

**APPENDIX B**

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**INFORMATION SHEET**

A randomised, double-blind comparative study to evaluate the safety, tolerability and effectiveness of tafenoquine and mefloquine for the prophylaxis of malaria in non-immune Australian soldiers deployed to East Timor

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Protocol No.  
***SB 252263/033 (ADMEC 216/00)***

You have been asked to take part in this research study. The purpose of this form is to explain this research study to you and to obtain your consent to take part in this study.

**PURPOSE OF THE STUDY**

Because you are deploying to an area where Malaria is known to occur, the decision has been taken by Land Command Health Services to provide you with drugs to protect you against this potentially life-threatening disease. The purpose of this study is to look at the safety and effectiveness of a new drug, ***tafenoquine***, for the prevention of malaria. We also wish to compare tafenoquine with another drug, ***mefloquine***, which has been widely used over the past decade and is one of the alternative drugs currently used by the ADF to prevent malaria.

**WHAT IS THE MEDICINE?**

If you agree to take part in the study, you will be assigned at random to one of two treatment groups. The study will be "*double-blinded*" which means that neither you nor your doctor will be aware which medication you are taking.

You will receive either one tafenoquine (200mg) capsule each day for three consecutive days during pre-deployment training followed by one tafenoquine capsule weekly throughout the deployment or one mefloquine (250mg) capsule each day for three consecutive days during pre-deployment training followed by one mefloquine capsule weekly throughout the deployment. You will have a 75% chance of being on tafenoquine and a 25% chance of being on mefloquine. You will take all medication with food to reduce side effects. The doses will be issued to you weekly so we can accurately record when you have taken your medication.

When you return to Australia, you will undergo treatment to get rid of any malaria parasites that may have collected in your liver. Those who received mefloquine will be given the standard drug used for this purpose called primaquine. You will take one capsule (15mg) twice a day for 14 days. If you received tafenoquine, this eradication course is not necessary, therefore you will take one capsule of placebo twice a day for

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14 days. As before, you will not know which treatment you are taking, but you will have a 75% chance of receiving placebo and a 25% chance of receiving primaquine.

While tafenoquine has been given to several thousand individuals safely (including more than 1,000 ADF personnel during trials in Bougainville and East Timor), it has not yet been registered with the regulatory authorities in Australia or the USA. Consequently it is still defined as an “experimental” compound.

## **WHAT IS THE STUDY?**

The study involves up to 700 volunteers receiving tafenoquine or mefloquine weekly throughout the deployment. Should you develop a fever within 12 months of returning home, you are asked to attend your local health facility and show them your study ID card. This ID card will contain details on how you should be investigated, how to contact the investigators, and how you should be treated if malaria is diagnosed.

## **LENGTH OF THE STUDY**

The study will begin during pre-deployment training in Townsville, continue during the deployment, with follow-up until 6 months after your deployment is completed. Your only involvement after redeployment will be normal follow-up (after 6 and 12 weeks) by your RAP according to LHQ directives, plus telephone interviews at 18 and 24 weeks after returning to Australia. Should you get malaria after this, your Doctor or RAP will undertake normal reporting to AMI. There are no additional blood tests during the follow-up period over those normally required for personnel re-deploying from overseas service.

## **STUDY TESTS**

As the investigators are looking at drug levels in your blood, checking your blood for malaria and measuring biochemical (liver and kidney function) and haematological (blood cell) levels in your blood to monitor safety, you will be requested to provide samples of blood from your arm. These tests involve the drawing of 9mls (two teaspoons) of blood on up to 9 occasions. Three (3) of these samples would be required anyway as part of your deployment requirements as directed by LHQ. Over the course of the study, a total of 81mls of blood will be collected.

A selected Company sized group will also have additional tests (including chest X-ray and ECG) done to look at other effects that either of the study drugs may have, as well as having eye and lung function tests done before and after the deployment. This will require an additional 20 mls of blood to be taken.

Female volunteers will have pregnancy testing performed on their blood samples on all occasions that blood is taken. No additional blood will be taken for this purpose.

## RISKS / DISCOMFORTS

There may be some bruising with blood taken from the veins in your arm.

Tafenoquine has a risk of producing a bleeding disorder if given to people who lack a particular enzyme called G6PD. You have been tested for this enzyme prior to deployment, and will not receive either drug if you have this deficiency. In eight previous clinical trials involving human subjects, including studies in ADF personnel on Bougainville, tafenoquine was noted to produce nausea, vomiting and diarrhoea in some subjects (usually self limiting and improved by taking the medication with food) and mild headache. Similar side effects are seen with mefloquine. In addition, mefloquine has also rarely (about 1:10,000) been associated with depression and anxiety. Both tafenoquine and mefloquine are considered to be safe, however, neither are recommended for use in pregnant females. Primaquine has similar side-effects to tafenoquine including the risk of producing the bleeding disorder related to a lack of G6PD, as described above.

Although you will be taking study medication designed to prevent malaria, there is a very small chance that you may contract malaria while on the study. However, if you do contract malaria you will be treated by your company medic or study investigator and followed up until you are better.

## BENEFITS

The benefit of taking part in the study is that you will be more closely monitored for the development of malaria during and after your deployment. You will be taking a medication once weekly rather than once daily with the ADF standard drug, doxycycline. In addition, the study results may provide a better understanding on how to prevent malaria infection on future overseas deployments.

## PRECAUTIONS

If you have had a significant response to any medications in the past, or have experienced urticaria (hives) or anaphylaxis (a significant allergic reaction involving collapse, swelling of the face and mouth, difficulty breathing) you may not be able to take part in the study. If you have experienced this type of reaction, please discuss this with the study Medical Officer.

