

Changing Landscape of Adult Immunisation and ZOSTAVAX® on the National Immunisation Program

ZOSTAVAX®
[Zoster Vaccine Live (Oka/Merck)]

- ### Learning Outcomes
- Understand the importance of adult immunisation for older Australians
 - Understand new provisions in the National Immunisation Program (NIP) for free herpes zoster (shingles) vaccination in individuals aged 70-79 years
 - Understand the role of herpes zoster vaccination (ZOSTAVAX®) in helping to prevent shingles in older adults and its complications

- ### Outline of Talk
- Vaccine preventable disease in Australian adults**
- Recommendations
 - Addition of shingles vaccine (ZOSTAVAX®) to the NIP schedule
 - Australian Immunisation Register
- About Herpes Zoster (Shingles)**
- Effects of shingles
 - Treatment
 - Prevention (vaccination)
 - Efficacy/safety of ZOSTAVAX®
- Strategies to implement vaccination programs in your practice**
- Recall strategies (Case studies)

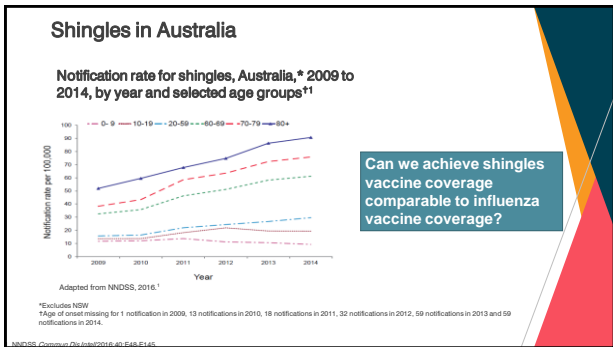
Addition of ZOSTAVAX® to the NIP from 1st November¹

Disease ²	Age group ²	Vaccine brands ²
Influenza	65 years and over	Influenza
Pneumococcal pneumonia	65 years and over	Pneumovax®23 (pneumococcal vaccine, polyvalent)
	50 years and over (Aboriginal and Torres Strait Islanders)	
Herpes-zoster (shingles)	70-79 years ^	ZOSTAVAX® (Zoster Vaccine Live (Oka/Merck))

[^] ZOSTAVAX® is to be provided free for 70 year olds, with a 5 year catch-up program for 71-79 year olds¹

Refer to the National Immunisation Program for the full Immunisation schedule¹

1. Department of Health. Shingles NIP announcement. www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/news-20152307. Accessed September 2016. 2. Australian Government Department of Health. National Immunisation Program Schedule. Available at: http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/5032D77C2F613F3ACCA3D7D4801E31755F5?OpenDocument. Accessed September 2016.



Australian Immunisation Register

Australia's Immunisation Registers have expanded

- From Sept 2016, the Australian Childhood Immunisation Register (ACIR) is expanded to become the Australian Immunisation Register (AIR)^{1,2}
- The AIR will capture all vaccines administered throughout a person's life given through General Practice and community clinics¹
- This will include all funded vaccines under the NIP; & private vaccines¹
- In September 2017 new functionality will be added to allow two-way communication between the AIR and Practice Management Software²

1. Australian Government Department of Health, Immunise Australia program. Fact sheet, UPDATE: Expansion of Australia's Immunisation Register, 23 October 2016. 2. Eastern Melbourne PHN, Immunisation Update, Australia. <http://www.emphn.org.au/183026/updates/immunisationupdate> Accessed July 2016.

Benefits of the AIR for GPs & other vaccine providers¹


- Broaden and improve immunisation data capture
- Enable greater understanding of current coverage**
- Give vaccination providers secure access to a range of due and overdue reports, to facilitate monitoring of vaccine uptake and help them identify the immunisation status of individuals**
- Assists in identifying areas of low coverage within Australia and enable targeted effort to boost immunisation rates in these areas

1. Australian Government Department of Health, Immunise Australia program. Fact sheet, UPDATE: Expansion of Australia's Immunisation Register, 23 October 2016.


