PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Participant Information Sheet- Genotype Testing (Optional component of CTM2002)

Title	A phase 1b study to evaluate the blood stage antimalarial activity of a single oral dose of tafenoquine in healthy subjects experimentally infected with *Plasmodium falciparum*.
Protocol Number	CTM2002
Ethics Number	P3646
Study Part	Genotype Testing (Optional component of CTM2002)
Sponsor	QIMR Berghofer Medical Research Institute
Principal Investigator	Associate Prof. Bridget Barber QIMR Berghofer Medical Research Institute 300 Herston Road, Herston, QLD 4006 AUSTRALIA Tel: +61 424 737 153
Location	USC Clinical Trials Unit 19-31 Dickson Road Morayfield QLD 4506 Australia Tel: +61 (0)7 54563965
Version / Date	Version 1.0 / 17 August 2020

INTRODUCTION

You are invited to take part in this optional research project, because you have consented to the malaria volunteer infection study **CTM2002: "A Phase 1b study to evaluate the blood stage antimalarial activity of a single oral dose of tafenoquine in healthy subjects experimentally infected with *Plasmodium falciparum*".** This optional research project involves donating approximately 4 mL of your blood. Your decision whether or not to participate has no bearing on your participation in the malaria volunteer infection study.

This Participant Information Sheet/Consent Form tells you more about the research project. Please read this information carefully as it explains the purpose of the additional sample and the risks of genetic testing. Understanding what is involved will help you decide if you want to take part in this research project. **If there is anything you do not understand after you have read this form, please ask the study doctor**.

Participation in this research project is voluntary. If you don't wish to take part, you don't have to. Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with USC Clinical Trials. You will receive the best possible care whether or not you choose to take part in this research project.

If you decide you want to take part in this research project, you will be asked to sign the consent section. Please refer to the information outlined in the malaria volunteer infection study Participation Information sheet and informed Consent Form (PICF) which also applies to this additional sample. This separate informed consent is only signed in combination with the malaria volunteer infection study PICF.

By signing this consent form you are telling us that you:

- understand what you have read
- consent to take part in the study
- consent to have the tests that are described
- consent to the use of your personal and health information as described

You will be given a copy of this Participant Information and Consent Form to keep.

You will be asked to provide a photo ID at your visit to the clinical trials site for this research project.

WHAT IS GENETIC RESEARCH?

Genes are made of DNA – the chemical structure carrying your genetic information that determines many human features such as the colour of your eyes or hair.
Researchers study genes in order to understand why some people have a certain condition such as Gilbert syndrome and why some people do not. Understanding a person's genes also may be able to explain why some people respond to a treatment, while others do not, or why some people experience a side effect and others do not.

WHAT IS THE PURPOSE OF THIS RESEARCH?

The purpose of the research is to check for genetic differences (called polymorphisms) which could be linked to changes in your body due to malaria. These differences may be different from one person to another. We would like to know if the interaction between malaria and the antimalarial drugs given during the study, has any possible effects on your liver. This is done by testing for polymorphisms in genes or nearby regions of DNA. Some examples of polymorphisms we may screen for include:

- Variations in a gene (UGT1A1) which cause Gilbert syndrome. Gilbert syndrome results in higher than normal blood levels of bilirubin (a breakdown product of red blood cells). This condition normally has no serious health consequences and does not require specific treatment.
- Variations in a DNA region with a role in regulation next to the haem oxidase-1 gene (HMOX-1). These variations have been associated with severe malaria in patients.
- Variations in a DNA region with a role in regulation next to the tumor necrosis factor alpha gene (TNFα). These variations have been associated with severe malaria in patients.
- Variations in currently unknown genes or nearby DNA regions which may be discovered in the future that could have an impact on liver function.

It is important for this malaria volunteer infection study that we know if any changes in liver function in participants are due to Gilbert syndrome or other inherited genetic differences that affect how the liver responds to malaria or how the liver handles antimalarial drugs used in this study.

WHAT DOES MY PARTICIPATION IN THIS RESEARCH INVOLVE?

If you agree to take part in this research project, a blood sample of approximately 4 mL (approx. 1 teaspoon) will be taken.

There are no additional costs associated with participating in this research project; you will not be paid for this additional sample collection.

WHAT DO I HAVE TO DO?

Participation in this research project is voluntary and does not affect your participation in the malaria volunteer infection study. If you don't wish to take part, you don't have to.

