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Participant Information Sheet

Researchers:
This study is being conducted at Dr Deb The Travel Doctor Clinic in Brisbane, and Travel-Bug Vaccination Clinic in Adelaide. The researchers conducting this study are:

- **Dr Colleen Lau** (primary investigator), an academic researcher at the Research School of Population Health at the Australian National University. Dr Lau has over 15 years of experience as a travel medicine doctor, and has conducted many research projects on travel vaccinations and travellers' health.
- **Dr Deborah Mills**, Medical Director of Dr Deb The Travel Doctor Clinic in Brisbane.
- **Ms Lani Ramsey**, Registered Nurse Practitioner and Senior Nurse Manager at Travel Bug Vaccination Clinic, Adelaide.
- **Dr Andrew Ebringer**, Senior Medical Director, International SOS, Brisbane.

The scientific aspects of the study have been reviewed and approved by **Professor Dennis Shanks**, Director of the Australian Army Institute, Brisbane. Prof Shanks is a world-renowned expert on many aspects of malaria, including prevention, treatment, and vaccine development. The ethical aspects of the study have been approved by the Human Research Ethics Committee of the **Australian National University**.

Project Title: The 3-Day Malarone Schedule: Acceptability and Tolerability for Malaria Prophylaxis

General Outline of the Project:

A. Description and Methodology: Malaria is one of the most common causes of fever in Australian travellers, with approximately 400 cases reported each year in Australia. Most travellers who develop malaria did not take anti-malarial medications, or did not take the medications properly (e.g. forgot to take tablets). Malaria is a serious illness and could potentially be life-threatening. This study aims to improve compliance and convenience of taking anti-malarial tablets, and therefore reduce the risk of malaria in travellers. Malarone (Atovaquone and Proguanil) is a safe and effective anti-malarial medication. Few people report significant side effects, and it is generally better tolerated than the other commonly used anti-malarial medications (doxycycline and mefloquine). The standard dosage of Malarone for prevention of malaria is one tablet per day, starting 2 days before travelling to a malaria area, daily while in a malaria area, and continuing until 7 days after leaving the malaria area. Research has shown that when people are given a 3-day course of Malarone for treatment of malaria, they are protected from malaria for at least 4 weeks afterwards. It is therefore possible to protect travellers for 4 weeks by giving them a 3-day course of Malarone, instead of having to take tablets daily for many weeks. This research will assess the tolerability, acceptability and compliance to the 3-day schedule of Malarone for malaria prevention.

B. Participants: Participants will be recruited from two specialist travel medicine clinics: Dr Deb The Travel Doctor clinic in Brisbane, and Travel-Bug Vaccination Clinic in Adelaide. Adult Australians (≥18 years of age) travelling to malaria endemic countries in Asia, the Pacific Islands, or South/Central America for ≤ 4 weeks will be invited to participate. The study aims to include approximately 220 travellers.

C. Use of Data and Feedback: It is anticipated that the results of the study will provide valuable information to support the tolerability, acceptability and compliance of the 3-day Malarone schedule for malaria prevention. On completion of the study, the research team plans to publish the results in an internationally recognised medical journal so that this important information can be shared with the medical and scientific community to improve the health of travellers.

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Individuals will not be identified when results are presented or published. A summary of the results will be posted on the websites of the travel medicine clinics, and shared with the participants.

D. Project Funding: This project does not have any specific funding. It is being conducted by the doctors and nurses at the participating clinics at their own cost, with the aim of improving clinical best practice in travel medicine.

Participant involvement:

A. Voluntary Participation & Withdrawal: Taking part in this study is entirely voluntary. There are no negative consequences if you decide not to participate, and you will continue to receive the usual high standard of pre-travel and post-travel advice from the doctors and nurses. The study involves pre-travel and post-travel questionnaires – you will need to participate in all questionnaires but you may decline to answer particular questions. You may decline to participate or decide to withdraw at any time without having to provide an explanation. If you decide to withdraw, your data will be destroyed and excluded from the pool of results. However, once the results have been published, we will not be able to withdraw your de-identified data from the overall findings. We recommend that you read this document carefully, and discuss any questions with Dr Colleen Lau, Dr Deborah Mills, or Ms Lani Ramsey (RN). Contact details are provided at the end of this document.

B. What does participation in the research entail? To participate in the study, you will be requested to attend a pre-travel consultation, take anti-malarial medications, fill in a symptom diary if you feel unwell after taking Malarone or during your travels, and complete a series of pre-travel and post-travel questionnaires.

