

BIO-004: ABBREVIATED PARTICIPANT INFORMATION SHEET

Understanding how the immune system responds to repeated malaria infections.

Why are we conducting this study?

Malaria is a disease caused by an infection transmitted by mosquitoes. It causes over 600,000 deaths every year, mainly in countries in Africa. Most of these are children under the age of 5 years who can experience breathing difficulties, kidney failure and seizures due to severe forms of the disease.



Severe malaria¹

Following repeated malaria infections, people develop natural immunity to the disease which protects them from severe illness. We think that there is an “overactive” immune response to the first malaria infection, which can be harmful rather than helpful. But in subsequent infections the immune system responds differently and learns to tolerate the infection, protecting the individual from severe forms of the disease. How this occurs is unknown.

The BIO-004 study is trying to understand how the immune system learns to tolerate malaria over the first few infections of life. It will provide us with the knowledge required to develop new treatments that can prevent childhood deaths due to malaria.

Thank you for your interest in the BIO-004 study. Help us in the fight against malaria!

Who can take part?

- ✓ Healthy adult age 18-45 years
- ✓ Not had malaria before
- ✓ Not received the yellow fever vaccine
- ✓ Able to attend study visits over a 20-month period

You may be able to take part!

Please see the full version of the [Participant Information Sheet](#) for a complete list of eligibility criteria

What does the study involve?

We would like to assess the immune response to repeated malaria infections by performing **malaria challenges**. A malaria challenge is where we introduce a deliberate malaria infection in carefully controlled conditions. We then monitor infection levels using blood tests and start treatment with effective malaria tablets when your infection levels are low to completely clear the infection. We will perform a malaria challenge on three occasions, each separated by around 5 months, and compare how your immune system responds to each infection.

This study also involves:

- **Blood tests**
- **Yellow Fever Vaccine**
- **Heavy Water**
- **Bone Marrow test**

Did you know that over 600 people have previously had a malaria challenge as part of a clinical trial in Oxford?

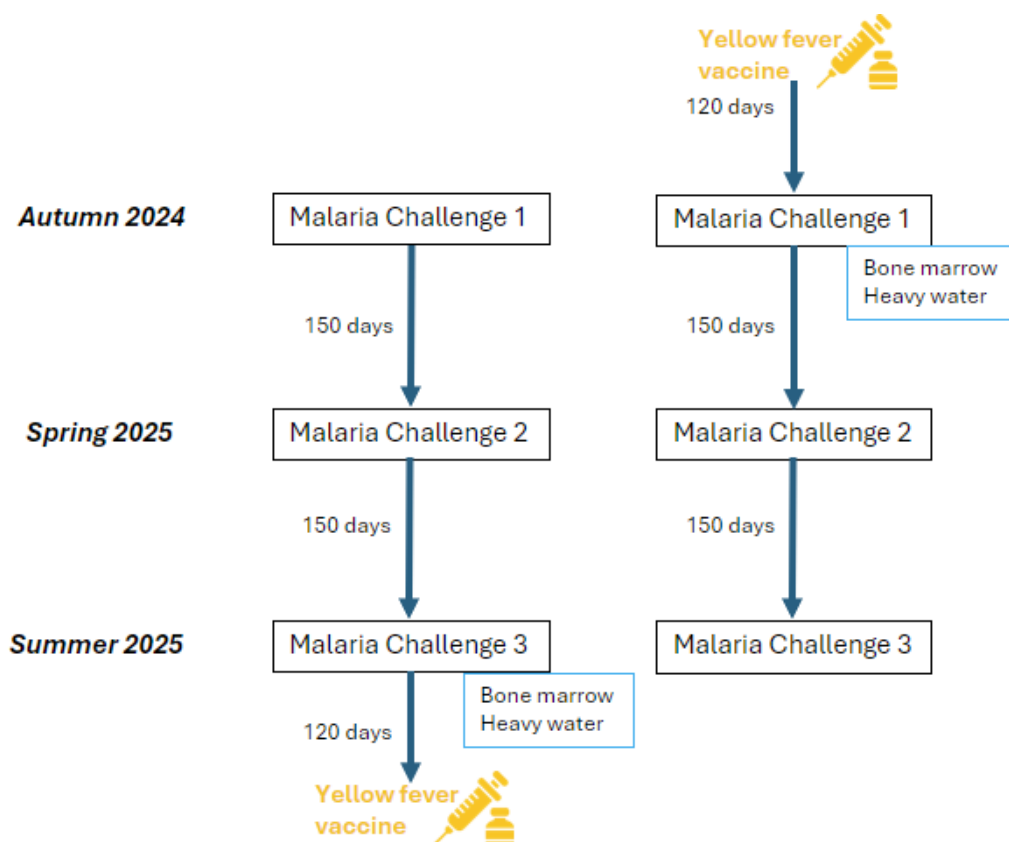
[Watch this video](#) hear about their experiences

See below for more details!

What does the schedule look like?

