Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

The Children's Hospital at Westmead

Title	**Q fever vaccine trial in Australian adolescents Safety and immunogenicity of Q fever vaccine (Q-VAX®) in children aged 10 to <15 years**
Short Title	Q fever vaccine in 10 to <15 year olds
Protocol Number	Qfevervax1/ CTC 0382
Project Sponsor	The University of Sydney
Coordinating Principal Investigator	Professor Nicholas Wood
Coordinating Centre	NHMRC Clinical Trials Centre
Principal Investigator	Professor Nicholas Wood
Associate Investigators	Dr Rama Kandasamy Dr Archana Koirala Dr Melanie Wong
Location	The Children's Hospital at Westmead

Part 1 What does my participation involve?

1 Introduction

This is an invitation for you to take part in this research project because you are at potential risk from Q fever infection and may benefit from the Q fever vaccine.

This research project aims to test the safety and immune responses of the Q fever vaccine in children aged 10 to < 15 years old. However we would like to compare the safety and immune responses of the Q fever vaccine in children with that seen in young adults (aged ≥15 to ≤ 30 years) and this is why you are being invited to participate.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not you can take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you do not wish to take part, you do not have to. You will receive the best possible care whether or not you take part.

If you decide you want you to take part in the research project, you will be asked to sign the consent section.

By signing it you are telling us that you:
• Understand what you have read
• Consent to taking part in the research project
• Consent to have the tests and treatments that are described
• Consent to the use of your personal and health information as described.

Please note, this consent form is to be completed by adults (≥ 18 years) that are participating in this study. A Young Person information sheet and separate Parent/Guardian consent form is to be completed for any participants under the age of 18.

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

2 What is the purpose of this research?

Q fever is a highly infectious disease caused by a bacteria called *Coxiella Burnetii*.

Each year in Australia there are over 450 cases notified, which equates to approximately 8-10 cases per week.

Q fever is usually spread from animals to humans by breathing in infectious droplets or dust. People thought to be most at risk of infection include farmers and abattoir workers, recreational shooters, shearers, livestock transporters and veterinarians.

Q fever causes a range of acute and chronic symptoms that can lead to significant medical problems. Most infections (60%) are mild, lead to non-specific influenza like symptoms and are self-limiting. However it can be more severe and lead to symptoms of pneumonia, liver infection (hepatitis), heart infection (endocarditis) or bone infection (osteomyelitis). Chronic disease, particularly endocarditis, can occur months or years later usually in adults. In addition, approximately 20% of adults experience post Q fever fatigue syndrome - protracted fatigue, joint and muscle pains - which may last years and is debilitating.

Currently there is an effective Q fever vaccine which is recommended for those considered to be in “occupational at risk” groups, such as abattoir workers, veterinarians and farmers. However, several recent studies have highlighted that the risk of contracting Q fever in the non-traditional “at risk” groups, such as children and those living in or close to cities, is higher than previously thought. The source of cases of Q fever disease in New South Wales and Queensland has changed. In the past most infections were seen in abattoir workers, we are now seeing an increased risk of infection in people who have contact with livestock, wildlife or feral animals.

Importantly the only registered vaccine available in the world is QVax®, manufactured by Seqirus in Australia and is only recommended for those over 15 years old according to the Australian Immunisation Handbook. As a result under current Australian Immunisation guidelines children under 15 years old, who may be at risk of contracting Q fever, because they live on farms, near abattoirs or, are children of “at risk” workers are not recommended to be vaccinated. The main reason for this age restriction is not because of an identified safety risk but because the initial trials did not include children under 15 years old and therefore restricted the licensure of the vaccine to only those aged 15 years and older.

Vaccinating children, particularly children of farmers or animal breeders, is an important protective measure against Q fever infection and has not been studied to date.

The aim of this study is to measure the safety and immunogenicity (meaning immune responses – specifically antibody levels) of the Q fever vaccine in children aged 10 to <15 years old.

In order to better understand the safety and immune responses in children we would like to include a comparison group of young adults (aged ≥15 to ≤30 years) given the licensed Q fever vaccine.