About herpes zoster ('shingles')

Shingles is unpredictable¹

Shingles is the reactivation of the varicella-zoster virus (VZV)²



97% of adults have VZV latent within them¹



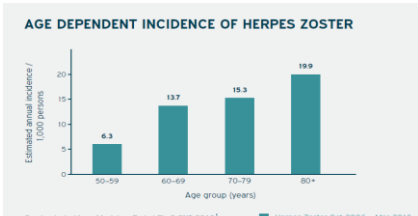
Only 4% of adults aged 60+ believe they are at high risk of shingles³

Shingles is on the rise in the 60+ age group⁴

1. Stein AN et al. Vaccine 2009;27:520-20. 2. Australian Technical Advisory Group on Immunisation (ATAGI). The Australian immunisation handbook 10th ed (2016 update). Canberra: Australian Government Department of Health, 2016. 3. Shingles Study 100000 n=1,000. Scgirus data on file, September 2015. 4:32. 4. MacIntyre R et al. Increasing Trends of Herpes Zoster in Australia. PLoS ONE 2014; 10(4):e0125025.

Incidence of shingles increases with age¹

AGE DEPENDENT INCIDENCE OF HERPES ZOSTER



Age group (years)	Estimated annual incidence / 1,000 persons
50-59	6.3
60-69	13.7
70-79	15.3
80+	19.9

Graph adapted from MacIntyre R et al. PLoS ONE 2015; 10(4):e0125025. ■ Herpes Zoster Oct 2006 – Mar 2013

1. MacIntyre R et al. Increasing Trends of Herpes Zoster in Australia. PLoS ONE 2015; 10(4):e0125025.

The risk of developing shingles is significant¹

120,000

Annual incidence of shingles per year in Australia¹

1 IN 3

Adults may develop shingles in their lifetime²
1 in 2 by 85 years old


1. MacIntyre R et al. Increasing Trends of Herpes Zoster in Australia. PLoS ONE 2014; 10(4):e0125025. 2. Herpasz R et al. MMRW Jun 6:57(Pp. 6): 1-30.

Shingles complications

Shingles pain can be excruciating: 'stabbing and burning'

Ophthalmic zoster

- Occurs in up to 25%¹
- Complications may include facial scarring and loss of vision^{1,2}




Stroke risk

- Shingles may also increase the risk of stroke in the next 6 months³
- 63% higher risk in the 4 weeks after shingles vs. baseline period³

1. Harpaz R et al. *MMWR* 2008 (June 6); 57 (RR-5): 1-30. 2. Osman MN et al. *Arvin AM et al. editors. 2009* 0246/75. 3. Langan SM et al. *Clin Infect Dis* 2014; 58: 1497-1503

Postherpetic neuralgia (PHN) is the most frequent debilitating complication of shingles¹

- PHN can last for months even years¹: min 3 months defines PHN
- Pain and nerve damage can begin before the shingles rash is visible²
- PHN may be severe^{1,2} especially if severe pain early on
- PHN patients report experiencing pain in the area of their shingles rash for an average of 3.5 years²



Up to 20% of adults may develop PHN⁴

1. Australian Technical Advisory Group on Immunisation (ATAGI). *The Australian immunisation handbook 10th ed* (2016 update). Canberra: Australian Government Department of Health, 2016. 2. Osman MN et al. *Arvin AM et al. editors. 2009* 0246/75. 3. Serpell M et al. *Health Qual Life Outcomes* 2014; 12: 92. 4. Harpaz R et al. *MMWR* 2008 (June 6); 57 (RR-5): 1-30

Treatment

Treatment options for shingles¹

- Antiviral treatment should be commenced in immunocompetent patients who present within 72 hours of the onset of the rash and in **all** immunocompromised patients regardless of rash duration
 - Antivirals help to reduce the severity and duration of shingles
- Adequate analgesia to manage pain include:
 - paracetamol, as well as corticosteroids, opioids and/or tricyclic antidepressants for severe pain
- Supportive care:
 - Cool compresses
 - Bathe lesions with saline to remove crusts and exudate
 - Cover the lesions with a light non-adherent padded dressing
 - Regular monitoring by GP to check that pain adequately controlled**

1. Herpes zoster: antiviral therapy (Published November 2014). In: eTG complete [Internet]. Melbourne: Therapeutic Guidelines Limited; 2016 Mar.

