Participant Information Sheet

JEVID - **J**apanese **E**ncephalitis **V**accination via **I**ntra**D**ermal route

Aim of the project: To determine the efficacy of intradermal administration of Japanese encephalitis vaccine

Researchers

This study is being conducted at Dr Deb The Travel Doctor Clinic. The laboratory analyses will be carried out at the QIMR Berghofer. The researchers conducting this study are:

- **Dr Luis Furuya-Kanamori**, NHMRC Early Career Fellow, UQ Centre for Clinical Research, Faulty of Medicine, The University of Queensland.
- **Dr Deborah Mills**, Medical Director of the clinic, Dr Deb The Travel Doctor.
- **Professor Colleen Lau**, NHMRC Fellow, School of Public Health, Faculty of Medicine, The University of Queensland, and travel medicine doctor at Dr Deb The Travel Doctor Clinic.
- **Associate Professor Gregor Devine**, Group Leader of the Mosquito Control Laboratory at QIMR Berghofer.
- **Dr Leon Hugo,** Senior Research Officer in the Mosquito Control Laboratory at the QIMR Berghofer.
- **Dr Narayan Gyawali,** Postdoctoral research fellow in the Mosquito Control Laboratory at the QIMR Berghofer.
- **Dr Kinley Wangdi,** Research fellow, Research School of Population Health, ANU College of Health and Medicine, Australian National University.

Outline of the project

Background

It is estimated that are more than 100,000 cases of Japanese encephalitis (JE) cases and 25,000 deaths worldwide per year. JE is endemic in Asia and Papua New Guinea, and outbreaks have occurred in the Torres Strait Islands. Travellers spending one month or more in endemic regions are recommended to receive JE vaccine. Effective JE vaccines with very few adverse events are currently available, but uptake of JE vaccines by travellers remain low, with the high cost of vaccines (approx. AU$ 300 for Imojev® in Australia) being one of the main reasons.

JE vaccines are licensed to be administered via subcutaneous or intramuscular injections; however, intradermal administration of vaccines using smaller doses have been shown to be as effective as subcutaneous or intramuscular administration for other vaccines, e.g. yellow fever and rabies. Intradermal injections are shallow injections into the dermis (the most superficial layer of the skin). The needle is inserted at approximately 5 degrees angle in the skin of the upper arm and 0.1mL of JE vaccine will be administered. The intradermal route uses a smaller volume of vaccine, thus it is less expensive than the subcutaneous and intramuscular routes of administration, and could potentially enable more travellers to afford the vaccination. Therefore, we aim to investigate whether intradermal administration could potentially be an economical yet effective route of administration for JE vaccine.

Sponsor

This clinical trial is sponsored by The University of Queensland, your decision to participate or not participate will not impact on your relationship with The University of Queensland.

Disclosure of conflict of interest

Dr Mills (Medical Director of the clinic Dr Deb The Travel Doctor) and Prof Lau (travel medicine doctor) are part of the research team. 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 from the clinic.

There are no financial benefits for the clinic derived from the research. If intradermal administration of JE vaccine is proven effective, the benefit will be translated to patients/travellers as immunisation would be more economical, and likely more travellers would be protected from this disease.

Use of data and feedback

It is anticipated that the results of the study will provide valuable information to support the use of intradermal administration of JE vaccine, making it affordable for more travellers. 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 worldwide. Individuals will not be identified when results are presented (e.g. conferences) or published (e.g. journal articles). A summary of the results will be posted in the clinic, on the website of the travel medicine clinic (www.thetraveldoctor.com.au) and distributed to participants.

Participant involvement

Participants

Participants will be recruited from our specialist travel medicine clinic: Dr Deb - The Travel Doctor in Brisbane, the study will be promoted through the clinic's patient database (i.e. patients who expressed their interest in receiving the vaccine during a prior pre-travel consultation), and its website. Adult Australian residents between 18 and 45 years of age, who have never received JE vaccine will be invited to participate. The study aims to recruit 50 participants.

Voluntary participation & withdrawal

Taking part in this study is entirely voluntary. The study involves 2 questionnaires and 3 visits to the clinic to collect blood samples. You will be requested to participate in both questionnaires, but you may decline to answer particular questions. You may decline to participate or decide to withdraw until the work is prepared for publication 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 the medical staff, or with the Dr Deborah Mills, Dr Luis Furuya-Kanamori, or Prof Colleen Lau. Contact details are provided at the end of this document.

What does participation in the research entail?