The results of this study may result in a change to Q fever vaccine recommendations in Australia and potentially allow younger children who are at risk of Q fever to be vaccinated.

This research has been initiated by Professor Nicholas Wood and associate investigators listed above and has been funded by a project grant from the NHMRC.

3 What does participation in this research involve?

You will be participating in a clinical vaccine trial and will be given the Q fever vaccine if you pass the screening tests as outlined below. This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions.

Healthy adults who are aged ≥15 to ≤30 years old and who are interested in receiving the Q fever vaccine can take part in this trial. The participant must not have had a Q fever vaccine previously or Q fever disease and have no contraindications to Q fever vaccination.

If you agree to participate in this study, we will first check in more detail whether the study is suitable for you. If the study is suitable for you and you agree to participate, you will be asked to sign the Participant Consent Form before any study-related procedures can commence. You will be in the study for 12 months, during which we will see you on five occasions. Your study doctor may inform your local doctor of your participation in this study. Please advise your study doctor if you do not wish this to occur.

Visit 1: On the first visit we will ask about your health and medical conditions, history of Q fever vaccination or disease and risk factors for Q fever disease including animal contact, collect a blood sample (7mls) and perform skin testing.

This visit will take a little over an hour.

Skin test and serology for pre-vaccine screening: During the skin test a qualified and experienced member of the study staff will inject a small amount of dilute Q fever vaccine in the skin of your forearm. This can be painful and itchy. The skin test will then be read one week later at Visit 2. The aim of this part of the study is to identify whether you have been exposed to Q fever previously and we will explain the meaning of the results to you:

- If the skin test and/or serology are positive then this means you have been exposed to Q fever in the past. This means you have natural immunity. In this case the Q fever vaccine CANNOT be given to you.
- If both the skin test and serology are negative then this indicates that you have not already been exposed to Q fever and CAN be vaccinated.

- If the skin test is positive but the serology negative this means you may have been exposed to Q fever in the past. This means you likely have natural immunity. In this case the Q fever vaccine CANNOT be given to you.
- If the skin test is negative but the serology positive this means you may have been exposed to Q fever in the past. This means you likely have natural immunity. In this case the Q fever vaccine CANNOT be given to you.

Visit 2: At the second visit we will tell you your serology result and a qualified and experienced member of the study staff will measure the skin test. They will look at and feel the area on your arm where the dilute Q fever vaccine was injected. If the area is raised or red then it is considered to be positive. Only those who are both negative to the skin and serology test will be given the Q fever vaccine.

Females will be asked to take a urine pregnancy test at visit 2 prior to the vaccine being given to make sure they are not pregnant. As Q fever vaccination is not routinely recommended during pregnancy and its safety has not been established we do not want to give the Q fever vaccine to any female who may be pregnant.

The vaccine will be given in your upper arm (in the deltoid region). You can choose which arm you would prefer the vaccine to be given.

Following vaccination we will give you a diary card to complete describing your daily symptoms for the next 7 days after vaccination, after which you will receive a weekly diary card for 3 weeks. We will explain how to use this paper or electronic diary card. We will ask you to measure your temperature under the armpit each evening and to look at the arm where the vaccine was given for any redness or swelling and measure it with a ruler we provide. This second visit will take a little over an hour.

Visit 3: At the third visit, which takes place at 28-42 days after vaccination, we will review your medical history, ask about any potential adverse events and collect a blood sample (7mls). This visit will take around 30 minutes.

Visit 4: At the fourth visit, which takes place at 180-210 days after vaccination, we will review your medical history, ask about any potential adverse events and collect a blood sample (7mls). This visit will take around 30 minutes.

Visit 5: At the fifth visit, which takes place at 365-395 days after vaccination, we will review your medical history and collect a blood sample (7mls). This visit will take around 30 minutes.

The following table describes the study visits. All visits may be conducted by study staff either at the medical facility or in the participant's home.