If you do decide to take part, you will be given this Participant Information and Consent Form to read and sign and you will be given a copy to keep. An additional sample of blood (approximately 4 mL) will be collected on the day you are injected with the malaria parasites (Inoculation Day). No additional clinic visits are required.

CAN I WITHDRAW FROM THE STUDY?

Your participation in this optional genetic research project is purely voluntary. You may refuse to take part or withdraw at any time and without any prejudice. You may be withdrawn from the genetic study if the Study Doctor feels it is best for you or if you do not comply with the requirements of the genetic study. If you decide to take part and later change your mind it may be that some of your blood has already been used for research purposes. If you do not want the information used, please contact the study staff.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

There are no health benefits to you from taking part in this optional genetic research project.

WHAT ARE THE POSSIBLE RISKS AND DISADVANTAGES OF TAKING PART?

RISKS OF GENETIC TESTING

Genetic testing involves the study of genetic material (typically DNA) that is shared with your blood relatives. Genetic research is undertaken for many reasons, including discovering more accurate ways of predicting disease within a group of people, or in people where there is strong family history or predisposition of disease.

Genetic testing may raise important issues. Although few may be expected to arise, your awareness of this is important for you to think about and carefully consider before agreeing to participate.

Learning about the results from genetic research might affect you and your family emotionally. You may learn information from your test result about inherited genetic variations that you have.

Statutory or contractual duties may require you to reveal results of genetic tests or analysis to third parties (e.g., insurance companies), particularly where results provide information about your future health. If the results of your genetic tests are not available to you or you choose not to have the results given to you, then your future requests for insurance may not be affected by participating in this research project.

If you do obtain the results of your genetic tests, you may then be obliged to disclose this on any future application for insurance should it be requested. As of 1st July 2019 Standard no. 11 of the Financial Services Council memorandum states that people can access life insurance without being asked about the result of a previously taken genetic test. Results can still be requested in certain circumstances, please review the standards at https://www.fsc.org.au/resources/standards/ for further information

To our knowledge, the genetic tests we are intending to do in this study have no implication for your health or insurance. Only authorised people will have access to your results and they will comply with privacy standards (see 'Confidentiality of Records' below).

RISKS OF BLOOD COLLECTION

There is some risk of pain or local bruising and infection at the site where blood is drawn for laboratory tests. The study doctor and clinical trial site personnel are very skilled in blood collection, but this study is not suitable for people who are afraid of needles or having blood collected.

There is also a small risk of a fainting episode, which can occur as a reaction to donating blood. However, the additional blood sample will be collected at a single time-point and will be only approximately 4 mL in total.

WILL I BE COMPENSATED?

As this genetic study falls alongside collection times for the malaria volunteer infection study, there are no additional compensation payments (which are provided for your time, travel expenses, parking and inconvenience).

WHAT WILL HAPPEN TO MY BLOOD SAMPLE?

Your blood sample will be stored indefinitely at QIMR Berghofer Medical Research Institute. It will be stored as a de-identifiable sample. This means that your sample will have all identifiers (e.g. name and personal details) removed and replaced by a code. To protect your privacy, only authorised people will be able to identify the sample as yours.

In the future, if we discover a reason why some people react differently to malaria infection and antimalarial drugs compared to other people, and we want to investigate this using your stored blood. Your stored blood sample will be sent directly to Sullivan Nicolaides Pathology, a diagnostic testing laboratory, to test for polymorphisms in genes or nearby regions of DNA as described in Question 3.

WILL I BE GIVEN THE RESULTS OF THE RESEARCH PROJECT?

Your genetic test results will only be made available to you if requested. Genetic information is complex and can be influenced by other factors including environment and lifestyle. If you decide to see your genetic test results the Study Doctor, or clinical staff authorised by the Study Doctor, will discuss the results with you. During this discussion you can also request to speak to a genetic counsellor who can give you further details that are relevant to you, answer your questions and discuss your concerns. If you wish to speak to a genetic counsellor, we can organise this with no cost to you.

CONFIDENTIALITY OF RECORDS

This study is being conducted under the Australian regulatory agency, the Therapeutic Goods Administration (TGA). All records are kept for a minimum of 15 years. All information obtained during this study including clinic and hospital records, personal information and research data will be kept confidential. Your personal information specifically relating to your health before, during and after your participation in this study is recorded on special forms by the Study Doctor and Q-Pharm staff. Your name is included on some of these forms, and only your initials

on others. Any information taken from these records will be coded by your study identification number and in some cases your gender and age will be included also.