The risk of developing PHN remains substantial¹

Virus replication causes inflammation and injury to the nerve before rash appears²

Rash Onset		Rash Healing	
Prodrromal Pain	Acute Pain	Subacute Herpetic Neuralgia	Chronic Pain: PHN
Nerve damage begins	Initiate antiviral within 72 hours of rash onset		
Day 0	2-4 Weeks	3 Months	

Cochrane Review: insufficient evidence to recommend antivirals to prevent PHN¹

1. Chan N et al. *Cochrane Database of Systematic Reviews* 2014, Issue 2. 2. Osman MN et al. *Arvin AM et al. (Eds). Varicella-Zoster Virus: Virology and Clinical Management* 2008: 748-775. 3. eTG complete (online) Therapeutic Guidelines 2015.

Prevention by vaccination



ZOSTAVAX®¹

- ZOSTAVAX® is a live-attenuated varicella-zoster virus vaccine¹
- ZOSTAVAX® is indicated for the prevention of:¹
 - shingles in individuals 50 years of age and older
 - postherpetic neuralgia (PHN) and for reduction of acute and chronic zoster-associated pain in individuals 60 years of age and older
- ZOSTAVAX® will be provided free from 1st Nov 2016 on the National Immunisation Program for 70-79 year olds²

1. ZOSTAVAX® Approved Product Information. 2. Department of Health, Shingles NIP announcement. <http://www.health.gov.au/about/newsroom/statements/2016/09/20160920-shingles-nip>. Accessed September 2016.

Shingles Prevention Study (SPS)¹

- The pivotal efficacy trial for ZOSTAVAX®
 - Randomised, double-blind, placebo controlled trial
 - Patients received either the vaccine or placebo, and were then followed up for a median of 3.1 years
- Conducted in 38,546 adults aged 60 years and over
- The **primary endpoint was the burden of illness** due to shingles;
 - a measure affected by the incidence, severity and duration of the associated pain and discomfort
- Secondary end point: incidence of post-herpetic neuralgia**

1. Corman MN et al. NEJM 2005; 352:2274-84

ZOSTAVAX® significantly reduced the incidence of shingles by 51% vs placebo in adults aged 60+^{1,2}

ZOSTAVAX® reduced the incidence of shingles by 51%

In vaccinated patients who developed shingles, ZOSTAVAX® significantly reduced shingles associated pain compared to placebo

A placebo controlled, double-blind clinical trial. 38,546 subjects aged 60 years or older were randomised to receive a single dose of either ZOSTAVAX® or placebo and were monitored for the development of shingles for a median of 3.1 years. Graph adapted from Corman et al. NEJM 2005.

ZOSTAVAX® Approved Product Information. 2. Corman MN et al. NEJM 2005; 352:2274-84

ZOSTAVAX® significantly reduced the incidence of PHN by 67% vs. placebo in adults aged 60+^{1,2}

ZOSTAVAX® reduced the incidence of PHN by 67%

Patients vaccinated with ZOSTAVAX® who did develop shingles had a significantly lower incidence of PHN compared to placebo

A placebo controlled, double-blind clinical trial. 38,546 subjects aged 60 years or older were randomised to receive a single dose of either ZOSTAVAX® or placebo and were monitored for the development of shingles for a median of 3.1 years. PHN – post-herpetic neuralgia defined as pain and discomfort associated with shingles rated as 3 or more, on a scale ranging from 0 (no pain) to 10 (pain as bad as you can imagine), persisting or appearing more than 90 days after the onset of rash. Graph adapted from Corman et al. NEJM 2005.

ZOSTAVAX® Approved Product Information. 2. Corman MN et al. NEJM 2005; 352:2274-84

Duration of protection

- The Shingles Prevention Study (SPS) demonstrated vaccine efficacy through 4 years post vaccination^{1,2}
- A follow on Short-Term Persistence Substudy (STPS) demonstrated persistence of vaccine efficacy for at least 5 years^{3,4}
- A Long-Term Persistence Substudy (LTPS) further showed vaccine efficacy remained significant against herpes zoster up to 8 years post vaccination
 - However the interpretation of this result is limited due to the methodological limitations in that study^{3,5}
- The need for a booster dose of ZOSTAVAX is not yet evaluated^{2,3}

1. Corman et al. In Arvin AM et al. editors. 2005; 246-275. 2. ZOSTAVAX® Approved Product Information. 3. Australian Technical Advisory Group on Immunisation (ATAGI). The Australian Immunisation Handbook 10th ed (2016 update). Canberra: Australian Government Department of Health, 2016. 4. Schmader et al. Clin Infect Dis 2012;34(7):932-939. 5. Morrison et al. Clin Infect Dis 2015;60(8):900-909.