Visit intervals and procedures

Visit Number (Timing)	Study procedure
Baseline visit 1 (Day 0)	Explanation and discussion of the study Sign consent form Medical history, Q fever risk factors, and examination Blood sample collection (7ml) QVAX® skin test

Visit 2 (7 days post visit 1)	Measure skin test results Medical history and examination Check temperature Urine pregnancy test only for females QVAX® vaccine administration **(ONLY if serology and skin test negative)** Observed for ½ hour post vaccine
Possible telephone call Week following Visit 1	Our study team will review the electronic diary cards remotely. If a paper diary card was used we will email/text you to remind you to return it. If there are any concerns on review we will make contact with you to check for any side effects after vaccination or other problems encountered.
Visit 3 (28-42 days post visit 2)	Check post-vaccination adverse events diary Medical history and examination Take blood sample (around 7mls)
Visit 4 (180-210 days post visit 2)	Medical history and examination Check adverse events Take blood sample (around 7mls)
Visit 5 (365-395 days after visit 2)	Medical history and examination Check ongoing adverse events Take blood sample (around 7mls)

We may also need to contact you at a later time in order to ask additional questions related to the study.

Diary card
We will give you either a paper or electronic diary card asking you to record any redness or swelling at the injection site and other symptoms you may have after vaccination. You will be given a thermometer to record your temperature each evening measured under the armpit

Blood tests
The blood samples are taken by a qualified and experienced member of the study staff. We will need to take about 7mls of blood from a vein in your arm. This can be painful and bruising can occur.

We take the blood to measure the level of antibody to Q fever. You will be given your individual results and their meaning.

Study costs
There are no additional costs associated with participation in this research project, nor will you or the participant be paid. The Q fever vaccination, tests and medical care required as part of the research project will be provided to you free of charge

If eligible under a financial assistance program (e.g. the Isolated Patients Travel and Accommodation Assistance Scheme (IPTAAS), you may be reimbursed for any reasonable travel expenses associated with the research project visit.

Your personal information will be kept confidential, and only study staff will have access to your data.

4 What do I have to do?

It is important that the diary card is completed as accurately and timely as possible and that all study visits are completed. You do not have to change any part of their lifestyle. There are no restrictions on your diet or exercise. You are allowed to take your routine medications.

You are not allowed to have a live vaccine, such as chickenpox vaccine, in the 4 weeks before or 4 weeks after the Q fever vaccine. You are also not allowed to have an inactivated vaccine, such as influenza or COVID-19 vaccine, in the 2 weeks before or 2 weeks after the Q fever vaccine. This is because we want to measure for any side effects after the Q fever vaccine and if another vaccine is given close in time to the Q fever vaccine it can be hard to know which vaccine may have caused the side effects.

5 Other relevant information about the research project

A total of 1000 children and a comparison group of 100 adults (aged 15 to ≤30 years) across multiple sites in NSW and Queensland are planned to take part in this Q fever vaccine trial. This trial is being conducted by a collaborative research group and involves paediatricians, vaccine trial specialists and experts in public health. It is being supported by both the Country Women's Association and the farmer's federations of both Queensland and New South Wales

6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide that you want to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide that you want to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision that you can or cannot take part, or that you can take part and then be withdrawn, will not affect your routine treatment, relationship with those treating you, or the relationship with The Children's Hospital at Westmead.

7 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, likely benefits include protection from Q fever disease. We also know that the Q fever vaccine is around 85% effective in preventing older children and adults from Q fever disease. You will also know after the skin and blood test whether you have already been exposed to Q fever disease.

8 What are the possible risks and disadvantages of taking part?

Medical treatments often cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or you

are worried about them, talk with the study doctor. The study doctor will also be looking out for side effects.

Tell the study doctor immediately about any new or unusual symptoms that you get.

The study doctor will discuss the best way of managing any side effects with you.

You may get at lump or sometimes a nodule, that can be painful and itchy, at the injection site of the pre-vaccination screening skin test, this rarely lasts long.

You may get some of the following side effects from the Q fever vaccine. Side effects can include feeling unwell within 48 hours of the injection, developing a fever or developing a small lump or some redness where you had the injection.

Injection site reactions are common (local tenderness (48%) and redness (30-50%)). Systemic symptoms occur in about 10% of vaccinees, including influenza-like symptoms (9%), fever (up to 15%), joint pain (10-20%), chills and minor sweating.

