AUSTRALIAN PRODUCT INFORMATION – Q-VAX® Q fever Vaccine and Q-VAX® SKIN TEST Q fever Skin Test (inactivated *Coxiella burnetii*) suspension for injection

1. NAME OF THE MEDICINE

Inactivated *Coxiella burnetii* as active ingredient.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Q-VAX® is a purified suspension of formalin-inactivated, *Coxiella burnetii* prepared from the Phase I Henzerling strain of the organism grown in the yolk sacs of embryonated eggs. Trace amounts of ovalbumin (<1 microgram) may also be present.

Q-VAX® Vaccine contains ≥ 25µg of antigen in 0.5 mL of aqueous solution.

Q-VAX® Skin Test contains ≥ 2.5 µg of antigen per 0.5 mL of aqueous solution. **Prior to administration**, Q-VAX® Skin Test is diluted with Sodium Chloride injection to ensure that 16.7 ng (nanograms) of antigen is delivered per 0.1 mL intradermal dose. (see **SECTION 4.2 – DOSE AND METHOD OF ADMINISTRATION**).

Each 0.5 mL Q-VAX® Vaccine also contains sodium chloride 4.1 mg, monobasic sodium phosphate dihydrate 120 microgram, dibasic sodium phosphate dodecahydrate 245 microgram thiomersal as preservative 50 microgram and water for injections to 0.5 mL.

Each 0.1 mL Q-VAX® Skin Test dose after dilution also contains sodium chloride 0.9 mg, monobasic sodium phosphate dihydrate 0.8 microgram, dibasic sodium phosphate dodecahydrate 1.6 microgram, thiomersal as preservative 333 nanogram and water for injections to 0.1 mL.

3. PHARMACEUTICAL FORM

Q-vax® Q-Fever Vaccine is a clear to slightly opaque, colourless suspension for subcutaneous injection.
Q-vax® Skin test is a clear to slightly opaque, colourless suspension for dilution prior to intradermal injection.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Q-VAX® Vaccine is indicated for the immunisation of susceptible adults at identifiable risk of infection with Q fever.

Abattoir workers (and those closely associated with the meat industry), farmers, veterinarians, stockyard workers, shearers, animal transporters and many others exposed to cattle, sheep or goats or their products should be considered for vaccination.

Note also that Q fever has occurred among persons culling and processing kangaroos and that laboratory personnel handling potentially infected veterinary specimens, or visiting abattoirs, are at risk.

Q-VAX® Skin Test is indicated for the pre-screening of potential vaccine recipients for prior sensitisation to Q fever antigens.

It is essential to test for sensitisation to Q fever antigens using Q-VAX® Skin Test in every individual prior to immunisation (see **SECTION 4.4 – SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

4.2 DOSE AND METHOD OF ADMINISTRATION

Q-VAX® Vaccine:

Q-VAX® Vaccine should not be administered until the results of serology and skin testing are known (see **SECTION 4.4 – SPECIAL WARNINGS AND PRECAUTIONS FOR USE).** Q-VAX® should be given only to those who have no demonstrable evidence of sensitisation to Q fever antigens.

The dose of Q-VAX® Vaccine is 0.5 mL given by subcutaneous [NOT INTRAMUSCULAR] injection. The container should be gently shaken before use.

The vaccine should never be administered intravenously.

No information is available on paediatric use.

Revaccination must never be undertaken due to the possibility of severe hypersensitivity reactions.

Q-VAX® Skin Test:

Preparation: Skin Test solution should be prepared by diluting 0.5 mL of the Q-VAX® Skin Test in 14.5 mL of Sodium Chloride Injection (to a final volume of 15 mL). The **diluted** Q-VAX® Skin Test should be freshly prepared, stored at 4°C and used within six hours**.**

Administration: The dose administered for skin testing is 0.1 mL of the **diluted** Q-VAX® Skin Test. This should be injected intradermally into the volar surface of the mid-forearm.

4.3 CONTRAINDICATIONS

Q-VAX® should not be administered to:

- Persons who have a history of Q fever
- Persons who have been previously vaccinated with Q fever vaccine
- Persons who 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
- Persons with known hypersensitivity to egg proteins or any component of the medicinal

product.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Prior to immunisation, all potential vaccines must have a serum antibody estimation and a skin test reported; administration of Q-VAX® to those who are already sensitised to Q fever antigens can cause serious hypersensitivity reactions.

As with other injectable vaccines, including Q-VAX® Skin Test solution, appropriate medical treatment and supervision should always be available in case of anaphylactic reactions. Adrenaline should always be readily available whenever the injection is given.