ZOSTAVAX® is contraindicated in patients with:¹

- History of hypersensitivity to any component of the vaccine, including gelatin
- History of anaphylactic/anaphylactoid reaction to neomycin
- Primary and acquired immunodeficiency states e.g. leukaemia, lymphoma, conditions affecting bone marrow or lymphatic system, immunosuppression due to AIDS, cellular immune deficiencies
- Immunosuppressive therapy (including high-dose corticosteroids)
- Active untreated tuberculosis
- Pregnancy

ZOSTAVAX® Approved Product Information

Persons significantly immunocompromised should not receive ZOSTAVAX®^{1,2}

- Unless a contraindication or precaution exists, ZOSTAVAX® may be given to patients receiving¹
 - topical/inhaled corticosteroids,
 - low-dose systemic corticosteroids or
 - corticosteroids as replacement therapy, e.g. for adrenal insufficiency
 - Seek specialist advice for immunocompromised patients^{1,2}
- and refer to NCIRS factsheet**

1. ZOSTAVAX® Approved Product Information. 2. Australian Technical Advisory Group on Immunisation (ATAGI). The Australian immunisation handbook 10th ed. 2015 update. Canberra: Australian Government Department of Health, 2016.

ZOSTAVAX® is generally well tolerated

- In clinical trials, ZOSTAVAX® has been evaluated for safety in more than 32,000 adults 50 years of age and older¹
- The most common adverse events (≥ 10%) reported in clinical trials were¹
 - Erythema, pain/tenderness, swelling and pruritus
- Over 33 million doses of ZOSTAVAX® have been distributed worldwide since 2006²
- Results from "real world" post marketing safety studies support the safety profile seen in clinical trials^{3,4}

To report an adverse event contact
 CSL Medical Information: 1800 642 865
 Email: MedicalInformation.Aust@csli.com.au

1. ZOSTAVAX® Product Information. 2. Seqirus Data on file. 3. Baxter et al Vaccine 2012; 30(47):6636-6641. 4. Tseng et al Journal of Internal Medicine 2012; 271(6):910-20

ZOSTAVAX® use with other vaccines¹

- ZOSTAVAX® can be administered concurrently with inactivated influenza vaccine as separate injections at different sites
- ZOSTAVAX® and PNEUMOVAX 23 should not be given concomitantly
 - concomitant use resulted in reduced immunogenicity of ZOSTAVAX®
 - Consider administration of the two vaccines separated by at least 4 weeks

1. ZOSTAVAX® Approved Product Information

ZOSTAVAX® dosage and administration¹

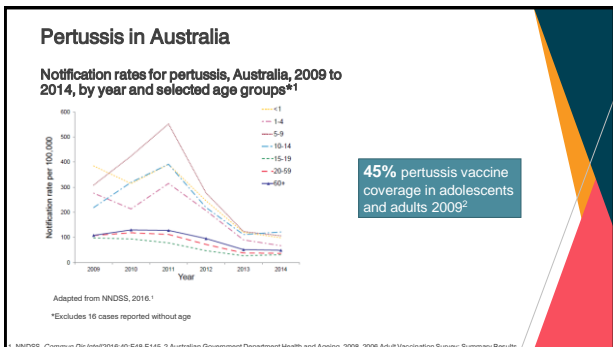
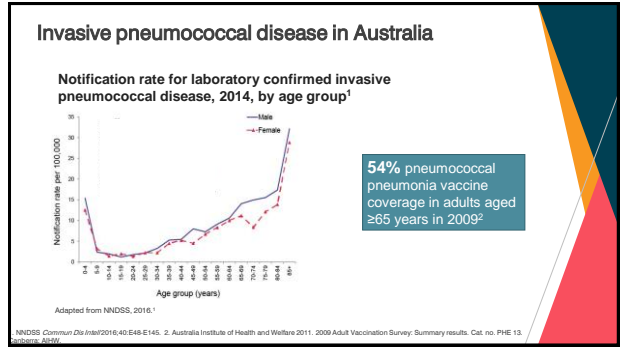
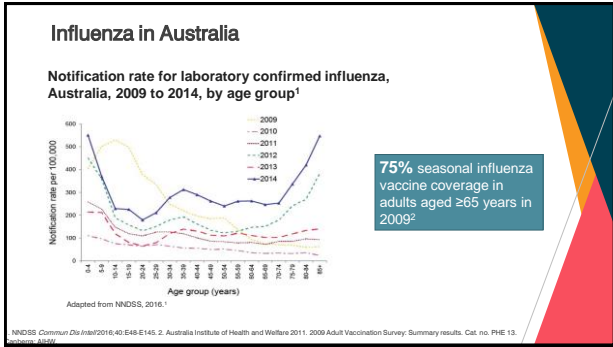
- Individuals should receive a single dose (0.65mL) of the vaccine **subcutaneously**
- Reconstitute immediately after removal from fridge
- Administer the vaccine immediately after reconstitution (discard if not used within 30 minutes)

