A CONCISE

GUIDE TO Q FEVER AND Q FEVER VACCINATION

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FOREWORD

Q fever is a world-wide problem, especially for people living in rural areas and particularly if they are exposed to animals. Parturient female animals (eg goats, cattle, sheep), who carry *Coxiella burnetii* in their genital tract, can infect people. While acute Q fever is a very unpleasant illness of 1-2 weeks duration, chronic Q fever is a life-threatening infection and the post-Q fever fatigue syndrome can debilitate patients for many months or even years.

Given that "prevention is better than cure", Australia is the only country in the world where an effective Q fever vaccine (Q-VAX®) is available. Australian healthcare professionals involved in vaccination can help prevent this infection in their patients due to the pioneering activities of the late Prof Barrie Marmion and a collaboration with the Commonwealth Serum Laboratories (CSL) at the time.

However, Q fever remains a challenge in Australia on many levels, including diagnosis, managing the risk of infection and utilising the non-conventional vaccine. Despite our increasing knowledge of the pathogen and the epidemiology, there is still a necessity to educate healthcare workers, policymakers and the wider community to continually improve our management of Q fever in Australia.

This guide is intended to provide a fundamental and hopefully, practical resource for healthcare professionals who are or want to be involved in managing and preventing Q fever.

Prof. Stephen R. Graves.

Prof. Stephen Graves
(May 2021)

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Q FEVER BACKGROUND IN AUSTRALIA

Q fever is a notifiable disease in all Australian States and Territories caused by an infection of an intracellular bacterium *Coxiella burnetii*.[1] The notification rates of the zoonotic disease across Australia broadly reflect the intensity of local cattle, sheep and goat husbandry and associated animal processing industries in those areas (Figure 1).[2,3]

Acute Q fever is often described as an influenza-like illness (ILI) and often with variable and non-specific symptoms, so that many Q fever cases are probably undiagnosed. Notifications of acute Q fever cases are likely to be an underestimate of the true burden of disease.[4] Almost 500 cases of Q fever are reported every year in Australia, mostly in Queensland and New South Wales (NSW).[5] A seroprevalence study of blood donors in metropolitan and non-metropolitan regions in NSW (Sydney and Hunter New England) and Queensland (Brisbane and Toowoomba) between 2014 and 2015 had determined crude antibody seroprevalence of 3.6% - lower in metropolitan cities and higher in non-metropolitan regions.[6] Overall, a recent study measuring Q fever seroprevalence using residual sera from diagnostic laboratories across Australia suggests 1 in 20 Australians may have been exposed to this bacterium (age standardised seroprevalence 5.6% (CI 4.5%-6.8%).[7]

There have been several Q fever outbreaks in Australia and these were generally occupationally related involving abattoir or rendering processes, farmers, sale yards and veterinary clinics.[8] Several work health and safety guidelines in Australia recommend vaccination for all those working, or intending to work, in a high-risk occupation unless prior immunity is evident.[9-11] However, increasing knowledge of Q fever epidemiology in Australia has demonstrated risk of *C. burnetii* infection is not limited to an occupational disease, but also by direct or indirect airborne exposure to the pathogen through close proximity (such as residing or visiting near an infected site).[12]

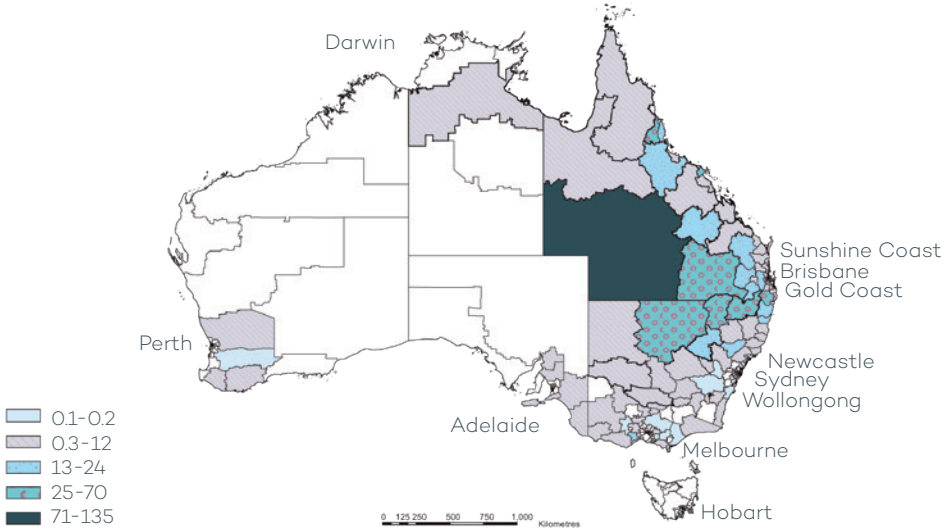


Figure 1: Notification rate for Q Fever, Australia, 2015 (cases per 100,000 population) by geographic areas.[2,3,#]

#Geographical areas defined by Australian Bureau of Statistics (ABS) as Statistical Area Level 3 (population generally between 30,000 and 130,000)

