the research data and sample itself) until the samples have been depleted or destroyed in order to comply with the Human Tissue Act. The blood samples may be used for further related research, including of the human body's immune system, vaccine research and/or your safety. Any such future research will have an appropriate ethical review. You may request that your remaining blood and bone marrow samples are destroyed at any time. If you decide to withdraw your consent to storage of leftover samples, they will be disposed of at the end of this study.

Urine samples will be destroyed immediately after testing.

Will any genetic tests be done?

Yes. Some blood will be used to look at the pattern of expression of your genes that can affect the immune system (so-called 'gene expression' analysis). This type of analysis looks at how information in

your genes is used to make proteins or a different type of genetic material called 'RNA'. 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.

Data will be collected and held by members of the Oxford Vaccine Group (OVG). It will be accessible to responsible staff at OVG and the University of Oxford who may monitor/audit the data collection process, and inspectors from the regulatory agencies responsible for research in the UK. The database servers are secure and held by the University of Oxford. We will keep identifiable information about you such as contact details for a minimum of 5 years after the study has finished. The need to store this information for longer will be subject to ongoing review. Pseudonymised research data will be stored indefinitely.

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 (e.g. if you request to be informed of other studies/trials), 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 CCVTM, personal information and medical information including blood test results may be accessed to avoid unnecessary repetition.

A photocopy of your ID (driver's licence, passport or national ID card) and either your national insurance or passport number for TOPS database registration (see below) and payment processing will be taken at the screening visit. We will securely retain copies until the end of the study.

Your information may also be shared with partners working with Oxford University. This information will be identified only by the unique study number. You will not be directly identifiable. All data received will be kept securely by these parties in line with all regulatory requirements. If the study is paused due to safety concerns relating to the yellow fever vaccine, medications prescribed by the study team, or heavy water, we will inform the local ethics committee, the study funders (MRC) and the manufacturers of vaccine/drug/heavy water as appropriate. The data shared would be pseudonymised.

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

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.

Involvement of the OVG Quality Assurance Team (Independent Monitors)

The OVG Quality Assurance Team act as independent monitors on behalf of the Sponsor to ensure we are complying with the clinical trial regulations. They 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 OVG Quality Assurance Team will comply with the University's Information Security Policies.

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. When we know the results of the study, we will send participants a summary of findings.

The anonymised data from this study will be shared with the partners who are organising and funding this research. 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. 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 postgraduate degree, for example an MD or PhD.

The results of this research study may be presented at scientific meetings or conferences and published in scientific or medical journals. 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.

A description of this clinical study will be available on https://www.isrctn.com/. 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 research studies

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 research studies. This is entirely optional. Taking part in this study will not be affected by your decision as to whether to allow storage of your contact details beyond your participation in this study.

Your details would be stored electronically on a secure server. Only authorised individuals at the CCVTM 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 and is funded by an Experimental Medicine grant from the UK Medical Research Council (MRC). The MRC is a UK-based organization which funds biomedical and clinical research. Neither your GP nor the researchers are paid for recruiting you into this study.

Who has reviewed the study?

This study has been reviewed by the National Research Ethics Service Committee South Central Berkshire 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.

Thank you for reading this information sheet. If you are interested in taking part in the study please complete the online pre-screening questionnaire at https://www.ovg.ox.ac.uk/studies/bio004 or

contact the study team at your local study site to arrange a screening appointment. You can also contact us with any questions about what you have read.

Contact details for further information:
Volunteer Recruitment Co-ordinator
E-mail: info@ovg.ox.ac.uk
Tel: 01865 611400
Oxford Vaccine Group, CCVTM, Churchill Hospital, Old Road, Headington, Oxford, OX3 7LE