1. Pre-travel consultation: You will be requested to attend either Dr Deb The Travel Doctor clinic in Brisbane or The Travel-Bug Vaccination Clinic in Adelaide for a pre-travel clinic, just as you would even if you were not participating in this study. A standard travel medicine consultation will be conducted, and you will be provided with expert advice on:

- Pre-travel health preparation
- Vaccinations
- Malaria tablets if you are travelling to a malaria endemic area
- Information about this research project

Women of child-bearing age will also be asked to have a pregnancy test.

2. Anti-malaria tablets: If you want to participate in the research project, you will be asked to take 4 tablets of Malarone per day for 3 days. You will need to start taking the Malarone tablets at least 4 days before you depart on your trip, and complete the course of tablets prior to leaving. If you do not want to participate in the research project, you will be provided with other options for anti-malarial medications, such as Malarone (standard daily schedule), doxycycline, or mefloquine. You will not be able to use the Malarone 3- day schedule unless you participate in this study.

3. Memory Aid and Symptom Diary: You will be provided with a one page Memory Aid and Symptom Diary. If you feel unwell after taking Malarone or during your trip, please record the type and severity of symptoms on the diary so that your doctors can accurately assess whether the symptoms are likely to be caused by Malarone or something else. Your travel health nurse will explain how to use the diary.

4. Questionnaires:

Q1. During your pre-travel consultation, a travel health nurse will help you complete a baseline questionnaire about your trip, general health, and previous experience with taking anti-malaria medications.

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Q2. A few days before your departure, a nurse will call you and ask a few short questions over the phone. The nurse will check that you have taken the Malarone tablets correctly, and ask if you experienced any side effects with the tablets. If you did not tolerate your first dose of Malarone (e.g. vomiting), please call your clinic immediately for further instruction. A doctor or nurse will assess whether you should continue with further doses, or switch to an alternate schedule or alternate medication.

Q3. One week after you return home, a travel health nurse will contact you by phone again and ask if you have had any health problems while overseas. You will also be reminded to return the Memory Aid and Diary to the travel clinic.

C. Location and Duration: The pre-travel consultation will take place at Dr Deb The Travel Doctor clinic in Brisbane or The Travel-Bug Vaccination Clinic in Adelaide. The consultation with the doctor and nurse will take about an hour, about the same time as a standard pre-travel consultation even if you do not want to participate in the study. The initial questionnaire (Q1) should only take about 10 minutes to complete, and a travel health nurse will help you do this. The follow-up telephone questionnaires Q2 and Q3 should take less than 5 minutes each. If you feel unwell and need to complete the Memory Aid and Symptom Diary, it should only take a minute or two. If you feel too unwell to complete the symptom diary on a particular day, you can do this when you feel better, but it is best to do it as soon as possible while the details are still fresh in your mind. In total, participation in the study should not take more than half an hour of your time. If you are unable to tolerate the Malarone tablets, you will need to make time to return to the clinic to collect alternative medications.

D. Remuneration: Taking part in the study will cost nothing apart from your time. You or your employer will need to pay for the pre-travel consultation, vaccinations, malaria tablets, and any other costs associated with your trip. We recommend that you have travel insurance that will cover any medical treatment required while you are overseas. You will not receive any special payments for being part of this research study.

E. Risks: The most common side effects of Malarone are nausea and headache, and serious side effects are rare. The 3-day schedule involves taking more tablets per day than the daily schedule, and it is possible that side effects are more common with the 3-day schedule. However, the 3-day schedule has been used for the *treatment* of malaria for many years, and found to be very safe and effective.

If you are unable to tolerate the 3-day schedule because of side effects, you will need to make time to return to the clinic and collect an alternative anti-malarial medication. In this situation, there will be no charge for the follow up visit, and an alternative medication (doxycycline) will be provided free of charge to cover for the same travel duration.

- If you feel unwell after taking your first dose of Malarone tablets and are concerned about whether you are able to complete the 3 days of tablets, please call your travel medicine clinic and ask to speak to a doctor. The doctor will assess whether you should try taking a second dose, or switch to an alternate schedule or alternate medication.
- If you develop a fever or feel unwell while you are in Australia (before or after your trip), please contact your travel clinic and ask to speak to a doctor.
- If you develop a fever or feel unwell while you are overseas, please see a doctor as soon as possible. Either contact your travel insurance helpline, or seek medical care locally. You can also contact your travel clinic by phone or email for medical advice – we provide 24 hour medical advice to our travellers but it will not be possible for us to organised blood tests or medications for you while you are overseas.