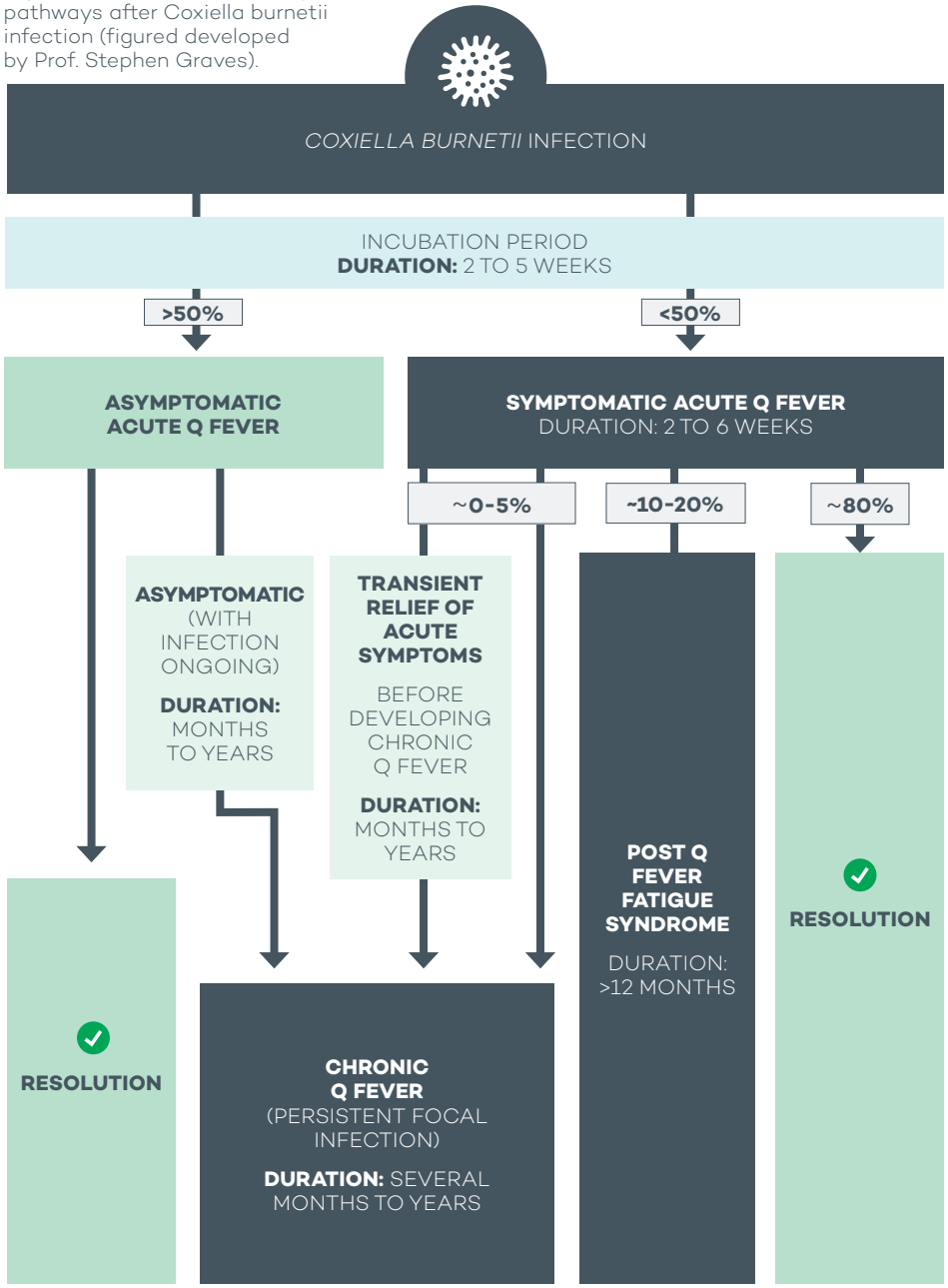
CLINICAL PRESENTATIONS

Q fever presentations are non-specific, variable and often misdiagnosed.[1, 2] In many cases people infected with *Coxiella burnetii* may be asymptomatic.[3] Up to 1 in 5 acute cases may develop post-Q fever fatigue syndrome (QFS) and up to 1 in 20 cases may develop chronic Q fever.[3, 4, 10]

Table 1: Clinical presentations of acute and chronic Q fever and for post Q-fever fatigue syndrome (QFS).

Disease state	Signs and Symptoms	Clinical Course
Acute Q Fever A severe acute febrile illness which is extremely debilitating and starts abruptly with symptoms mimicking those of influenza.[5]	Symptoms are highly variable, non specific[5] and may include: [1, 3, 5, 6] • Rapid onset of fever and chills that can last for 7-10 days • Profuse sweating • Severe headache • Aching muscles and joints • Extreme fatigue and mental confusion. • Nausea and diarrhoea • Photophobia or blurred vision • Pneumonia • Weight loss • Hepatitis (rarely with jaundice) • Rash (rare) • Acute endocarditis.	Symptoms appear 2-5 weeks after infection.[3, 5] In most cases the acute illness lasts from 2-6 weeks.[3, 5]
Chronic Q Fever *(Persistent focal infection)* Due to persistent focal *Coxiella burnetii* infection at one or more anatomical sites.[5] Occurs in up to 5% of acute Q fever cases.[4]	Chronic Endocarditis: Most common (60-70% of chronic Q fever cases)[1, 3] and most serious manifestation.[5] Symptoms are typically suggestive of cardiac involvement (heart failure due to cardiac valve dysfunction).[5] High morbidity and mortality if left untreated.[5, 7] Other manifestations[1, 3, 5] • Osteomyelitis or recrudescent granulomatous lesions in bone, joints, soft tissue or other organs • Vascular infections, especially aneurysms or infected prostheses • Late stage pregnancy infection • Hepatitis.	May appear months or years after acute Q fever illness even if the initial episode was mild or asymptomatic.[1, 4, 5]
Post Q fever fatigue syndrome (QFS) Up to 20% of acute patients will go on to experience a post-Q fever fatigue syndrome.[3, 5, 10]	Typical features of QFS include:[8] • Profound fatigue • Nausea • Constant headache • Aching muscles/joints • Concentration and memory problems • Sleeping problems • Night sweats.	Symptoms continue to persist for more than 12 months after the onset of the acute illness.[3, 5] Symptoms can last for years and have the potential to be highly incapacitating.[3, 9]

Figure 2: Clinical disease progression pathways after Coxiella burnetii infection (figured developed by Prof. Stephen Graves).



RISK

People at increased risk of contracting Q fever include those in direct contact or in close proximity to infected animals, their products (such as faeces, urine, milk, wool and especially products of conception) and contaminated material (such as dust, aerosols, soil, grass, straw, clothes).[1-3]

Assisting in birthing and slaughtering of animals are particularly high risk activities.[4] However, Q fever is by no means restricted to these groups, and individuals in the community may be infected, especially rural communities.[2] Certain pre-disposing factors have also been identified and linked to developing chronic Q fever or post-Q fever fatigue syndrome.[5, 6]

Table 2: Examples of risk factors for acute Q fever, chronic Q fever and post-Q fever fatigue syndrome.

Acute Q fever risk factors:[4]	
Meat & livestock	Abattoir workers and others associated with the meat industry
	Farm workers
	Shearers
	Stockyard workers
	Livestock transport workers
	Tanning and hide workers
Animal carers	Veterinarians, veterinary staff and veterinary nurses and students
	Wildlife carers, hunters, zoo keepers (working with high risk animals)
	Animal breeders and anyone regularly exposed to parturient animals
	Staff in veterinary microbiology laboratories
Environmental	Maintenance engineers, electricians, plumbers etc in at-risk environments
	Visitors to at-risk environments e.g. research workers, teachers, school students, insurance agents, sales people etc, especially in rural communities
	People with indirect contact to livestock e.g. those living down-wind of livestock transport routes, processing plants, feedlots and abattoirs
	People involved in rural mowing due to aerosolised dust potentially contaminated with infected animal excreta, especially kangaroos and bandicoots
	Family members of the at-risk occupational groups through exposure to contaminated clothing, boots or equipment

Chronic Q fever risk factors:[5]				
Valvular heart disease / valve prosthesis	Aortic aneurysms	Vascular grafts	Immuno-compromised	Pregnancy

Post Q-fever fatigue syndrome risk factors:[6]	
Severity of initial acute Q fever	Likely genetic factors

Table 3: Suggested Risk Assessment Tool for Patient Exposure to Q Fever.[7]
(**Y**=Yes; **N**=No; **U**=Unknown)
Note: At-risk sites of *C. burnetii* infection is a developing area of research.