**Pregnancy** - If you think (females only) that you may be pregnant or intend to become pregnant within one month of returning to Australia, please discuss this with the study Medical Officer. It is recommended not to become pregnant within 3 months of ceasing the medication.

**Contraception** – While taking this medication, it is recommended that females use an accepted form of contraception\*, which may include abstaining, barrier methods or pharmaceutical methods (“the pill”). Tafenoquine and mefloquine are not considered to interact with Oral Contraceptive Pills. If you are concerned about such interactions or have any questions about contraception while on the medication, please discuss this

with the study Medical Officer. Continue precautions for 3 months after stopping treatment.

\*It should be remembered that no barrier or pharmaceutical method of contraception is 100% effective.

## **CONFIDENTIALITY**

In all reports, publications or presentations about this research, information about you and your participation in this study will be kept in the strictest confidence and will not be released in any form that personally identifies you (a study number only will be used). The investigators will have your contact details and full name to allow them to make sure you can be contacted if necessary. This information will not be passed on to anyone else. Your medical records will be kept confidential and only released to medical personnel to assist in any care that you may need. Your name will not appear on any reports about this study.

From time to time a monitor representing the sponsors of the study (SmithKline Beecham / US Army Medical Research and Materiel Command), or a regulatory authority such as the Therapeutic Goods Administration in Australia or the US Food and Drug Administration, may require access to your medical records to ensure that the study is being carried out to the international standards under Good Clinical Practice (GCP). This access will be supervised by one of the study team and all monitors are bound by a confidentiality agreement.

It is the policy of the USAMRMC that data sheets are to be completed on all volunteers participating in research for entry into the Command's Volunteer Registry Database. This is a confidential database and the data entered include name, address, social security number (or equivalent) and details of the clinical trial. This information is needed to answer questions concerning subjects participating in research sponsored by USAMRMC, and to ensure that subjects can be contacted if there is new information on the study drug. The information will be stored for 75 years.

## **COMPENSATION**

All necessary medical care for injury or disease caused by your participation in this study will be provided at no cost to yourself. Compensation other than medical care will be provided according to the compensation provided as a member of the Australian Army. You should also understand that this is not a waiver or release of your legal rights. You should discuss this issue thoroughly with the principal investigator before you enroll in this study. Should you consider injury or illness has resulted from your participation in the study, you should seek immediate assistance from your nearest medical facility. The study investigators may be advised by calling the pager number on your study ID card.

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## YOUR RIGHTS

If during the course of the study you have any questions, or believe you have sustained a research-related injury or illness you can contact the study investigators, or your medical facility. Additionally, any concerns can be raised with the Executive Secretary of the Australian Defence Medical Ethics Committee as detailed below:

**Executive Secretary  
Australian Defence Medical Ethics Committee  
CP2-7-66  
Department of Defence  
Canberra, ACT, 2600  
Tel: (02) 6266 3925**

## INVESTIGATOR RESPONSIBILITIES

The investigators are responsible for ensuring that the study is conducted according to accepted Good Clinical Practice (GCP) standards, and for ensuring that the well being of study participants is always considered over all other considerations. Additionally, they are required to advise you in a timely manner should any other information become available that may be relevant to your willingness to participate in the study.

## YOUR RESPONSIBILITIES

Should you agree to enter the study, you should be prepared to undertake all doses of drug required during the deployment, as well as all tests and follow-up required. Should you experience any medical problems, including suspected side effects to the study drugs, you should report these promptly to your Company medic, RAP or study investigator. If you want any further information on the study, please contact the study investigator named on the attached consent form.

## VOLUNTARY PARTICIPATION

Your decision to participate in this study is entirely voluntary and refusal to participate will involve no penalty or loss of benefits to which you might otherwise have been entitled. Should you choose to be omitted from the study, or to withdraw from the study at any stage, there will be no detriment to your medical care or your career. If you choose to leave the study you should advise the study investigators. The study doctor has the right to withdraw you from the study if he/she feels it is appropriate to do so. This will be done if he/she feels that it is not in your best interest to continue either because of side effects of the drugs, or other injuries or illnesses you may experience during the deployment.

Should you not wish to participate in the study, you will require:

- a) the normal prevention course for malaria of **doxycycline daily** during the deployment,

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- b) a malaria eradication course on returning to Australia including:
  - i) two weeks of **doxycycline daily** and
  - ii) two weeks of **primaquine three times a day**, and
- c) all the required **blood samples** taken for deployment and post deployment screening.

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**Volunteer ID:** \_\_\_\_\_

**INFORMED WRITTEN CONSENT**

I have carefully read the information provided to me in this information sheet (dated.....). All questions raised by me have been answered to my satisfaction. I have been given a copy of this Information Sheet and Consent Form. I understand that I am free to withdraw from the study at any time without incurring any disadvantage to me in the future.

I consent to my participation in the study

**VOLUNTEER’S SIGNATURE** \_\_\_\_\_

**Printed Name:** \_\_\_\_\_

**Date:** \_\_\_\_\_

**INVESTIGATOR’S SIGNATURE** \_\_\_\_\_

**Printed Name:** \_\_\_\_\_

**Date:** \_\_\_\_\_

**WITNESS SIGNATURE** \_\_\_\_\_

**Printed Name:** \_\_\_\_\_

**Date:** \_\_\_\_\_

**ADDRESS OF SUBJECT:** Lavarack Barracks, Townsville, Queensland, Australia.

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