Q-VAX® should never be administered intravenously.

There is no information available on the efficacy and safety of Q-VAX® in immunodeficient or immunosuppressed individuals.

Those who have a confirmed positive antibody test or a positive skin reaction must not be given Q-VAX® (see Pre-vaccination testing).

If the skin test is negative or equivocal and antibodies are present at low titres (reported as a borderline laboratory test result), it cannot be concluded that the subject has adequate *protective* immunity against Q fever. The low-level presence of antibodies may be non-specific or due to technical factors of the assay. The risk-benefit decision of being vaccinated or not should be individually assessed and discussed with the subject, in order to decide whether potential adverse events following vaccination outweigh the potential risk to that subject from Q fever infection and its associated complications.

It should be noted that a very small number of people may have had Q fever in the past and yet show no response to serological or skin testing. Such persons may have severe reactions to Q-VAX®. For this reason, subjects should be carefully questioned regarding the possibility of previous exposure to Q fever and the duration of such exposure.

Workers who are at risk of contracting Q fever should be immunised prior to commencement of work or as soon as possible after they commence work as the risk of infection is highest in the first few years.

Vaccination during the incubation period of Q fever does not prevent the onset of the disease.

Despite the significant efficacy of Q-VAX® in clinical trials, cases of Q fever following vaccination have been reported (see **SECTION 5.1 – PHARMACODYNAMIC PROPERTIES, Clinical Trials**).

Pre-vaccination Testing

Serology: People who are being considered for Q fever vaccination must have serum antibody testing. Subjects in whom antibodies are unequivocally positive should not be given Q-VAX® (see **SECTION 4.4 – SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

Skin Test:

Preparation: Skin Test solution should be prepared by diluting 0.5 mL of the Q-VAX® Skin Test in 14.5 mL of Sodium Chloride Injection (to a final volume of 15 mL). The diluted Q-VAX® Skin Test should be freshly prepared, stored at 4°C and used within six hours**.**

Administration: The dose administered for skin testing is 0.1 mL of the diluted Q-VAX® Skin Test. This should be injected intradermally into the volar surface of the mid-forearm.

A positive reaction is indicated by any induration at the site of injection read seven days after the test dose. Any person with a positive reaction must not be vaccinated.

Use in the elderly

No data available

Paediatric use

No data available

Effects on laboratory tests

No data available

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No data available.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy (Category B2)

Safety of use in pregnancy has not been established. Deferral of vaccination is recommended.

Use in lactation

No data available.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effect of this medicine on person's ability to drive and use machines were not assessed as part of its registration

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Vaccination of already immune subjects may result in severe local or general reactions, with the possibility of local abscess formation.

Clinical trial data
In a clinical trial in South Australia the following adverse events were recorded amongst 464 persons who received Q-VAX®.

Table 1 Q-VAX® vaccine Clinical Trial Adverse Events

Reaction	Frequency of vaccine reactions (%)
Local	
Tenderness	48
Erythema	33
Induration/oedema	< 1
Systemic	
Headache	9
Fever	0.2

There was a single case report of abscess formation at the injection site.

Post-marketing data

A range of adverse reactions has been reported with clinical use of Q-VAX®. The reactions are summarised below and categorised by frequency according to the following definitions. Very common: ≥ 1/10; common: <1/10 and ≥ 1/100; uncommon: <1/100 and ≥ 1/1000, rare: <1/1000 and ≥ 1/10,000 and very rare: <1/10,000.

Blood and Lymphatic System Disorders
Very rare: Lymphadenopathy

Nervous System Disorders
Common: Headache
Very rare: Dizziness

Gastrointestinal Disorders
Uncommon: Nausea, vomiting and diarrhoea

Skin and subcutaneous tissue Disorders
Common: Delayed skin reaction (presenting up to 6 months after vaccination) at injection site (either vaccination and/or skin test site)
Uncommon: Hyperhidrosis

Musculoskeletal and connective tissue Disorders
Uncommon: Myalgia
Very rare: Arthralgia

General disorders and administration site conditions
Very common: Injection site inflammation (e.g. erythema, pain, warmth and swelling).

Uncommon: Injection site induration and/or oedema, pyrexia, malaise, fatigue
Rare: Injection site abscess formation, granuloma
Very rare: Chills, chronic fatigue syndrome

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PARTICULARS

5.1 Pharmacodynamic properties

Mechanism of action

Q fever is caused by *Coxiella burnetii*, an obligate, intracellular, Gram-negative coccobacillus. The *C. burnetii* is shed in the products of conception, and on the neonate of the infected animal. It may also be present in the udder and milk of infected animals and is passed on within their faeces and urine. Infection is transmitted to humans primarily by inhalation of infected airborne particles or dust during the handling or processing of these materials or by close proximity to infected animals and their products.