General	**Y**	**N**	**U**
1. Environmental - Resides in a rural or regional area?			
2. Animal - Occupation involves direct or indirect contact with animals?			
1. Environmental Exposure	**Y**	**N**	**U**
1a. Lives on any of the following:			
• farm/station or rural property			
• near an abattoir / animal grazing area / sale yards			
1b. Visited or travelled to any of the following:			
• farm/station or rural property			
• a facility that processes animal products (e.g. abattoir, factory)			
• rural/regional communities			
1c. Exposure to any of the following:			
• dust from paddock or animal yards			
• trucks transporting livestock			
• clothes worn by someone who works with animals			
• ticks (incl. any bites from a tick)			
• faeces from wildlife (e.g. kangaroos) – e.g. while mowing grass			

2. Animal Exposure	**Y**	**N**	**U**
2a. Direct contact with the following animals:			
• Domestic ruminants - cattle, sheep, goats (incl. feral goats)			
• Native fauna – kangaroos, small marsupials (e.g. bandicoots)			
• Other mammals – pigs, cats, dogs			
2b. Direct contact with animal tissues or fluids:			
• blood, bone, viscera, skin/hides, faeces or urine			
• slaughtering, skinning or meat processing			
• assisted or observed animal birth (incl. handling new-borns)			
• directly undertaking veterinary practices			
• observing veterinary practices			
• shearing, wool processing or wool classing			
• contact with pelts or hides (incl. tanning)			
• contact with straw or animal bedding			
• consuming unpasteurised milk or milk products			
• hunting or shooting			
• attending an animal sale yard or animal show			
• taxidermy			

DIAGNOSIS

The signs and symptoms of Q fever are non-specific and can be associated with a wide variety of diseases. In addition to clinical symptoms and risk assessment that raise suspicion of Q fever, diagnosis almost always requires laboratory testing.

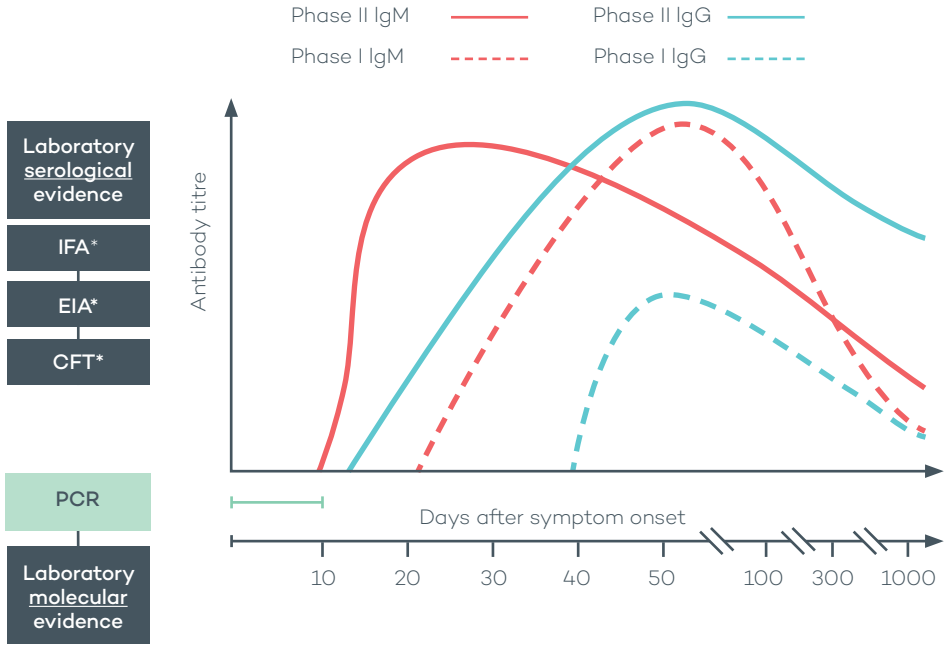
Nucleic acid testing (Polymerase Chain Reaction, PCR)
This test provides the fastest turnaround time to achieve diagnosis, avoiding the need to wait for a convalescent serum.[1] A positive PCR result is confirmatory alongside the clinical findings. It may be performed on blood (EDTA) or biopsy (e.g. cardiac valve post-operatively). False-negative PCR results are common however, as bacteraemia declines and can become undetectable approx. 10 days after the onset of illness (Figure 3)[2] - **DO NOT rely solely on a negative PCR result to rule out Q fever.**

Serology
Serology is the most widely used diagnostic technique for Q fever testing.[2] It is important to note that antibody detection is highly dependent on the timing of the specimen collection (Figure 3)[3]. Q fever results in two antibody types produced - phase I antibody and phase II antibody. There are different patterns of antibody response during the course of acute Q fever and chronic Q fever.[3] False-negative serological results may also occur due to declining antibody titres, particularly in patients infected many years previously.[2] As a result the interpretation of Q fever serology results can be challenging and specialist input may be required.

There is no serological pattern that correlates with the post-Q fever Fatigue Syndrome (QFS).[1] Diagnosis of QFS depends on a characteristic set of 8-10 symptoms and evidence of past antigenic stimulation.[2] Specialist referral is suggested if QFS is suspected.

Differential diagnosis[4]	
Q fever must be differentiated from other, more common causes of: • fever • chronic fatigue • weakness • other non-specific flu-like symptoms • endocarditis.	Q fever must also be differentiated from other atypical pneumonias - pneumonia caused by infection with bacteria such as: • Chlamydia • Mycoplasma • Bartonella • Rickettsia • Legionella • Brucella.

Figure 3. Typical *C. burnetii* serological and nucleic acid response in Acute Q fever (figure developed by Prof. Stephen Graves).



IFA= immunofluorescence assay; EIA= enzyme immunoassay; CFT= complement fixation test; PCR= polymerase chain reaction; *IFA, EIA & CFT require seroconversion or significant increase in antibody level to Phase II antigen in paired sera to confirm acute Q fever diagnosis.

Note: In most patients infected with *C. burnetii* there is a short period of overlap when both PCR and serology assays are positive, however there may be a window of period for some patients when neither of the assays are positive.

Table 4a: A clinician's guide to laboratory diagnosis of suspected acute Q fever.[1-3]

	Possible Acute Q fever	
	PCR	Serology
Specimens required	5-10 mL of unclotted (EDTA) blood.	5-10 mL of serum (clotted blood).
When to take specimens	Ideally **within one week of disease onset** to enable the detection of *C. burnetii* DNA in blood through polymerase chain reaction (PCR).	Initial - **As soon as the patient is seen** AND Convalescent - collected **again at 12-25 days after** onset of illness. During the acute phase of Q fever Phase II IgM and later IgG antibodies are usually detected.
Comments	Interpretation of PCR results require care; the bacteria are rapidly eliminated from the bloodstream, so a negative PCR test does not exclude the possibility of Q fever.	The collection of convalescent sera from all cases is critical even if the patient has since recovered. Diagnosis can be **confirmed by a 4-fold rise in antibody titre.** Advice from a clinical microbiologist and/or infectious disease physician may be required to assist in the interpretation of the serological results and other aspects of diagnosis.