Refer to product information for further information




ZOSTAVAX® Approved Product Information

Strategies to implement vaccination programs in your practice



Case studies

Case 1



- Dawn is a healthy 70-year-old woman who moved from Vietnam to Australia 20 years ago
- She is not sure if she has had chickenpox before
- She has heard about the free shingles vaccine and would like to be vaccinated

Question

Would you assume Dawn has been exposed to VZV?

Question

Would you offer the shingles vaccine to Dawn?

Vaccination of varicella-zoster virus-naïve individuals

- VZV exposure may be significantly lower in some tropical countries¹
- However, neither history of previous varicella infection nor evidence of prior immunity to VZV is required prior to the routine administration of the shingles vaccine²
- Studies of the administration of a high-dose VZV-containing vaccine to VZV seronegative adults, compared with previously infected adults, suggest that the vaccine was well tolerated and immunogenic in seronegative persons³

1. Cunningham AL et al. *MMWR* 2008; 188: 171-76. 2. Australian Technical Advisory Group on Immunisation (ATAGI). *The Australian immunisation handbook* 10th ed (2016 update). Canberra: Australian Government Department of Health, 2016. 3. MacLachlan N et al. *Vaccine* 2007; 25: 2139-44.

Could varicella vaccination be more appropriate?

- If there *is* laboratory evidence of a lack of immunity to VZV, and the patient does not have a history of age-appropriate varicella vaccination, they should be vaccinated with 2 doses of varicella vaccine, rather than shingles vaccine

Australian Technical Advisory Group on Immunisation (ATAGI). *The Australian immunisation handbook* 10th ed (2016 update). Canberra: Australian Government Department of Health, 2016.

Case 2



- Bob is 77 years old
- He says he had shingles 8 years ago, and he was in excruciating pain (he is not a regular patient, so you do not have a record of this)
- He is in good health
- He knows someone who recently had shingles twice, and he wants to ensure that doesn't happen to him

Question

Would you recommend shingles vaccination for Bob?

It's possible to develop shingles more than once

- While recurrence is uncommon among immunocompetent persons, having an episode of shingles does **not** ensure protection against future episodes¹
 - Estimated 5% recurrence rate^{1,2}
 - Recurrence more likely in:¹
 - Immunocompromised patients
 - Patients who experienced longer duration of pain with initial episode
- ZOSTAVAX® can be given to someone who has had shingles^{2,3}
 - The length of time following an episode of shingles after which it would be reasonable to vaccinate has not been established.
 - The Australian Immunisation Handbook suggests that the vaccine could be given at least one year after the shingles episode.²

1. Yawn et al. *Mayo Clin Proc* 2011;86:88-93. 2. Australian Technical Advisory Group on Immunisation (ATAGI). *The Australian immunisation handbook* 10th ed (2016 update). Canberra: Australian Government Department of Health, 2016. 3. ZOSTAVAX® Approved Product Information.

Question

Bob is planning to attend the clinic for flu & pneumococcal vaccination next month, and he would like to receive the shingles vaccine on the same day. Would you recommend this?