- *Clinic visit 1 - Day 0:* To participate in the study, the medical staff will assist you to fill out the first questionnaire with basic demographic details. The nurse will draw 10mL of blood, which will be sent to Queensland Institute of Medical Research (QIMR) Berghofer to test for JE antibodies (we expect that you will not have antibodies at this stage). Once the blood sample has been collected, the nurse will give you a single dose of intradermal JE vaccine in the arm.
- *Day 10:* The clinical staff will call you to ask if you have experienced any side effects from the vaccine.
- *Clinic visits 2 & 3 - Days 28 and 56:* You will need to return to the clinic for a second and third blood test, respectively.
- *Day 70:* You will be telephoned by research staff and be given the results of your blood tests.

Location and duration

The consultations will take place at Dr Deb The Travel Doctor's clinic in Brisbane. The first visit may take 45 minutes (including 30 minutes of observation after receiving the vaccine). The second and third visits will take about 15-30 minutes.

Remuneration

Taking part in the study will cost nothing apart from your time. The cost of the blood tests and the JE vaccine will be covered by the study. You will receive $50 at the completion of the study to assist with costs of transport and parking to come to the clinic, which is located in Brisbane city. Otherwise, you will not receive any special payments for being part of this research study.

Project funding

The project is partially funded by the International Society of Travel Medicine (ISTM). The clinic will cover other costs of the study, with the aim of improving clinical best practice in travel medicine.

Vaccine

Imojev® will be used for this study. Imojev® is a live attenuated JE vaccine, and it is approved for use in Australia in people aged ≥9 months. Each 0.5 mL reconstituted dose contains 4.0–5.8 log plaque-forming units of live attenuated recombinant JE, mannitol, lactose, glutamic acid, potassium hydroxide, histidine, and human serum albumin. The medical staff will determine if you do not have contraindications for this vaccine. The intradermal dose will be one fifth the standard dose (0.1mL)

Risks

The most common side effects of blood collection are soreness and bruising at the site of the blood collection. The side effects of JE vaccine are a red, sore and/or itchy injection site. Very occasionally persons vaccinated may experience fever, a rash or fatigue. We encourage you to ring the clinic (07) 3221 9066 to discuss any side effects with the medical staff. Clinic medical staff are on call for our patients by phone 24 hours a day to discuss vaccine side effects or other issues. In the event that you experience an adverse reaction to the vaccination that prompts you to see your regular GP, we would like to contact your doctor and ask them about the reaction and also provide medical details about the side effects or other issues related to the research or vaccine to that doctor. We will

seek your consent to do this in the consent form. All adverse events will be reported by the research team to The University of Queensland, and reported in the final scientific publication.

Benefits

We expect that the results from this study will confirm that a single intradermal dose of JE vaccine (Imojev) is effective and economical. If it is shown to be successful, you will be protected against JE. We will not know how long the protection will last with the intradermal route, and when you travel again, you can attend Dr Deb's for a blood test to check immunity and a free booster of the standard dose of Imojev to ensure that you have long-term protection for future trips.

Exclusion criteria

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

- You are under 18 or over 45 years of age
- You have lived in a JE risk area for 12 months or more
- You have had dengue fever
- You have previously had vaccines against JE, yellow fever, or dengue or are planning to have yellow fever or dengue vaccines during the next two months
- You have contraindications to the Imojev vaccine or live vaccines
- You are pregnant or planning to get pregnant (If clinically relevant, a urine pregnancy test can be done at the clinic prior to enrolment)
- You are breastfeeding
- You have a disease or are on any medication that suppresses your immune system (e.g. cancer or on chemotherapy)
- You are travelling or planning to travel to areas of high risk for JE within the next two months

The medical staff will assist you to determine if you are eligible to participate in the 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 need to record your date of birth on the blood test form as it will form part of your usual medical record as it will be important for your future medical care for your treating doctors to have access to this information. We will keep your participation in

this research study confidential to the extent permitted by the law. For publication, the results of all participants will be pooled, and no individual will be identified.

Data Storage

Electronic data will be stored in password-protected computers owned by the clinic, the University of Queensland, and the researchers. Data will be stored for a period of at least 15 years from the date of any publication arising from the research. After 15 years, the research data will be completely de-identified (name and date of birth of the participants will be deleted from the dataset) and archived in the servers of the University of Queensland.

Ethics Committee Clearance

This study adheres to the Guidelines of the ethical review process of The University of Queensland and the National Statement on Ethical Conduct in Human Research. Whilst you are free to discuss your participation in this study with project staff (contact details below), if you would like to speak to an officer of the University not involved in the study, you may contact the Ethics Coordinators on +617 3365 3924 / +617 3443 1656 or email: humanethics@research.uq.edu.au

Queries and concerns

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. Deborah Mills	Email: email@drdeb.com.au	Phone: (07) 3221 9066
Dr. Luis Furuya-Kanamori	Email: l.furuya@uq.edu.au	Phone: (07) 3346 5064
Prof. Colleen Lau	Email: colleen.lau@uq.edu.au	Phone: (07) 3346 4747