Table 4b: A clinician's guide for laboratory diagnosis of suspected chronic Q fever or post Q fever Fatigue Syndrome (QFS).[1-3]

	Possible Chronic Q fever		Possible QFS
	PCR	Serology	Serology
Specimens required	5-10 mL of unclotted (EDTA) blood or biopsy specimens of fresh tissue.	5-10 mL of serum (clotted blood).	5-10 mL of serum (clotted blood) to confirm past exposure to *C. burnetii.*
When to take specimens	DNA may be detected by PCR in peripheral blood mononuclear cells or in biopsy specimens from focally infected tissue (e.g. heart valves, bone, synovium).	Serum specimens should be collected as soon as the patient is seen (or as soon as chronic Q fever is suspected) and collected again approx. a fortnight later. In chronic Q fever cases Phase I IgG and Phase I IgA antibodies are usually detected in high concentration (titre).	On presentation.
Comments	The sensitivity of PCR in blood in patients with endocarditis or vascular infection can vary significantly and can be as low as 23%.[5] Any case of culture-negative endocarditis may be Q fever.	Clinicians should be aware that late-stage "burnt-out" Q fever endocarditis (i.e. distorted/ fibrosed/ calcified valves without obvious vegetations) may not exhibit the characteristic serological pattern of chronic Q fever endocarditis.	Clinical diagnosis only. No laboratory tests are available to confirm diagnosis other than evidence of past exposure to *C. burnetii* by serology.
	Note: A diagnosis of chronic Q fever may not be made based on laboratory results alone. Diagnosis relies on the test results supported by compatible clinical findings. Investigations include: - documented evidence of a previous acute Q fever episode. - chest X-ray; and full blood workup including liver function tests and inflammatory markers; and results of ultrasound imaging (for endocarditis).		

INFECTIVITY AND RESISTANCE OF *COXIELLA BURNETII*

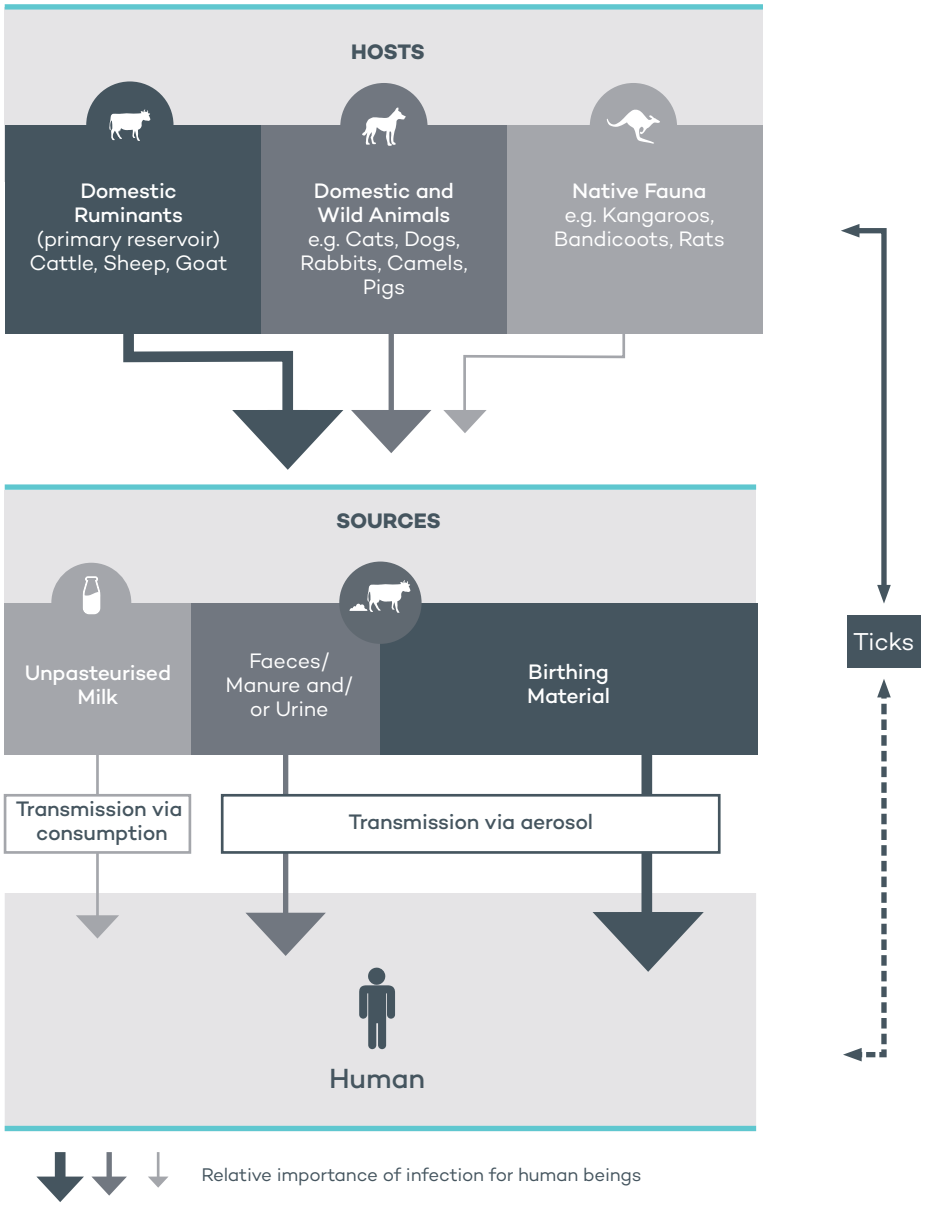
Infectivity

C. burnetii is a highly infectious and readily-transmitted pathogen.

Common mode of *C. burnetii* infection for humans[1]	**Inhalation** of airborne dust or droplets contaminated by secretions from infected animals (e.g. birthing products, faeces and urine).
Other possible modes of transmission[1,2]	**Subcutaneous and intramuscular inoculation** (e.g. following cuts with contaminated knives, or needle stick injury). **Consuming** unpasteurised milk or unpasteurised milk products from infected animals. **Tick** bites or inhalation of tick excreta (this has been infrequently documented). **Human to human transmission** (e.g. blood transfusion, sexual transmission) has been reported, though this is very rare.
Median inhaled infectious dose of *C. burnetii* for humans[3,4]	1 to 15 organisms.
Location of *C. burnetii in vivo*[1]	The principal host cell for *C. burnetii* is the alveolar **macrophage** and other monocytic cells. After infection, *C. burnetii* survives and multiplies intracellularly within the host cell phagolysosome.