Whether you are part of this study or not, please remember that anti-malaria tablets are not 100% effective, regardless of the type of tablet or the schedule used. It is therefore very important to avoid mosquito bites, and see a doctor promptly if you develop any fevers. We do not expect the 3-day schedule to be any less effective than taking the standard schedule of daily Malarone. The initial symptoms of malaria are very non-specific, and include fever, shakes, chills, flu-like

illness, headache, tiredness, and body aches. These symptoms can develop from ***1 week to 1 year after being bitten by a malaria-infected mosquito***. If you develop any fevers, you should be tested for malaria as soon as possible. If you are given proper and prompt treatment for malaria, you will recover completely. If you do not seek treatment quickly, malaria can be fatal.

F. Benefits: The advantages of taking the 3-day schedule for Malarone are:

- You only need to take tablets for 3 days prior to departure (instead of the usual schedule of daily tablets for Malarone and doxycycline, or weekly tablets with mefloquine)
- You will not need to carry or remember to take anti-malarial medications during your trip
- The 3-day schedule will involve fewer tablets and will therefore be cheaper

We expect that the results from this study will confirm that the 3-day Malarone schedule is well tolerated, and the findings could provide support for more widespread use of this schedule in travellers in the future.

Exclusion criteria:

Participant Limitation: You will not be able to participate in this study if:

- You have previously experienced side effects from taking Malarone.
- You are taking other medications that may adversely interact with Malarone, including metoclopramide, rifampicin, tetracyclines, fluvoxamine. Your travel medicine doctor will be able to advise on this.
- You are pregnant or planning a pregnancy.
- You have diabetes, heart problems, asthma, epilepsy, depression, kidney dysfunction, digestive problems that require medications, or taking long-term antibiotics.
- You are travelling to an area with a very high risk of malaria, e.g. sub-Saharan Africa. Your travel medicine doctor will assess whether your trip is suitable for this study.

Confidentiality:

The information provided by you will only be accessible by your travel medicine doctors and nurses, and the researchers. We will need to record your name and contact details so that we can contact you for the follow-up questionnaires. We will keep your participation in this research study confidential to the extent permitted by the law. However, it is possible that other people may become aware of your participation in this study. For example, The University's Human Research Ethics Committee might inspect records pertaining to this research, but the university will ensure that your information personal remain confidential. For publication, the results of all participants will be pooled, and no individual will be identified.

Privacy Notice:

In collecting your personal information within this research, the ANU must comply with the Privacy Act 1988. The ANU Privacy Policy is available at https://policies.anu.edu.au/ppl/document/ANUP_010007 and it contains information about how a person can:

- Access or seek correction to their personal information;
- Complain about a breach of an Australian Privacy Principle by ANU, and how ANU will handle the complaint.

Data Storage: Medical and research records will be kept at the travel medicine clinics. Electronic data will be stored in password-protected computers owned by the clinics, the Australian National University, and the researchers. Data will be stored for a period of at least five years from the date of any publication arising from the research. After 5 years, the

research data will be completely de-identified and archived at computers at the Australian National University, but your medical records will continue to be kept at the travel medicine clinics.

Queries and Concerns:

A. Contact Details for More Information: You have the right to ask any questions about this research. If you have questions, complaints or concerns related to this research, please contact one of the following people:

- Dr. Colleen Lau (Primary Investigator) Email: colleen.lau@anu.edu.au Phone: (07) 3221 9066
- Dr. Deborah Mills (Brisbane) Email: email@drdeb.com.au Phone: (07) 3221 9066
- Ms. Lani Ramsey (Adelaide) Email: ramseylani@hotmail.com Phone: (08) 8267 3544

B. Contact Details if in Distress: If you require emergency medical care while overseas, please call your travel insurance Helpline or go to a local hospital. You can also contact your travel clinic 24 hours a day by phone or email, but please note that the clinic will not be able to prescribe medications or order tests for you while you are overseas. For emergencies, medical staff are on call after hours for registered patients, please call the following numbers:

- Dr Deb – The Travel Doctor, Brisbane Phone: +61 7 3221 9066
- Travel-Bug Vaccination Clinic, Adelaide Phone: +61 400 930 818

Ethics Committee Clearance:

The ethical aspects of this research have been approved by the ANU Human Research Ethics Committee (Protocol 2016/87). If you have any concerns or complaints about how this research has been conducted, please contact:

Ethics Manager
The ANU Human Research Ethics Committee
The Australian National University
Telephone: +61 2 6125 3427
Email: Human.Ethics.Officer@anu.edu.au