We will recruit two groups of 11 volunteers. Both groups will undergo the malaria challenges at the same time. The timing of the other study procedures will depend on group allocation (see below).

- **The total study duration is 20 months***
- **The expected number of visits is approximately 70 (between 50-85 visits)**
- **We will provide compensation for your participation. This will be up to £9,100**



**Optional follow up visits at 23 and 35 months*

What are the study procedures?

1. Malaria Challenge

A small volume of fluid (approximately 5ml) that contains the malaria infection will be introduced through a drip (“cannula”) in your arm.

- Group 1: receive *Plasmodium falciparum* malaria at each challenge
- Group 2: receive *Plasmodium falciparum* malaria at the first and second malaria challenge. The third challenge is with a slightly different malaria sub-type called *Plasmodium vivax*

After the malaria challenge, you can go home and continue with your usual activities. However, we will need to check you every day so that we can start antimalarial tablets once you have a detectable infection (no more than 2.5 weeks after challenge). People may experience some early symptoms of malaria such as mild flu-like symptoms. We ask that you remain in the Oxford area during this time so that we can start treatment promptly. The study doctor is available 24/7.

The malaria infection is prepared from a diluted human blood donation. This has been rigorously screened and tested and has been safely used in all our previous studies. However, it is regarded as a tiny blood transfusion and therefore, under current UK guidance, you would not be allowed to be a blood donor in the future.

2. Yellow Fever Vaccine

This vaccine is widely used in countries where the yellow fever virus, another infectious disease transmitted by mosquitoes, is found (e.g. countries in South America). It is a very effective vaccine and produces a reliable immune response. We want to see how these yellow fever-specific immune cells behave before, during and after the malaria challenges to give us an idea of what the immune system is doing.

3. Heavy Water

This looks and tastes exactly like normal tap water and is just as safe but is made from a slightly different water molecule. It will help us identify your immune cells so that we can monitor them during the malaria challenges. We will ask you to drink a small amount of Heavy Water for 2-3 weeks after one of your malaria challenges.

4. Blood tests

Blood samples will be taken at most study visits. We will use these to check:

- Routine blood counts, kidney and liver function.
- Measure malaria infection levels.
- Assess your immune response.

5. Bone marrow test

We want to understand how your immune system remembers to tolerate malaria infections. We think this happens in your bone marrow because most of your immune cells that have “memory” live in the bone marrow. To examine these cells more closely, we would like to perform a procedure called a bone marrow test once during the study. During this procedure, we will take a small sample of bone marrow from your pelvic bone. This bone can be reached with a small needle at the lower back area where it is close to the skin surface. We will use local anaesthetic to minimise any discomfort. The procedure we are performing in this study is safe and commonly performed as a routine outpatient investigation for people with certain blood disorders. We will provide you with more information and the opportunity to ask any questions before undertaking this procedure.

Is there anything else I should know?

▪ Are there any risks or benefits of participating?

Untreated malaria infection can result in serious illness. Therefore, it is important that you attend all the clinic visits and take the anti-malarial treatment as advised. The malaria challenge can be associated with flu-like symptoms. Symptoms following the yellow fever vaccine, such as arm pain and fever, may also occur. There is a small risk of pain, bleeding and infection following a bone marrow test. More information can be found in the [Participant Information Sheet](#). Participating in this study will not benefit you directly. However, it will greatly improve our understanding of the immune response to repeated malaria infections. This will help us develop more effective treatments and strategies to stop children dying because of malaria.

▪ How do I sign up?

Thank you for your interest! To express an interest in participating in the BIO-004 study, please complete our online questionnaire.

➤ [Visit our website](#)

➤ Scan the QR code



The questionnaire takes 5-10 minutes and will ask questions to see if you could be eligible for participation. It will also ask for your contact details and permission to contact you so that we can arrange an in-person appointment.

▪ What happens next?

The next step is a screening appointment with one of the study doctors. This appointment lasts 1-2 hours and involves a detailed discussion about the trial, review of the full eligibility criteria, blood tests and a medical examination.

▪ How long are the other visits?

The malaria challenge will require you to be present for most of the morning on the day of challenge. However, the other study visits are much quicker and generally take no more than 30 minutes. These generally fit around normal working or studying patterns for most people.

▪ How do I find out more information?

➤ More detailed information about this study can be found in the [Participant Information Sheet](#) – full version. **We require you to read this document before you can be part of this study.**

➤ Watch our [video about the BIO-004 study](#)

➤ Find out more about participating in a malaria challenge study from some of our previous volunteers in our [malaria challenge video](#)

➤ Contact us using the details below. We would be more than happy to answer any queries!

Dr Andrew Duncan, Clinical Research Fellow

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References

1. **Image from Medicines for Malaria Venture, Africa-Europe partnership launches study to evaluate emergency response tools for severe malaria in highly isolated rural settings.** Available at <https://www.mmv.org/newsroom/news-resources-search/SEMAREACT-PR>. Accessed 30th November 2023