Resistance	Pathogenesis[1]
C. burnetii is able to resist physical and chemical stressors such as elevated temperatures, desiccation, osmotic shock, UV light, and chemical disinfectants.[1] The organism may spread on fomites such as wool, hides, clothing, straw and packing materials.[8] Pasteurisation temperatures inactivate the organism.[8] Examples of the *C. burnetii* resistance to harsh environmental stresses include its ability to survive in:[1,2] • wool at 15-20°C for 7 to 9 months (and almost twice as long at 4-6°C) • fresh meat in cold storage for >1 month • salted meat for 5 months • dried cheese for 30-40 days • skim milk at room temperature for >40 months • dry tick faeces for >18 months • dust for months to years (windborne spread of contaminated dust can disperse the organisms over several kilometres)	• The principal host cell for *C. burnetii* is the macrophage and cells of the monocyte lineage. After infection, *C. burnetii* survives and multiplies in the host cell phagolysosome. • The host's innate and adaptive immune responses appear to be inhibited during the long incubation period, but eventually effective humoral and cell mediated immunity (CMI) responses develop. • Interferon-gamma and other pro-inflammatory cytokines plays a key role in restoring macrophage function leading to elimination of *C. burnetii*. • Symptoms of acute Q fever are due in part to the CMI and acute phase cytokine responses.

Figure 4: Example of *C. burnetii* infected hosts and zoonotic modes of transmission.



TREATMENT

Antibiotic therapy is used to treat individuals with acute Q fever. Most commonly a tetracycline is used to treat acute Q fever and doxycycline 100 mg twice daily for 14 days is recommended for adults. Referral to an infectious diseases physician for management of children and pregnant women is recommended.[1]

Chronic Q fever is more difficult to treat. Q fever endocarditis may require a long course of antimicrobial treatment and specialist input.[1,2] In some individuals with damage to the heart valves or evidence of heart failure, surgery may be necessary.[3]

There is no effective treatment for QFS apart from general medical support and gentle exercise.

RISK REDUCTION METHODS OF *COXIELLA BURNETII* INFECTION

Measures that may help reduce the risk of Q fever infection can include:*[1,2]

Washing hands and arms thoroughly with soapy water after handling animals, carcasses or relevant clothing potentially exposed to the bacteria.

Keeping yard facilities for sheep and cattle well away from domestic living areas. A one kilometre house free zone is recommended around any worksite at risk of Q fever.

Minimising dust and rodents in slaughter and animal housing areas.

Proper handling of animal products and proper disposal of animal tissues, especially birthing products.

Removing protective and/or other clothing that may carry bacteria before returning to the home environment. Consider careful washing of clothing.

Limiting access to high risk facilities for those not vaccinated.

When working in at-risk environments wearing disposable face masks that are properly fitted (P2/N95 masks) to help filter small air particles and reduce the risk of airborne transmission of Q fever.

Vaccination can help prevent Q fever infection and may be recommended for those who are at risk and are appropriate candidates for vaccination.

*For a complete list of risk reduction strategies refer to local state government safe work guidelines.

PRE-VACCINATION SCREENING

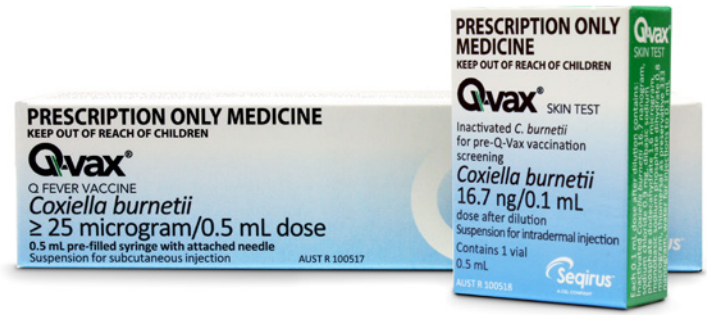


Figure 5. Q-VAX® Vaccine (left) and Q-VAX® Skin Test (right)

The primary method of preventing Q fever is through the vaccination of appropriate individuals.[1-4] An effective vaccine against Q fever (Q-VAX® Q Fever Vaccine, Seqirus) has been available in Australia since 1989. However, administering this vaccine to someone who has already been exposed to *C. burnetii* can cause serious hypersensitivity reactions and is contraindicated.[5] To help prevent these adverse reactions from occurring, a pre-vaccination screening process is required to exclude individuals from vaccination who are already sensitised to Q fever antigens from a prior Q fever infection or prior exposure to *C. burnetii* or previous vaccination.[5]

The three components of Q-VAX® pre-vaccination screening are patient history, blood (serology) testing and the administration of the Q-VAX® Skin Test. All three components are required and can be performed on the same day, however the Q-VAX® Skin Test should be administered after the blood collection for serology testing if they are not done on the same day (see Figure 7).[1,5]

Pre-Vaccination Blood (Serology) Test

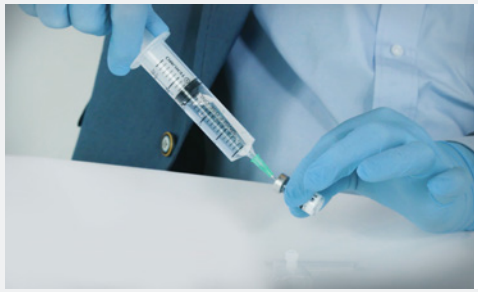
Serological testing during pre-vaccination screening measures IgG antibodies in the individual's blood to *C. burnetii* phase 2 antigen. This is aimed at detecting antibody patterns indicative of past exposure to *C. burnetii*. It is an additional safeguard in case the Q-VAX® Skin Test is performed incorrectly. Immunofluorescent assay (IFA) and enzyme immunoassay (EIA) are the preferred tests as a complement fixation test (CFT) at a 1 in 2.5 dilution is subject to false positive and false negative reactions.[1]

Q-VAX® Skin Test

The Q-VAX® Skin Test is a purified solution of ≥2.5 µg/0.5mL formalin-inactivated, *C. burnetii* prepared from the Phase I Henzerling strain of the organism.[5] The main purpose of Q-VAX® Skin Test is to detect the presence of cell-mediated immunity (CMI) and exclude susceptible adults at risk of experiencing hypersensitivity reactions to the vaccine.[1,5] It requires preparation by diluting the 0.5 mL with 14.5 mL of sodium chloride for injection (a 1 in 30 dilution) and administering 0.1 mL of the diluted solution (16.7 ng) via the intradermal route into the volar surface of the mid-forearm (see Figure 6 and 7).[1,5]

Figure 6. Q-VAX® Skin Test: Preparation by dilution with 0.9% sodium chloride - full video available at www.qfeverfacts.com.au/login/ (access open to Australian healthcare professionals only).

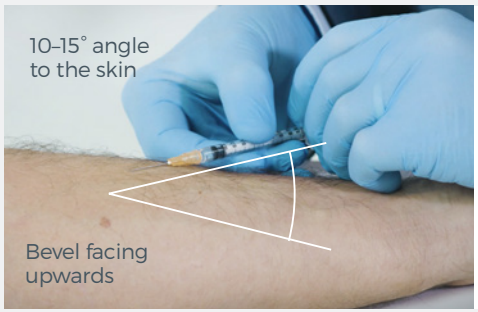
Draw 14.5mL of 0.9% sodium chloride for injection into syringe.