It is anticipated that the results of this research project may be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified. Only your study identification number (and in some cases your gender and age) will be included in such reports.

Your records (which will include your name, some personal particulars, your medical history, the results of your blood and urine tests, your medical examinations, and the blood levels of the drugs you take for the study) may, however, be inspected by relevant authorities, the Sponsor and their authorised representatives, and the Research Ethics Committee at the clinical study site only. The representatives of these organisations all comply with privacy standards.

We will not use your personal health information for a different research project without the permission of a Human Research Ethics Committee. Once all personal identification is removed, the information might be used or released for other purposes without asking you.

In accordance with Australian and Queensland privacy and other relevant laws, you have the right to request access to your information collected and stored by the study team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

WHO HAS REVIEWED THE RESEARCH PROJECT?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the QIMR Berghofer HREC.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007, updated May 2018. This statement has been developed to protect the interests of people who agree to participate in human research studies.

WHO SHOULD I CONTACT IF I HAVE QUESTIONS?

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

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

General contact details

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

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Phone	(07) 5459 4759

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

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	QIMR Berghofer HREC
Telephone	07 3362 0117
Email	HREC.Secretariat@qimrberghofer.edu.au

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

INFORMED CONSENT FOR GENETIC TESTING

A Phase 1b study to evaluate the blood stage antimalarial activity of a single oral dose of tafenoquine in healthy subjects experimentally infected with *Plasmodium falciparum*

Protocol Number	CTM2002
Project Sponsor	QIMR Berghofer Medical Research Institute
Principal Investigator	Associate Professor Bridget Barber
Location	USC Clinical Trials Unit 19-31 Dickson Road Morayfield QLD 4506 Australia Tel: +61 (0)7 54563965

I have read and understood this additional study information related to genetic testing. I have had the opportunity to discuss and ask questions about this additional study and my questions have been answered to my satisfaction. I hereby give my consent to provide the additional blood sample.

I also understand that all statements in my main consent form that I have already signed are still in effect. I understand that I am free to withdraw from the study:

- at any time
- without having to give a reason for withdrawing
- and without affecting my future medical care

I understand that I will be contacted if the testing shows important information about me, and I will be asked if I wish to know the results.

In respect to the storage and use of my genetic samples, I give permission for the use of my blood sample/DNA for the purpose of:

1. This research project only Yes ☐ No ☐
2. This research project and any closely related future research projects Yes ☐ No ☐
3. Future research projects that may or may not be related to this research project Yes ☐ No ☐

Participant:				
	Full Name	Signature	Date	Time

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

Study Doctor:				
	Full Name	Signature	Date	Time

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

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

FORM FOR WITHDRAWAL OF PARTICIPATION

A Phase 1b study to evaluate the blood stage antimalarial activity of a single oral dose of tafenoquine in healthy subjects experimentally infected with *Plasmodium falciparum*

Protocol Number	CTM2002
Project Sponsor*	QIMR Berghofer Medical Research Institute
Principal Investigator	Associate Professor Bridget Barber
Location	USC Clinical Trials Unit 19-31 Dickson Road Morayfield QLD 4506 Australia Tel: +61 (0)7 54563965

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with USC Clinical Trials Unit or QIMR Berghofer Institute of Medical Research.

In respect to the use of information that may have already been collected from this research project, I would like:

1. All information collected to be discarded. Yes ☐ No ☐
2. Existing information may be kept but my sample will be discarded. Yes ☐ No ☐

Participant:

Full Name	Signature	Date	Time

Declaration by Study Doctor

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Study Doctor:

Full Name	Signature	Date	Time

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.

This page is the manifestation of an electronic signature certifying that I have reviewed the electronic copy of this document and certify that it is an exact copy having all of the same attributes and information as the original document.

Document Name: CTM2002_PICF Tafenoquine_Genetic - Version 1.0_17Aug2020
Document ID: 4216
No. Pages: 9
Study: QIMR Berghofer Medical Research Institute - QIMR Tafenoquine Malaria - CTM2002

Electronic Signature for: Fiona Groom
Electronically Signed by: fgroom
Date & Time: 20/OCT/2020 12:51 PM AEST
IP Address: 203.29.104.121