Administration of inactivated *Coxiella burnetii* in Q-vax vaccine stimulates production of an immune response in the vaccinated individual. The immune response provides protection against clinical illness in a high proportion of vaccinated individuals, but may not be effective in some individuals.

Early antibody response to the vaccine is predominantly with the IgM subclass; IgG antibodies appear later. Although the seroconversion rate is low (50-80%) and antibody levels are transient, cell mediated immunity develops. Clinical trials have demonstrated a high degree of efficacy (see **SECTION 5.1 – PHARMACODYNAMIC PROPERTIES, Clinical Trials**). As Q fever is often asymptomatic or misdiagnosed due to its non-specific nature, many abattoir workers develop immunity to Q fever without an obvious illness.

The duration of protective immunity following immunisation is unknown, but is believed to be in excess of five years.

Revaccination must never be undertaken due to the possibility of severe hypersensitivity reactions (see SECTION 4.3 – CONTRAINDICATIONS).

Clinical trials

A randomised, blind, controlled study comparing Q-VAX® and influenza vaccine for the prevention of Q fever amongst 200 workers in three Queensland abattoirs was undertaken, using sequential analysis for determining the efficacy of Q-VAX®. A statistically significant difference in the incidence of symptomatic Q fever was noted 15 months after commencement of vaccination, with 7 cases in those given the control vaccine and no cases in those given Q-VAX®. At 15 months, 24% of those who had not been vaccinated and had not developed symptomatic infection had serological evidence of exposure to Q fever, indicating subclinical infection.

A retrospective cohort study in three South Australian abattoirs was undertaken to compare the incidence of Q fever in vaccinated and unvaccinated subjects between 1985 and 1990. There were two cases of Q fever amongst 2555 vaccinated employees compared with 55 cases in 1365 unvaccinated subjects. Both cases of Q fever in the vaccinated group occurred within two weeks of receiving the vaccine. For workers who were vaccinated, the mean duration of employment following vaccination was 1.9 years; 203 workers were employed for all five years of the study. Protection against clinical infection over this period was demonstrated.

Although the dose in each of these studies was nominally 30 µg, one batch which contained only 20 µg in each dose was shown to be as effective. However, as with all vaccines, 100% effectiveness for generation of protective immunity against Q fever cannot be guaranteed (see **SECTION 4.4 – SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

5.2 PHARMACOKINETIC PROPERTIES

Not applicable

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available

Carcinogenicity

No data available

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Refer to **SECTION 2 – QUALITATIVE AND QUANTITATIVE COMPOSITION**.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this

medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Q-VAX® Vaccine and Q-VAX® Skin Test should be protected from light and stored at 2°- 8°C. Refrigerate. DO NOT FREEZE.

6.5 NATURE AND CONTENTS OF CONTAINER

AUST R 100517

Q-VAX® Vaccine is available as a pre-filled syringe containing ≥ 25 µg of antigen, in 0.5 mL solution.
The syringe and all associated syringe components do not contain natural rubber latex. The Q-VAX® Vaccine syringe is supplied in a moulded plastic blister with peel-off paper cover. Do not use if the blister pack encasing the syringe is damaged or missing.

AUST R 100518

Q-VAX® Skin Test is available as a pre-filled vial containing ≥ 2.5 µg of antigen, in 0.5 mL solution. **Q-VAX® Skin Test must be diluted prior to use in pre-vaccination screening (see SECTION 4.2 – DOSE AND METHOD OF ADMINISTRATION).** The vial and all associated components do not contain natural rubber latex. The Q-VAX® Skin Test vial is packaged with a plastic tear away cap covering the vial septum. Do not use if the tear away cap on the vial is damaged or missing.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements,

6.7 PHYSICOCHEMICAL PROPERTIES

Not applicable

7. MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (S4)

8. SPONSOR

Seqirus Pty Ltd
ABN 26 160 735 035
63 Poplar Road
Parkville, VIC 3052
Australia

9. DATE OF FIRST APPROVAL

9 July 1999

10. DATE OF REVISION

26 August 2019

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
2	Replace 'Excess egg proteins are removed by fractionation and ultracentrifugation' by "**Trace amounts of ovalbumin (<1 microgram) may also be present."**
6.2	Update ingredient names for compliance with AAN
6.5	Addition of latex statement
All	Updated as per TGA Form for providing PI dated Mar 2018