Dilute the Q-VAX® Skin Test solution (0.5 mL) by drawing it into the syringe with sodium chloride (total volume 15 mL).

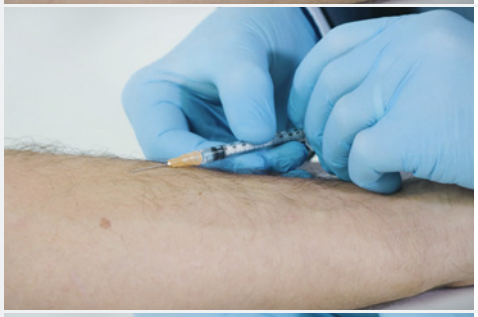
Transfer the diluted solution to a sterile container. MIX well and store as directed. When ready, a smaller syringe is used to draw 0.1 mL for administration.

Figure 7. Q-VAX® Skin Test: Intradermal injection technique - full video available at www.qfeverfacts.com.au/login/ (access open to Australian healthcare professionals only).

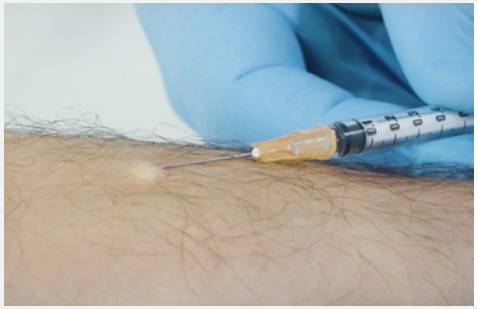


Only Q-VAX® Skin Test solution that has been diluted in 0.9% sodium chloride for injection (see Figure 6) should be administered for skin testing.

Insert needle into volar surface of mid-forearm. Place syringe at 10-15° angle to the skin. Bevel up.



The needle should be clearly visible through the skin.



Slowly inject 0.1mL of diluted Q-VAX® Skin Test solution, until a bleb (fluid filled blister) can be seen.

Tips	Potential Errors
- Diluted skin test solution can be used for more than one person if stored at 4°C and used within 6 hours. - 1 mL syringes with integrated extra fine needles (i.e. insulin needles) are useful. - Record/note the site of the intradermal injection.	- Diluted skin test solution injected too deeply (i.e. subcutaneous instead of intradermal). - Not confirming a patient can return in 7 days (to have the test results read) before administering Q-VAX® Skin Test.

Figure 8. Q fever pre-vaccination clinic flowchart.

1.

Patient History Screening Questions

- Does the patient have a prior history of Q fever infection confirmed at the time of illness?
- Has the patient previously been vaccinated with Q-VAX® vaccine?
- Does the patient have a known hypersensitivity to egg proteins or other components of Q-VAX® vaccine?

If **ANY** answer = **YES**

Q-VAX® VACCINE IS **CONTRAINDICATED**

If **ALL** answers = **NO**
(And the patient is an adult* + not pregnant)

Confirm patient can return in exactly 7 days to have skin test read

CONDUCT PRE-VACCINATION **BLOOD (SEROLOGY) TEST** AND **Q-VAX® SKIN TEST**

2.

Pre-Vaccination Blood (Serology) Test

A. **Collect** 5-10 mL blood in plain tube in clinic or in Pathology.

B. **Request** pathology for 'Q-VAX® pre-vaccination screening for *Coxiella burnetii* phase 2 IgG antibodies.'

3.

Q-VAX® Skin Test

A. **Prepare** the Q-VAX® Skin Test solution. Dilute 0.5 mL of Q-VAX® Skin Test solution in 14.5 mL of sodium chloride for injection (to a final volume of 15 mL) and MIX well. The diluted solution can be stored at 4 °C but must be used within six hours.[5] It is suggested to label the diluted solution with the preparation details (e.g. time).

B. **Inject** 0.1 mL of the diluted Skin Test solution via intradermal injection into the volar surface of the mid-forearm. NOTE: Do NOT inject subcutaneously or intramuscularly.[5]

Schedule Follow-up Appointment in 7 Days

Patient must come back 7 days after the Q-VAX® Skin Test dose for interpretation of pre-vaccination screening results (serology and skin) and for their vaccination (if appropriate).

*Q-VAX® Vaccine and Skin Test are indicated for use in adults.[5] The Australian Technical Advisory Group on Immunisation (ATAGI) advises that Q-VAX® can be used in people aged ≥15 years.[6]

Interpreting Pre-Vaccination Screening Test Results

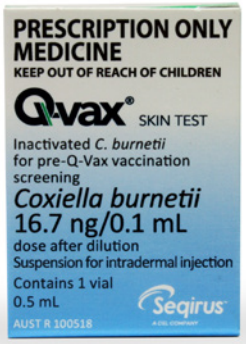
Pre-Vaccination Blood (Serology) Test

A positive antibody test is indicated by:

- Immunofluorescent antibody (IFA)-positive (at 1 in 25 or greater dilution); or
- Definitive positive absorbance value in enzyme immunoassay (EIA); or
- Complement fixation test (CFT) antibody-positive (at a 1 in 2.5 dilution)[1]

An equivocal serology test may be due to detection of low antibody titers. The low-level presence of antibodies may be non-specific or due to technical factors in the assay. An equivocal serology result alone does not necessarily exclude vaccination.[5]

Antibody levels will decline with time and may be negative in a patient infected many years previously.[1]



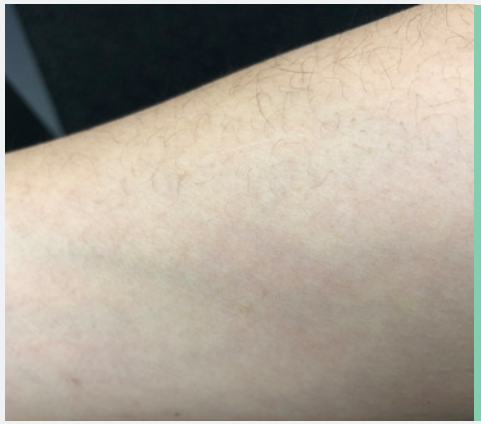
Q-VAX® Skin Test

A positive reaction is any induration at the site of injection read seven days after the test dose was given.[5]

An induration means a palpable, raised, hardened area or swelling.[1,5,6]
An induration is not necessarily visible and will require assessment of the skin test site via:

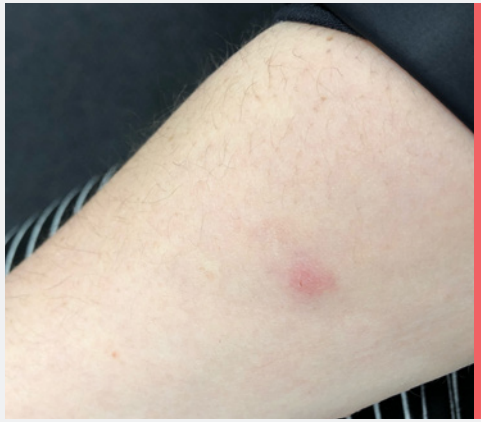
- palpation method (using fingers to feel for an induration); or
- ballpoint pen technique (using a ballpoint pen to draw perpendicular lines 1-2 cm from skin test site and moving to the centre – if resistance is felt then the margin of an induration has been detected).