Importantly individuals who have had previous infection or vaccination may develop a severe local reaction (injection site abscess) and systemic symptoms resembling post Q fever fatigue syndrome, hence the importance of pre-vaccination screening to make sure we don't give these people a dose of the Q fever vaccine.

Rarely, a severe lump/abscess, called a "non-necrotising granuloma" can develop at the injection site 1-8 months after vaccination. These granulomas are reported to resolve over several months. In Australia, 86 adverse events following Q fever immunisation were reported to the Therapeutic Goods Administration between 2001 and 2004. Most (80%) were for injection site reactions, including 5 sterile injection site abscesses.

Having a vaccine injected or blood sample taken may cause some discomfort, bruising, minor infection or bleeding. If this happens, it can be easily treated.

The effects of Q fever vaccine on the unborn child and on the newborn baby are not known. Because of this females must not participate in the research if they are pregnant or trying to become pregnant, or breast-feeding at the time of vaccination. Females will be asked to have a urine pregnancy test at visit 2 prior to Q fever vaccination.

Side effects you report to your study doctor may be reported to Seqirus, Australia (the manufacturer of the Q fever vaccine) and the Therapeutic Goods Administration (TGA) Australia, but the report will not contain any identifying details about you. This reporting allows continued monitoring of the benefit-risk balance of the vaccine.

9 What will happen to my test samples?

This study is an investigator-initiated study. Your blood sample will be sent to the Australian Rickettsial Reference Laboratory in Geelong, Victoria, (and tested locally where available) for Q fever antibody testing. This laboratory will be analysing the de-identified blood samples to check your antibody levels. They are specialist reference laboratory that has extensive experience in the conduct of Q fever serology in Australia. The analysis and interpretation of results will be performed by study investigators

Your blood samples will be stored at secure, expert central laboratories in the Australian Rickettsial Reference Laboratory. All samples that are not used for the study analysis will be transferred to and stored securely at the Children's Hospital at Westmead Research Laboratories.

Your samples will never be sold. You will not benefit financially if this research leads to development of a new treatment or medical test.

10 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, the study doctor will tell you about it.

11 Can I have other treatments during this research project?

Whilst you are participating in this research project, you will be able to take all of the medications or treatments you have been normally taking for your condition or for other reasons. It is important to tell the study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments.

You should also tell the study doctor about any changes to these during your participation in the research project.

12 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. If you do withdraw during the research project, the study doctor and relevant study staff will not collect additional personal information, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the Project Sponsor up to the time of withdrawal will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

13 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:
• Unacceptable side effects
• Decisions made by local regulatory/health authorities

Part 2 How is the research project being conducted?

14 What will happen to information about me?

Your individual serology results will be given to you with an explanation of the meaning of the results.

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Your information will only be

used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

All data collected will be held in strict confidence to protect your privacy. All information about you (including your email address and mobile phone number) will be stored securely with access restricted to authorised members of the research team from the University of Sydney (NHMRC CTC), and research teams at your study site. Only these people will access your personal data as they need to manage your participation in the trial. Personal data will be kept separate to your de-identified health data.

No material which could personally identify you will be used in any reports on this study. Results from the analysis will be stored in computer files and in written form in locked cabinets at the local research site and the coded data will be stored by the NHMRC Clinical Trials Centre at the University of Sydney in a secure database. The study data will be kept, for a minimum of 15 years, OR until the youngest participant turns 25 (whichever is the later after which time the information will be destroyed securely. You may ask to see or correct your data. We will give you a written copy and explanation of your immune responses once they have been tested. The data and samples obtained from this study may be used in future related or unrelated research by other researchers, following appropriate approval.

In accordance with relevant Australian and State 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 form if you would like to access your information.

Your health records and any information obtained during the study are subject to inspection and monitoring, both remotely and at the location where it is held (for the purpose of verifying the procedures and the data) by the relevant authorities and authorised representatives of the University of Sydney and NHMRC Clinical Trials Centre, the Australian Therapeutic Goods Administration and other relevant regulatory authorities, the approving Human Research Ethics Committee (HREC) and The Children's Hospital at Westmead, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

It is anticipated that the results of this research project will 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, except with your permission.