Co-administration with ZOSTAVAX®

- Can be administered concurrently with inactivated influenza vaccine as separate injections at different sites
- ZOSTAVAX® and PNEUMOVAX® 23 should not be given concomitantly because concomitant use resulted in reduced immunogenicity of ZOSTAVAX®. Consider administration of the two vaccines separated by at least 4 weeks.
- Refer to Product Information for further information

Case 3



- Judy is 72 years old
- Currently taking 15 mg/day prednisolone for polymyalgia rheumatica
- She has heard about the free availability of the vaccine and would like to be vaccinated

Question

Would you recommend vaccination for Judy?

Contraindications

- Primary and acquired immunodeficiency states due to conditions such as: acute and chronic leukaemias; lymphoma; other conditions affecting the bone marrow or lymphatic system; immunosuppression due to HIV/AIDS; cellular immune deficiencies.
- Immunosuppressive therapy (including high-dose corticosteroids);

Persons significantly immunocompromised should not receive the zoster vaccine

Unless a contraindication or precaution exists, ZOSTAVAX® may be given to:

- Patients receiving
 - topical/inhaled corticosteroids,
 - low-dose systemic corticosteroids or
 - corticosteroids as replacement therapy, e.g. for adrenal insufficiency



Before prescribing, please review the Product Information available at www.seqirus.com.au/P1

MINIMUM PRODUCT INFORMATION

ZOSTAVAX® Zoster Virus Vaccine Live (Qualicel®), Refrigerator stable

Indications: Prevention of herpes zoster (shingles) in individuals 50 years of age and older. Prevention of postherpetic neuralgia (PHN) and reduction of acute and chronic zoster-associated pain in individuals 60 years of age and older. ***Contraindications:** History of hypersensitivity to any component of the vaccine, including gelatin. History of anaphylactic/anaphylactoid reaction to recombinant primary and acquired immunodeficiency states due to conditions such as acute and chronic leukaemias, lymphoma, other conditions affecting the bone marrow or lymphatic system, immunosuppression due to HIV/AIDS, cellular immune deficiencies, immunosuppressive therapy (including high-dose corticosteroids, but not topical inhaled corticosteroids). ZOSTAVAX is a live attenuated varicella-zoster vaccine and administration may result in disseminated disease in immunosuppressed or immunodeficient patients. Active untreated tuberculosis. Pregnancy (see PRECAUTIONS).

Precautions: Adequate treatment provisions, including adenovirus injection (1:1000), should be available for prophylactic use should an anaphylactic/anaphylactoid reaction occur. Consider **Use in Pregnancy (Category B2)** in the presence of fever >38.5 °C. Safety and efficacy not established in adults known to be infected with HIV. **Use in Lactation:** It is not known whether ZVZ is secreted in human milk. **Use in the elderly:** The mean age of subjects enrolled in the largest (N=38,340) clinical study of ZOSTAVAX was 69 years (range 59-99 years). ZOSTAVAX was demonstrated to be generally safe and effective in this population. **Interactions with other vaccines:** ZOSTAVAX can be administered concurrently with inactivated influenza vaccine, ZOSTAVAX and PNEUMOVAX 23 should not be given concomitantly because concurrent administration may result in reduced immunogenicity of ZOSTAVAX. Consider administration of the two vaccines separated by at least 4 weeks. **Adverse Effects:** headache, erythema, pain/tenderness, swelling, pruritus, fatigue, haematoma, warmth, induration, pain, itchy redness. **Post-marketing experience:** necrotic zoster ulcers, encephalitis, myelitis, injection-site rash, injection-site urticaria, pruritus, transient injection-site lymphadenopathy, hypersensitivity reactions including anaphylactic reactions, rash, necrotizing retinitis. **Dosage and Administration:** A single dose (0.5mL), administered subcutaneously. Administer vaccine immediately after opening/bottle to improve shelf of potency. ZOSTAVAX is not a treatment for zoster or PHN. Based on Approved Product Information dated 26 April 2016. Date of preparation May 2016.

*Please see change(s) in Product Information

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

Seqirus (Australia) Pty Ltd ABN: 66 120 398 067 63 Poplar Road, Parkville VIC 3052 www.seqirus.com.au distributor for Merck, Sharp and Dohme (Australia) Pty Ltd. CSL Medical Information: 1800 642 865. ZOSTAVAX® is a registered trademark of Merck & Co. Inc. Whitehouse Station, NJ, USA. Seqirus™ is a trademark of Seqirus UK Limited or its affiliates. SEQ/ZOST/0916/0190 Date of preparation September 2016