Figure 9. Example of Q-VAX® Skin Test results (7 days post administration).



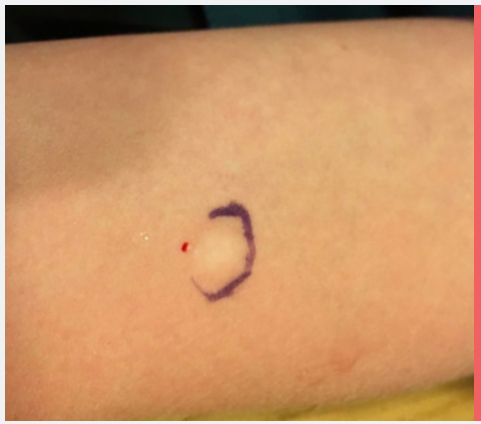
Negative

Subsiding erythema but no raised, hardened area.



Positive

A visible induration that is raised and palpable.



Positive

An invisible induration that is raised and hardened.

Table 5. Interpretation of pre-vaccination results on day 7 post administration and recommended action.

Blood Test	Skin Test	Likely Immune Status	Recommended Action
Positive	Positive	Sensitised	Do not vaccinate
Positive	Negative	Sensitised	Do not vaccinate
Negative	Positive	Sensitised	Do not vaccinate
Equivocal	Positive	Sensitised	Do not vaccinate
Equivocal	Negative	Unknown	Indeterminate
Negative	Negative	Non-immune	Vaccinate

Note: For any questions regarding the pre-vaccination screening, please contact Seqirus (a CSL company) Medical Information on 1800 642 865.

Do not vaccinate	The patient is most likely sensitised to *Coxiella burnetii* due to unknown prior exposure. Therefore, vaccination with Q-VAX® is contraindicated. Consider documenting the patient's pre-vaccination screening results with their consent on the Q Fever Register (www.qfever.org) and the Q Fever Pre-screening and Immunisation Record Card (available from Seqirus) for the patient's record.
Indeterminate	The patient may have a low-level of *C. burnetti* antibodies, but cannot be assumed to have adequate protective immunity. The risk-benefit decision of being vaccinated or not should be individually assessed and discussed with the patient to decide whether the potential risk of adverse effects following vaccination outweighs the potential benefits of prevention of Q fever and its associated complications. **For further support or information, please enquire with Seqirus (a CSL company) Medical Information (phone: 1800 642 865).**
Vaccinate	The patient does not demonstrate a prior history of Q fever infection, nor sensitisation to Q fever antigens that may lead to serious hypersensitivity reactions if vaccinated. Proceed to vaccination (see next section).

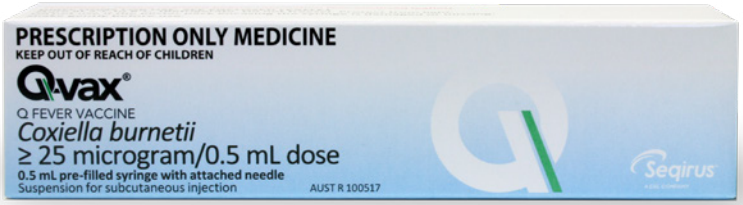
VACCINATION AND ADVERSE EFFECTS

What is Q-VAX® Vaccine?

Q-VAX® is a purified suspension of inactivated *C. burnetii* (Henzerling strain) in the phase I antigenic state. The organisms are grown in the yolk sac of embryonated eggs, extracted, inactivated with formalin, and purified from excess egg proteins. Thiomersal 0.01% w/v is added as a preservative.[1]

Each Q-VAX® Vaccine dose contains a minimum of 25 µg of antigen in a 0.5 mL aqueous solution. Q-VAX® Vaccine is supplied as a prefilled syringe.[1]

Figure 10: Q-VAX® Vaccine



Who is Q-VAX® Vaccine indicated for?

Susceptible adults who are at an identifiable risk of Q fever infection (see section 3) and have demonstrated no prior history or sensitisation to Q fever antigens (see section 8).[1,#]

What is the efficacy of Q-VAX® Vaccine and duration of immunity?

- A retrospective analysis estimated vaccine efficacy at 83-100%, however, like all vaccines, 100% effectiveness cannot be guaranteed.[1,5]
- The duration of protective immunity following immunisation is unknown, but it is believed to be in excess of 5 years. Re-vaccination must never be performed due to the possibility of severe hypersensitivity reactions.[1]

Note: Immunity to Q fever typically develops 2 weeks after vaccination.[2]

Q-VAX® Vaccine and Skin Test are indicated for use in adults.[1] The Australian Technical Advisory Group on Immunisation (ATAGI) advises that Q-VAX® can be used in people aged ≥15 years.[3]

What is the suggested vaccination process of Q-VAX® Vaccine?[1]

1.

Ensure the patient has passed the pre-vaccination screening (see section 8):
- A susceptible adult who is at identifiable risk of Q fever infection.
- Not pregnant (deferral of vaccination is recommended).
- No prior history of likely *Coxiella burnetii* exposure (including previous Q fever vaccination) followed by illness strongly suggestive of Q fever infection.
- No known hypersensitivity to egg proteins or any component of the Q-VAX vaccine.
- Negative Q-VAX® Skin Test at day 7 after administration.
- Negative serology antibody test result.

2.

Prepare for vaccination:
- Ensure adrenaline is available in case of anaphylaxis.
- Check that the blister pack encasing the Q-VAX® vaccine syringe is not damaged or missing – do not use if this is the case.
- Shake the Q-VAX® Vaccine pre-filled syringe gently before use.

3.

Administering Q-VAX® Vaccine:
- Inject 0.5 mL of the Q-VAX® Vaccine solution **subcutaneously** (45° angle to the skin). Do NOT administer the vaccine intravenously or intramuscularly.

4.

Post-vaccination:
- Cover injection site with cotton wool and tape and advise patient to apply gentle pressure on the injection site for 1-2 minutes.
- Monitor patient for 15 minutes for any immediate adverse effects.
- Document relevant details (e.g. batch record, date of administration, etc.) and consider recording in the **Q Fever Register** (www.qfever.org) with the patient's consent, as well completing the **Q Fever Pre-screening and Immunisation Record Card** (available from Seqirus).
  Please note that the **Q Fever Register** website may also contain potentially useful resources (i.e. forms) to assist in the running a Q fever vaccination clinic.

What are possible adverse effects of Q-VAX® Vaccine?