The date and batch of your Q fever vaccine that is received during this research project will be recorded in the Australian Immunisation Register.

15 Complaints and compensation

If you suffer any injuries or complications as a result of this study, you should contact the study doctor as soon as possible who will assist you in arranging appropriate medical treatment.

You may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available if the injury or complication is sufficiently serious and is caused by unsafe drugs or equipment, or by the negligence of one of the parties involved in this study (for example, the researcher, the hospital or the treating doctor). If you receive compensation that includes an amount for medical expenses, you will be required to pay

for your medical treatment from those compensation monies. You do not give up any legal rights to compensation by participating in this study.

If you are not eligible for compensation for the injury or complication under the law, but are eligible for Medicare, then you can receive any medical treatment required for the injury or complication free of charge as a public patient in any Australian public hospital.

16 Who is organising and funding the research?

This research project is being conducted by the above named investigators and coordinated by the NHMRC Clinical Trials Centre and sponsored in Australia by The University of Sydney. The study is being funded by the NHMRC. The Children's Hospital at Westmead will receive a payment from the NHMRC CTC for undertaking this study. No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

17 Who has reviewed the research project?

The conduct of this study has been also authorised by The Sydney Children's Hospitals Network Human Research and Ethics Committee. If you have any concerns about the conduct of the study, or your rights as a study participant, you may contact: the Secretary of the Ethics Committee (phone 02 7825 3017) and quote reference 2022/ETH00624.

This information sheet is for you to keep. We will also give you a copy of the signed consent form.

18 Further information and who to contact

You have the right to ask questions at any time about this study or the potential risks associated with it. You will be informed of any significant new information pertaining to your safety.

Clinical contact person

Name	Professor Nicholas Wood
Position	Staff specialist
Telephone	0429 849 440
Email	nicholas.wood@health.nsw.gov.au

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	The Sydney Children's Hospitals Network HREC
HREC Executive Officer	Caitlin Braude
Telephone	02 7825 3017
Email	SCHN-Ethics@health.nsw.gov.au

Consent Form - *Adult providing own consent*

Title	**Q fever vaccine trial in Australian adolescents Safety and immunogenicity of Q fever vaccine (Q-VAX®) in children aged 10 to <15 years**
Short Title	Q fever vaccine in 10 to <15 year olds
Protocol Number	Qfevervax1/ CTC 0382
Project Sponsor	The University of Sydney
Coordinating Principal Investigator	Professor Nicholas Wood
Coordinating Centre	NHMRC Clinical Trials Centre
Principal Investigator	Professor Nicholas Wood
Associate Investigators	Dr Rama Kandasamy Dr Archana Koirala Dr Melanie Wong
Location	The Children's Hospital at Westmead

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to The Children's Hospital at Westmead concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

I understand that, if I decide to discontinue the study treatment, I may be asked to attend follow-up visits to allow collection of information regarding my health status. Alternatively, a member of the research team may request my permission to obtain access to my medical records for collection of follow-up information for the purposes of research and analysis.

Future use of samples

I consent to the storage and use of blood and tissue samples taken from me for use, as described in the relevant section of the Participant Information Sheet, for:

- This specific research project
- Any future ethically approved research.

Name of Participant (please print) _____

Signature _____ Date _____

Name of Witness* to
Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning the research project.

Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation - *Adult providing own consent*

Title	**Q fever vaccine trial in Australian adolescents Safety and immunogenicity of Q fever vaccine (Q-VAX®) in children aged 10 to <15 years**
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Coordinating Principal Investigator	Professor Nicholas Wood
Coordinating Centre	NHMRC Clinical Trials Centre
Principal Investigator	Professor Nicholas Wood
Associate Investigators	Dr Rama Kandasamy Dr Archana Koirala Dr Melanie Wong
Location	The Children's Hospital at Westmead

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 The Children's Hospital at Westmead.

Name of Participant (please print) _____

Signature _____ Date _____

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.

Declaration by Study Doctor/Senior Researcher†

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.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.