Vaccination of already immune subjects may result in severe local or general reactions, with the possibility of local abscess formation. The most common reactions after vaccination observed during clinical trials are minor local and systemic reactions (Table 6).[1,2]

Table 6: Common minor reactions to Q-VAX® Vaccine (data relates to a clinical trial in South Australia in 464 vaccinated subjects).[1,4]

Reaction	Frequency of reactions (%)
Local tenderness	48
Local erythema	33
Other reactions (aching joints; swollen glands; flu-like symptoms; feeling faint; itching and induration at injection site)	15
Headache	9

A range of adverse reactions have been reported during post-marketing use of the vaccine (Table 7).[1]

Table 7: Post Marketing data: Q-VAX® Vaccine adverse reactions.[1]

Disorders of:	Adverse reactions	Frequency of adverse reaction*
General and administration site	Injection site inflammation (e.g. erythema, pain, warmth and swelling)	Very common
Nervous system	Headache	Common
Skin and subcutaneous tissue	Delayed skin reaction (presenting up to six months after vaccination) at injection site (either vaccination and/or skin test site)	Common
Gastrointestinal system	Nausea, vomiting and diarrhoea	Uncommon
General and administration site	Injection site induration and/or oedema, pyrexia, malaise, fatigue	Uncommon
Musculoskeletal system and connective tissue	Myalgia	Uncommon
Skin and subcutaneous tissue	Hyperhidrosis	Uncommon
General and administration site	Injection site abscess formation or granuloma	Uncommon
Blood and lymphatic system	Lymphadenopathy	Rare
General and administration site	Chills, chronic fatigue syndrome	Very rare
Musculoskeletal system and connective tissue	Arthralgia	Very rare
Nervous system	Dizziness	Very rare

*Very Common: (≥1/10); common: <1/10 and ≥1/100; uncommon: <1/100 and ≥1/1000; rare: <1/1000 and ≥1/10,000; very rare: 1<10, 000

REFERENCES AND OTHER RESOURCES

Resources

Listed below are links to various helpful resources about Q fever. Please note that some information in these links may not comply with the Australian regulatory requirements. Further information relevant to the Australian environment is available from Seqirus and the Approved Product Information.

Resource	Description	Website
Q Fever Facts	A Seqirus website that aims to educate members of the Australian public and healthcare professionals about Q fever. Healthcare professionals can find training videos on the Q-VAX® vaccination process, including access to other information resources. Access to the healthcare professional section is granted only to Australian healthcare professionals with a valid AHPRA number.	www.qfeverfacts.com.au
Q Fever Register	An online register owned and funded by the Australian Meat Processor Corporation (AMPC), dedicated to recording the Q fever immune status of individuals in Australia. It also contains useful forms and resources for use in running Q fever vaccination clinics.	www.qfever.org
Australian Immunisation Handbook	The Australian Immunisation Handbook provides clinical advice for healthcare professionals on the safest and most effective use of vaccines in their practice.	https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/q-fever

Q fever background

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Infectivity and Resistance of *Coxiella burnetii*

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PBS Information: This product is not listed on the National Immunisation Program (NIP) or the PBS.

Before prescribing Q-VAX® Vaccine or Q-VAX® Skin Test, please review the Approved Product Information available at seqirus.com.au/products

MINIMUM PRODUCT INFORMATION: Q-Vax® Vaccine: Formalin-inactivated *Coxiella burnetii* suspension for injection (≥25 µg/0.5mL). **INDICATIONS:** Immunisation of susceptible adults at identifiable risk of infection with Q fever. **CONTRAINDICATIONS:** Persons who: have a history of Q fever; have previously been vaccinated with Q fever vaccine; have a history of likely exposure followed by an illness strongly suggestive of Q fever; persons with positive serology for Q fever antibody or a positive Q fever Skin Test; known hypersensitivity to egg proteins or any components of the medicinal product.**PRECAUTIONS:** Prior to immunisation, all potential vaccinees must have serum antibody estimation and a skin test reported; administration of Q-Vax® to those already sensitised to Q fever antigens can cause serious hypersensitivity reactions. Subjects with a confirmed positive antibody test or a positive skin reaction must not be given Q-Vax®. Q-Vax® Vaccine should never be administered intravenously. Efficacy and safety have not been established in immunodeficient or immunosuppressed individuals. Use in Pregnancy (Category B2): Safety not established. Deferral of vaccination is recommended. Use in Lactation: No information available. Use in Children: No information available. **ADVERSE EFFECTS:** Vaccination of already immune subjects may result in severe local or general reactions. Very common: injection site inflammation eg: erythema, pain, warmth, swelling. Common: headache; delayed skin reactions. **DOSAGE AND ADMINISTRATION:** Do not administer vaccine until results of serology and skin testing are known. Administer 0.5mL subcutaneously [NOT INTRAMUSCULARLY]. Do not revaccinate due to possibility of severe hypersensitivity reactions. Q-Vax® Skin Test: 2.5 µg antigen/0.5mL aqueous solution. **INDICATIONS:** Pre-screening of potential vaccine recipients for prior sensitisation to Q fever antigens. **DOSAGE AND ADMINISTRATION:** Dilute 0.5mL in 14.5mL Sodium Chloride Injection before administration. Administer 0.1mL diluted Q-Vax® Skin Test intradermally into the volar surface of the mid-forearm.

Based on TGA Approved Product Information: 26 August 2019. Seqirus Pty Ltd. ABN 26 120 735 035. 63 Poplar Road, Parkville VIC 3052 Australia. Seqirus™ is a trademark of Seqirus UK Limited or its affiliates. Q-Vax® is a registered trademark of CSL Limited. Seqirus Medical Information: 1800 642 865. ANZ-QVAX-21-0008. Date of preparation: 06/2021.

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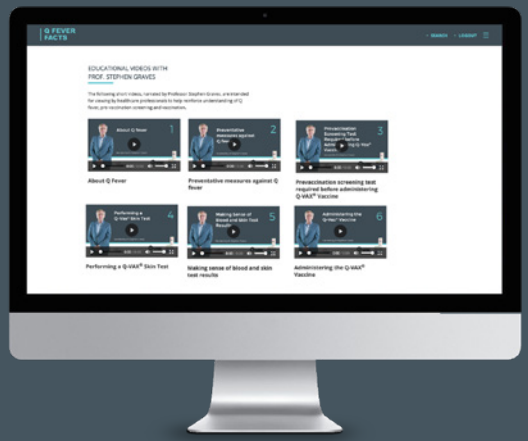

WAKE UP TO THE FACTS ON
Q FEVER

For more information on Q fever please visit www.qfeverfacts.com.au

Access a range of helpful resources to better understand who is at risk of contracting Q fever and how to implement preventative measures against Q fever.

Educational resources and clinic support materials are available to download from the website. Healthcare professionals can request printed copies of brochures and posters for use in their surgeries, plus access to educational videos.

CONTENT INCLUDES:

- Downloadable patient & clinic support materials
- Educational videos
- Q fever related case studies
- Podcasts

A CONCISE

GUIDE TO Q FEVER AND Q FEVER VACCINATION

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